Volume 3 Datasheets – Chemical and physical determinands

Part 2.3: Pesticides

2019

2.3 Pesticides

### Introductory notes

1. Pesticides can have more than one common name, trade name and chemical name. The CAS Registry Number (Chemical Abstracts Systematic names) is a single identifier aimed to remove any ambiguity arising from the various nomenclatures. An internet site for finding pesticide names for a CAS number is http://www.alanwood.net/pesticides/index\_rn2\_frame.html. Or to find a CAS number for a pesticide: http://www.alanwood.net/pesticides/index\_cn\_frame.html.

2. The Drinking-water Standards for New Zealand (DWSNZ) define a MAV as the concentration of a determinand, below which the presence of the determinand does not result in any significant risk to a consumer over a lifetime of consumption. For carcinogenic chemicals, the MAVs set in the DWSNZ generally represent a risk of one additional incidence of cancer per 100,000 people ingesting the water at the concentration of the MAV for a lifetime of 70 years.

The World Health Organization (WHO) states that a drinking-water guideline value (equivalent to our MAVs) normally represents the concentration of a constituent that does not result in any significant risk to health over a lifetime of consumption.

3. **USEPA**

(a) **MCL**: Some datasheets include the USEPA’s MCL. Title 40, Protection of Environment, Chapter I: Environmental Protection Agency, Part 141, National Primary Drinking Water Regulations, § 141.1 40 CFR Ch. I (7–1–02 edition) defines MCL (maximum contaminant level) as the maximum permissible level of a contaminant in water which is delivered to any user of a public water system.

(b) **RfD**: Some datasheets also include the reference dose (usually meaning the chronic reference dose) or RfD, which the USEPA defines as “an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime”.

An ARfD or acute reference dose, is defined as the maximum quantity of an agricultural or veterinary chemical that can safely be consumed as a single, isolated, event. Note that the 2001 JMPR defined the acute reference dose as “The acute RfD of a chemical is an estimate of the amount of a substance in food and/or drinking-water, normally expressed on a body-weight basis, that can be ingested in a period of 24 hours or less without appreciable health risk to the consumer on the basis of all known facts at the time of the evaluation”.

(c) **HHBPs**: The USEPA maintains a table of Human Health Benchmarks for Pesticides that includes RfDs and ARfDs for (currently) 363 pesticides. The HHBPs were originally developed in 2012. The table includes a column for “acute or one-day HHBPs”, another for “chronic or lifetime (non-cancer) HHBPs”, and one for “carcinogenic HHBPs”. HHBPs are the concentrations in water at or below which adverse health effects are not anticipated from one-day or lifetime exposures. HHBPs are derived for the most sensitive population group. Details can be accessed at http://www.epa.gov/sites/production/files/2015-10/documents/hh-benchmarks-techdoc.pdf or http://iaspub.epa.gov/apex/pesticides/f?p=HHBP:home.

The acute HHBP = [aRfD (mg/kg bw/day) x BW (kg) x 1,000 (µg/mg)] / [Drinking Water Intake (L/day)] where BW = 10 kg for children and 66 kg for females 13–49 years and Drinking Water Intake = 1 L/day for children and 2 L/day for females 13–49 years. In essence, these can be considered to be one day MAVs.

The chronic HHBP = [cRfD (mg/kg bw/day) x BW (kg) x 1,000 (µg/mg) x 0.2 RSC] / [Drinking Water Intake (L/day)] where BW = 70 kg for general population and 66 kg for females 13–49 years and Drinking Water Intake = 2 L/day for general population as well as for females 13–49 years and RSC = Relative Source Contribution assumed as 20 percent. This calculation is basically the same as that used by the WHO in deriving their guideline values, and hence our MAVs.

The formula for deriving carcinogenic HHBP = [10–6 or 10–4/Drinking Water Unit Risk (ppb-1), where Drinking Water Unit Risk (ppb-1) = [CSF (per mg/kg/day) x 2(L/day)]/[70 kg x1000 (µg/mg)].

Because pesticides should only be found rarely in New Zealand waters, and for short periods, the acute one day HHBP (where available) has been included in the datasheets.

(d) **DWEL**: The USEPA also uses the concept of Drinking Water Equivalent Level or DWEL, which is defined as “a lifetime exposure concentration protective of adverse, non-cancer health effects, that assumes all of the exposure to a contaminant is from drinking water”. The DWEL is calculated by multiplying the oral chronic RfD (mg/kg/d) by 70 (kg body weight) divided by 2 (L/day consumption).

The USEPA review their MCLs, DWELs and RfDs regularly. The 2012 values can be found at: http://water.epa.gov/action/advisories/drinking/upload/dwstandards2012.pdf.

(e) **Carcinogenicity**: The USEPA classification of carcinogenicity as at 24 September 2008, has been included where available. See latest list at http://envirocancer.cornell.edu/turf/chemseval.pdf. This also explains their classification groups.

4. The Australian guideline values for pesticides are not always based on health issues. For pesticides that are not approved for use in water or in water catchments, the guideline value is often set at or about the analytical limit of determination. Where a pesticide is approved for use in water or in water catchments, the guideline value is set at a level consistent with good management practice and which would not result in any significant risk to health of the consumer over a lifetime of consumption. These datasheets only include their health based guideline values, see http://www.nhmrc.gov.au.

5. The Australian Government’s Department of Health and Ageing, Office of Chemical Safety and Environmental Health has a document that lists the Acceptable Daily Intakes (ADIs)\* for Agricultural and Veterinary Chemicals, where “the acceptable daily intake (ADI) for humans is considered to be a level of intake of a chemical that can be ingested daily over an entire lifetime without any appreciable risk to health. It is calculated by dividing the overall NOEL from the animal studies by a safety factor. The magnitude of the safety factor is selected to account for uncertainties in extrapolation of animal data to humans, variation between humans, the completeness of the toxicological data base and the nature of the potential adverse effects”. Their ADIs (which are updated regularly) appear in these datasheets. See http://www.health.gov.au/internet/main/publishing.nsf/Content/ocs-adi-list.htm. They also publish Acute Reference Doses for Agricultural and Veterinary Chemicals (called the ARfD List), see http://www.health.gov.au/internet/main/publishing.nsf/content/ocs-arfd-list.htm.

**Note:** The acceptable daily intake (ADI) is similar in definition and intent to terms such as reference dose (RfD), reference concentration (RfC) and tolerable daily intake (TDI). They are an estimate of the daily exposure to humans that is likely to be without appreciable risk of deleterious effects during a lifetime of continuous exposure. The derivation of a TDI involves identifying the critical effect(s), and selecting the pivotal study, the point of departure, and appropriate uncertainty factors (UFs).

6. A MAV had been developed for most of the early pesticides because of their usually general and high level of toxicity and/or persistence. Many of these products now have restricted use in New Zealand or have been withdrawn. Despite this, most of these MAVs have been retained because traces of some of these older pesticides can still be found in the soil or possibly groundwater.

Most pesticides included in this section of the datasheets do not have a MAV but are registered for agricultural use in New Zealand and appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). Many of these are fairly new products with a much more specific application, are usually a lot less persistent, and are mostly used at a much lower dose. Many of these are yet to be evaluated in the WHO *Guidelines for Drinking-water Quality*.

7. The WHO has developed a classification of pesticides by hazard, where:

* Class IA is extremely hazardous
* Class IB is highly hazardous
* Class II is moderately hazardous
* Class III is slightly hazardous

See The WHO Recommended Classification of Pesticides by Hazard. http://www.who.int/ipcs/publications/pesticides\_hazard/en/.

8. Pesticides can participate in a number of transformation processes resulting in a large number of degradation products. The AWWA Research Foundation produced in 2008 “*Pesticide Degradates of Concern to the Drinking Water Community*”: 143 pages. See http://www.waterrf.org/PublicReportLibrary/2938.pdf.

They report that 92 pesticide degradates have been detected in the environment with 29 detected in groundwater and 27 detected in surface waters. Degradates of alachlor, acetochlor, atrazine, cyanazine, dichloropropene, dicamba and 2,4‑D were likely to be the greatest concern to water supplies in the USA, whereas in the UK they were cyanazine, isoproturon and flufenacet. All are used in New Zealand.

9. DWI (2010) published a 478-page report “A Desk Study on Pesticide Metabolites, Degradation and Reaction Products to Inform the Inspectorate’s Position on Monitoring Requirements”, DWI Project: 70/2/232. See http://dwi.defra.gov.uk/research/completed-research/2000todate.htm.

10. “Review of Trends in Agricultural Pesticide Use in New Zealand” (1999) MAF Policy Technical Paper 99/11 (www.maf.govt.nz/mafnet/rural-nz/sustainable-resource-use/resource-management/pesticide-use-trends/PesticideTrends.pdf) discusses how pesticides were used in New Zealand up to 1998.

11. IUPAC (2003) Technical Report: “Significance of impurities in the safety evaluation of crop protection products”, includes:

There may be substantial differences in the chemical composition of technical-grade products of the same active ingredient manufactured under different conditions, from different raw materials, or by different routes of synthesis. Resulting differences in impurity content may significantly affect the toxicological properties of pesticide products.

See *Pure Appl Chem* 75(7) 2003, pp 937–73, for details of the more significant impurities. Available at: http://old.iupac.org/publications/pac/2003/pdf/7507x0937.pdf.

12. Dow Chemical Company maintains a “Product Safety Assessment Finder” on their website: http://www.dow.com/productsafety/assess/finder.htm.

13. ESR coordinates a survey of pesticides in groundwater throughout New Zealand. The survey has been completed every four years since 1990 with 2014 being the seventh. The report for the 2014 survey covers 165 groundwaters; pesticides were detected in 28 wells (17 percent), with 10 of these having two or more pesticides. Seven pesticides were detected in one well and 21 different pesticides were detected. Herbicides were the most frequently detected group with four insecticides and two fungicides also detected. There were 31 detections (61 percent) of triazine herbicides with terbuthylazine being the most frequently detected (16 detections). There were four pesticide detections exceeding 0.001 mg/L. One sample exceeded the MAV: dieldrin was detected at 0.000043 mg/L, slightly in excess of the MAV of 0.00004 mg/L. The next highest detection relative to the MAV was terbuthylazine at 17 percent of the MAV with the remainder of detections being less than 5 percent of the MAV. For details, see: Humphries B, Close M (2015) *National Survey of Pesticides in Groundwater 2014*, Client Report No CSC 15003, 33 pp. http://www.marlborough.govt.nz/Environment/Groundwater/~/media/Files/MDC/Home/Environment/Groundwater/2015%20Reports/National\_Survey\_of\_Pesticides\_in\_Groundwater\_Report\_final.pdf.

14. The most commonly used pesticides in New Zealand up to 2004 (excluding domestic) appear in the following table. Source: Manktelow et al 2005, Trends in Pesticide Use in New Zealand 2004: Report to the Ministry for the Environment, Project SMF4193 – modified – copied from “Literature Review of Organic Chemicals of Emerging Environmental Concern in Use in Auckland”, Auckland Regional Council, Technical Report No. 028, December 2008, 193 pp. http://www.arc.govt.nz/albany/fms/main/Documents/Plans/Technical%20publications/Technical%20reports/1-50/TR2008-028%20-%20Literature%20Review%20of%20Organic%20Chemicals%20of%20Emerging%20Environmental%20Concern%20in%20Use%20in%20Auckland.pdf.

The table does not include mineral oils (ca. 25 t/y). A number of other pesticides are used in domestic, roadside and specialty applications, including pyrethroids, neonicotinoids, and anticoagulant rodenticides. Some of these, while used in much lower volumes, are likely to be more hazardous to the environment.

|  |  |  |  |
| --- | --- | --- | --- |
| **Chemical compound type (FAO category)** | **Active ingredient** | **Percentage of sales** | **Mode of action** |
| phenoxy hormones | MCPA, 2,4-D, mecoprop, MCPB | 25 percent | synthetic auxin (herbicides) |
| dithiocarbamates | mancozeb, metiram, thiram, ziram | 11 percent | lipid synthesis inhibitors (fungicides) |
| phosphonyls | glyphosate, glufosinate-ammonium | 8.4 percent | amino acid inhibitor (herbicides) |
| triazines | terbuthylazine, hexazinone, atrazine, simazine, propazine | 7.6 percent | photosynthesis inhibitors (herbicides) |
| plant growth regulators | hydrogen cyanamide, ammonium thiosulphate, chlomequat-chloride, mepiquat-chloride | 6.9 percent | growth inhibitors/ retardants (herbicides) |
| inorganics | copper compounds, sulphur compounds, phosphorous acid | 6.9 percent | mostly fungicides |
| organophosphates | diazinon, methamidophos, chlorpyrifos, fenamiphos, pirimiphos-methyl, phorate | 3.6 percent | neurotoxic (insecticides) |
| chloroacetanilides | acetochlor, alachlor, propachlor | 3.0 percent | seedling shoot inhibitors (herbicides) |
| other fungicides | captan, chlorothalonil, metalaxyl-m, tolylfluanid | 2.4 percent | fungicides |
| urea derivatives | isoproturon, linuron | 2.0 percent | photosynthesis inhibitors (herbicides) |
| other hormone types | triclopyr, pichloram | 1.3 percent | synthetic auxin (herbicides) |
| dinitroanilines | trifluralin | 0.4 percent | – |
| N-methyl carbamate insecticides | aldicarb, carbaryl, carbofuran, formetanate HCl, methiocarb, methomyl, oxamyl, pirimicarb, propoxur and thiodicarb | 0.4 percent | inhibition of the acetylcholinesterase enzyme |

15. Some physical data have been included for some pesticides. The following discussion has mostly been taken from http://npic.orst.edu/ingred/ppdmove.htm and http://pubs.usgs.gov/circ/2005/1291/ (accessed 2013).

The soil half-life is a measure of the persistence of a pesticide in soil. Pesticides can be categorised on the basis of their half-life as non-persistent, degrading to half the original concentration in less than 30 days; moderately persistent, degrading to half the original concentration in 30 to 100 days; or persistent, taking longer than 100 days to degrade to half the original concentration. A ”typical soil half-life” value is an approximation and may vary greatly because persistence is sensitive to variations in site, soil, and climate.

**Note:** The United Nations Environment Programme (UNEP), Secretariat of the Stockholm Convention on Persistent Organic Pollutants, as amended in 2009, Annex D (b) Persistence:

(i) evidence that the half-life of the chemical in water is greater than two months, or that its half-life in soil is greater than six months, or that its half-life in sediment is greater than six months; or

(ii) evidence that the chemical is otherwise sufficiently persistent to justify its consideration within the scope of this convention.

This definition is consistent with the European Union definition for a very persistent pesticide of a half-life in soil of greater than six months (Regulation EC No 1107/2009 concerning the placing of plant protection products on the market).

Two of the parameters used most often to describe the partitioning of a compound among environmental media are (1) the Henry’s Law constant (KH), which describes partitioning between air and water, and (2) the soil organic carbon-water partition coefficient (Koc), which describes partitioning between water and the organic matter in soil or sediment.

A pesticide with a high KH is volatile and thus, primarily tends to reside in and be transported by air. As a result, such compounds are rarely retained for long in streams or soil, but if they reach groundwater, they may remain for substantial periods of time because there is comparatively little exposure to the atmosphere.

The sorption coefficient (Koc) describes the tendency of a pesticide to bind to soil particles. Sorption retards movement, and may also increase persistence because the pesticide is protected from degradation. The higher the Koc, the greater the sorption potential, ie, the lower the mobility. Koc is derived from laboratory data. Many soil and pesticide factors may influence the actual sorption of a pesticide to soil. Because they associate more strongly with organic matter than with water, pesticides with high Koc values are sometimes referred to as hydrophobic. Compounds with low Koc values (which therefore tend to favour water over organic matter) are described as hydrophilic. As a result of their affinity for organic matter, the more persistent hydrophobic pesticides are likely to accumulate not only in soils and sediments, but also in fish, birds, mammals, and other biota. Pesticides with high Koc values are typically not very water soluble and will preferentially adhere to soils rather than be dissolved in water. This means that pesticides in this class are unlikely to be carried offsite in run-off as dissolved substances; instead, they are transported on sediment particles. For example DDT with a Koc of 100,000 adheres strongly to soil. Diazinon has a Koc of 1,580 and is readily transported as the free substance dissolved in water. The California Department of Pesticide Regulation has determined that pesticides with a Koc less than 1,900 have potential to contaminate groundwater.

The GUS or Groundwater Ubiquity Score is an empirically derived value that relates pesticide persistence (half-life) and sorption in soil (sorption coefficient, Koc). The GUS may be used to rank pesticides for their potential to move toward groundwater. The pesticide movement rating is derived from the GUS. GUS = log10 (half-life) x [4 – log10 (Koc)]. Movement ratings range from extremely low to very high. Pesticides with a GUS less than 0.1 are considered to have an extremely low potential to move toward groundwater. Values of 1.0–2.0 are low, 2.0–3.0 are moderate, 3.0–4.0 are high, and values greater than 4.0 have a very high potential to move toward groundwater.

16. **Threshold values indicating potential for groundwater contamination by pesticides**: The USEPA developed the following values in 1986 (taken from http://psep.cce.cornell.edu/facts-slides-self/facts/pest-gr-gud-grw89.aspx):

|  |  |
| --- | --- |
| **Chemical or physical property** | **Threshold value** |
| Water solubility | greater than 30 mg/L |
| Henry’s Law constant | less than 10-2 atm/m3 mol |
| Kd | less than 5, usually less than 1 or 2 |
| Koc | less than 300 to 500 |
| Hydrolysis half-life | more than 25 weeks |
| Photolysis half-life | more than 1 week |
| Field dissipation half-life | more than 3 weeks |

The likelihood of a pesticide to volatilise is a function of both its vapour pressure and its solubility. This function is expressed by Henry’s Law constant. (Unfortunately there are many different ways to express Henry’s Law constant, and many different units are used.)

Kd = the concentration of chemical adsorbed divided by the concentration of chemical dissolved. The major drawback of using Kd to predict leaching of pesticides is that it is highly dependent on soil characteristics. Organic matter is the most important soil constituent determining pesticide retention. It therefore is useful to adjust the Kd value by the percent organic carbon in the soil. This yields another adsorption coefficient, Koc, which is relatively independent of soil type. Koc = Kd divided by the percent organic carbon in the soil.

17. An excellent primer on toxicology has been prepared by the Australian Pesticides and Veterinary Medicines Authority (APVMA). See http://apvma.gov.au/node/1036.

18. Neonicotinoids (or neonics) are a class of neuro-active insecticides chemically similar to nicotine. These compounds account for about 25 percent of the current (2013) global insecticide market. The neonicotinoids include (on ACVM Register as at October 2013):

|  |  |
| --- | --- |
| **acetamiprid (no)** | **clothianidin (yes)** |
| dinotefuran (no) | imidacloprid (yes) |
| nitenpyram (yes) | nithiazine (no) |
| thiacloprid (yes) | thiamethoxam (yes) |

On 24 May 2013, the European Commission imposed a number of use restrictions on neonicotinoid insecticides, which are suspected to be a contributing factor of bee colony collapse disorder. The European Commission has adopted a proposal (Regulation (EU) No 485/2013) to restrict the use of three pesticides belonging to the neonicotinoids family (clothianidin, imidacloprid and thiametoxam) for a period of two years from December 2013. See: http://ec.europa.eu/food/animal/liveanimals/bees/neonicotinoids\_en.htm.

Clothianidin is a primary metabolite of thiamethoxam. The chloronicotinyl insecticides (thiamethoxam, clothianidin, imidacloprid) are more toxic than the cyano substituted (thiacloprid, acetamiprid). See also: FERA (2013) Neonicotinoid Pesticides and Bees, The Food and Environment Research Agency (UK), 133 pp. http://www.fera.defra.gov.uk/scienceResearch/scienceCapabilities/chemicalsEnvironment/documents/syngentaNeonicotinoidReportJan13.pdf.

19. Drinking water standards in England and Wales are now set out in European and UK legislation. They are called Prescribed Concentrations or Values (PCVs) and many are different from WHO’s Guideline Values. See: DWI (2010) The Water Supply (Water Quality) Regulations 2010, *Water, England and Wales* 994 (W.99): 42 pp. http://dwi.defra.gov.uk/stakeholders/legislation/wsr2010wales.pdf.

20. Many vertebrate toxic agents (VTAs) are used in New Zealand. Datasheets have been prepared for brodifacoum, bromadiolone, chloralose, 3-chloro-p-toluidine hydrochloride, cholecalciferol, coumatetralyl, difethialone, diphacinine, flocoumafen, norbormide, PAPP, phosphine, pindone, strychnine and 1080.

21. **Triazole derivatives**: These are generally considered to comprise triazole alanine (TA), 1,2,4-triazole (1,2,4-T), triazole acetic acid (TAA) and triazole lactic acid (TLA). They are common metabolites of the triazole-containing fungicides which includes the following 18 triazole active fungicides:

bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, ipconazole, metconazole, myclobutanil, paclobutrazol, penconazole, propiconazole, prothioconazole, tebuconazole, tetraconazole, triticonazole.

Others that are sometimes mentioned are azaconazole, hexaconazole, triadimefon, triadimenol and uniconazole.

An abbreviated datasheet for the triazoles has been included. For further detail, refer to the individual fungicide datasheets.

Contents

The datasheet for [*Bacillus thuringiensis israelensis*](#_Toc350766576) is included in the Bacteria datasheets. Abamectin and streptomyces – see actinomycetes (bacteria section) for brief discussion.

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Metamitron 988

Metam sodium 991

Methabenzthiazuron 995

Methamidophos 997

Methiocarb 1002

Methomyl 1006

Methoprene 1012

Methoxychlor 1016

Methoxyfenozide 1021

1-Methylcyclopropene 1025

Methylene bisthiocyanate 1028

Methyl isothiocyanate 1031

Methyl parathion 1034

Metiram 1041

Metofluthrin 1045

Metolachlor 1048

Metrafenone 1056

Metribuzin 1059

Metsulfuron 1067

Milbemectin 1072

Mirex 1075

Molinate 1079

Monocrotophos 1084

Myclobutanil 1087

Naphthenates 1091

1-Naphthylacetic acid 1094

Neem oil 1098

Nicarbazin 1102

Niclosamide 1106

Nicosulfuron 1109

Nitenpyram 1112

Norbormide 1114

Norflurazon 1116

Novaluron 1120

Octhilinone 1124

N-octyl bicycloheptene dicarboximide 1127

Oryzalin 1129

Oxadiazon 1134

Oxamyl 1138

Oxathiapiprolin 1143

Oxine-Copper 1146

Oxyfluorfen 1149

Paclobutrazol 1152

PAPP, para-aminopropiophenone 1155

Paraquat 1159

Parathion 1164

Penconazole 1170

Pencycuron 1173

Pendimethalin 1176

Pentachlorophenol 1182

Penthiopyrad 1192

Permethrin 1195

Phenmedipham 1204

d-Phenothrin 1207

Phenylphenol 1210

Phorate 1215

Phosphine 1220

Phoxim 1223

Picloram 1226

Picoxystrobin 1234

Pindone 1237

Pinoxaden 1240

Piperonyl butoxide 1243

Pirimicarb 1246

Pirimiphos methyl 1250

Pirimisulfuron methyl 1258

Polyoxin D 1262

Posaconazole 1264

Prochloraz 1266

Procymidone 1269

Prohexadione-calcium 1274

Prometryn 1277

Propachlor 1280

Propamocarb 1286

Propanil 1290

Propargite 1296

Propazine 1300

Propetamphos 1307

Propham 1310

Propiconazole 1313

Propineb 1319

Propoxur 1324

Propyzamide 1328

Proquinazid 1332

Prothioconazole 1335

Prothiofos 1339

Pymetrozine 1341

Pyraclostrobin 1345

Pyrazophos 1348

Pyrethrin and Pyrethroids 1351

Pyridate 1356

Pyrimethanil 1360

Pyriproxyfen 1364

Pyroxasulfone 1369

Pyroxsulam 1372

Quinoxyfen 1375

Quintozene 1379

Quizalofop-p-ethyl 1384

Resmethrin 1388

Rotenone 1391

Saflufenacil 1395

Sethoxydim 1399

Simazine 1402

Sodium tetrathiocarbonate 1410

Spinetoram 1414

Spinosad dt 1419

Spiromesifen 1424

Spirotetramat 1427

Spiroxamine 1432

Streptomycin 1435

Strychnine 1438

Sulfentrazone 1441

Sulfoxaflor 1444

Sulphaquinoxaline 1447

2,4,5-T 1450

Tau-fluvalinate 1456

Tebuconazole 1460

Tebufenozide 1464

Tebuthiuron 1467

Temephos 1470

Tepraloxydim 1474

Terbacil 1477

Terbufos 1482

Terbumeton 1487

Terbuthylazine 1489

Terbutryn 1495

Tetrachlorvinphos 1498

Thiabendazole 1502

Thiacloprid 1507

Thiamethoxam 1511

Thidiazuron 1515

Thifensulfuron-methyl 1518

2-(thiocyanomethylthio) benzothiazole 1521

Thiodicarb 1525

Thiophanate-methyl 1529

Thiram 1534

Thymol 1540

Tolclofos-methyl 1543

Toltrazuril 1547

Tolylfluanid 1550

Topramezone 1554

Toxaphene 1557

Tralkoxydim 1562

Triadimefon and Triadimenol 1565

Tri-allate 1571

Triazole metabolites 1575

Triazophos 1578

Tribenuron 1581

Trichlorfon 1584

Triclopyr 1588

Trifloxystrobin 1596

Trifloxysulfuron sodium 1600

Triflumuron 1603

Trifluralin 1606

Triforine 1613

Trinexapac-ethyl 1617

Triticonazole 1621

Uniconazole 1623

Zinc pyrithione 1626

Zineb 1630

Ziram 1634

1080 1638

# Abamectin, avermectin

Abamectin (CAS No. 71751-41-2) is a mixture of [avermectins](http://en.wikipedia.org/wiki/Avermectin) containing more than 80[percent](http://en.wikipedia.org/wiki/%25) avermectin B1a (CAS No. 65195-55-3) and less than 20 percent avermectin B1b (CAS No. 65195-56-4). There are four major homologues and four minor homologues of the lactones.

Abamectin is a macrocyclic lactone product derived from the soil micro‑organism *Streptomyces avermitili* – see Actinomyctes datasheet in Bacteria section.

### Maximum Acceptable Value

No MAV has been set for abamectin or avermectin in New Zealand drinking-water.

EPA established an environmental exposure limit of 0.001 µg/L for abamectin in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to drinking-water

Abamectin is a broad-spectrum acaricide with additional insecticidal action on a limited number of insects. Abamectin is also used as an anthelmintic drug in veterinary medicine.

Abamectin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Abamectin and avermectin have very similar biological and toxicological properties. The abamectins are broad spectrum insecticidal and anthelmintic compounds derived from various laboratory broths fermented by the soil [bacterium](http://en.wikipedia.org/wiki/Bacterium) [Streptomyces avermitilis](http://en.wikipedia.org/w/index.php?title=Streptomyces_avermitilis&action=edit&redlink=1) (EXTOXNET 1994, EMEA 2002). Abamectin is a natural fermentation product of this bacterium, and is sold by a large number of companies in New Zealand.

### Forms and fate in the environment

Abamectin is rapidly degraded in soil. At the soil surface, it is subject to rapid photodegradation, with half-lives of eight hours to one day reported. Abamectin is rapidly degraded in water. After initial distribution, its half-life in artificial pond water was four days. Its half-life in pond sediment was two to four weeks.

NPIC (1994) quotes for abamectin (avermectin) a soil half-life of 28 days, water solubility of 5 mg/L and a sorption coefficient (soil Koc) of 5,000. This resulted in a pesticide movement to groundwater rating of very low.

JMPR (2015) reports that Avermectin B1a degraded in aerobic soils with a half-life ranging from 12 to 52 days, and a mean of 29 ± 14 days (n=14). Light accelerates the degradation in water and soil, and isomerises the compound to its 8,9-Z isomer. Aqueous hydrolysis is not a significant degradation route for avermectin B1a at environmentally relevant pHs and temperatures.

EFSA (2016) stated that the surface water and sediment exposure assessments for the metabolites [8,9-Z]-avermectin B1a, 8a-oxo-avermectin B1a, 8a-hydroxy-avermectin B1a, 4,8a-dihydroxy-avermectin B1a, 8a-oxo-4-hydroxy-avermectin B1a and 4”-oxo-avermectin B1a were not finalised. Consequently, while it cannot be concluded that there will not be aquatic metabolites present in surface water at the point of abstraction for drinking water, so a further data gap was identified for the effect of water treatment processes on the nature of residues in surface water treated for drinking water purposes to be addressed. The potential for groundwater exposure from the representative uses of abamectin was concluded to be low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The RfD for avermectin was calculated at 0.0025 mg/kg/d (USEPA. 1989. For all other populations (containing females, infants and children) an acute population adjusted dose (PAD) of 0.00083 mg/kg/day was used and reflects an appropriate 300X UF. For the male subpopulation, chronic exposure was compared with the chronic RfD of 0.0012 mg/kg/day from a two-generation reproduction study in rats and a 100X UF. A 300X UF was utilised for populations containing females (13+ years old) and infants and children and the exposures were compared to a PAD of 0.0004 mg/kg/day.

EXTOXNET (1996) quotes an ADI of 0.0001 mg/kg/d and a RfD of 0.0004 mg/kg/d for abamectin. USEPA (2004) reports an acute RfD for abamectin of 0.0025 mg/kg/day based on a NOAEL of 0.25 mg/kg/day from a one-year dog study and a 100X uncertainty factor (UF).

JMPR (2000) initially adopted an ADI of 0–0.0002 mg/kg bw for abamectin on the basis of a NOAEL of 0.12 mg/kg bw per day for toxicity in pups in a study of reproductive toxicity in rats. A safety factor of 500 was applied because of concern about the teratogenicity of the 8,9-Z-isomer, a photodegradation product that has been detected as a residue in plants. JMPR agreed in 1995 that the ADI of 0–0.0002 mg/kg bw was not appropriate for abamectin residues that do not contain the 8,9-Z-isomer, and it allocated an ADI of 0–0.001 mg/kg bw to abamectin, on the basis of a NOAEL of 0.12 mg/kg bw per day observed in the study of reproductive toxicity in rats, with a safety factor of 100. New toxicological data were evaluated by the JMPR in 1997. In view of the finding that rats are hypersusceptible postnatally, the meeting agreed to reduce the interspecies safety factor in establishing an ADI. A safety factor of 50 was therefore applied to the NOAEL of 0.12 mg/kg bw in the multigeneration study in rats, which is corroborated by a NOEL of 0.24 mg/kg bw per day in a one-year study in dogs, with a safety factor of 100. It was considered appropriate to establish a single ADI for abamectin and its 8,9-Z-isomer, since the potential teratogenicity of the isomer had been satisfactorily explained. An ADI of 0–0.002 mg/kg bw was established for the sum of abamectin and its 8,9-Z-isomer.

The Acceptable Daily Intake (ADI) adopted in Australia for abamectin is 0.0005 mg/kg body weight with a NOEL of 0.5 mg/kg bw. The ARfD is 0.005 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0004 mg/kg/d, and a ARfD of 0.005 mg/kg/d for abamectin and for avermectin B1a. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for abamectin is 0.05 mg/L.

The toxicological profile of abamectin was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.0025 mg/kg bw per day and 0.005 mg/kg bw, respectively (EFSA 2014/2016). The metabolite included in the residue definition was considered to be of the same toxicity as the parent active substance.

Studies on genotoxicity were negative. Studies (combined with chronic toxicity studies) in mice and rats gave no evidence for an oncogenic potential of abamectin (EMEA 2002).

The JMPR 2015 Meeting established a new ADI of 0–0.001 mg/kg bw, based on the NOAEL of 0.12 mg/kg bw per day for lower body weights and delayed time of vaginal opening observed at 0.20 mg/kg bw per day in post-weaning pups in the two developmental neurotoxicity studies in rats, using a safety factor of 100. The meeting withdrew the existing ADI of 0–0.002. The ADI also applies to the 8,9-Z isomer and the 24‑hydroxymethyl metabolite of abamectin. The meeting established an ARfD of 0.003 mg/kg bw, based on the overall NOAEL of 0.25 mg/kg bw per day for clinical signs in dogs (mydriasis) observed in the first week of treatment at 0.5 mg/kg bw per day. This ARfD also applies to the 8,9-Z isomer and the 24-hydroxymethyl metabolite of abamectin. Because of the very similar biological and toxicological properties of the B1a and B1b components, they can be considered to be equivalent (JMPR 2015).

In view of the lack of genotoxicity and the absence of carcinogenicity in mice and rats, the meeting concluded that abamectin is unlikely to pose a carcinogenic risk to humans (JMPR 2015).

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for abamectin since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Acephate

CAS No. 30560-19-1. The IUPAC name for acephate is (RS)-(O,S-dimethyl acetylphosphoramidothioate) or (RS)-N-[methoxy(methylthio)phosphinoyl]acetamide. The CAS name is O,S-dimethyl acetylphosphoramidothioate.

### Maximum Acceptable Value

Acephate is not mentioned in DWSNZ, or in the WHO Guidelines.

The USEPA concluded on 22 September 2009 that acephate is known or anticipated to occur in PWSs and may require regulation. Therefore they added acephate to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.008 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Acephate is a broad-spectrum organophosphate systemic insecticide. In New Zealand, acephate is used on avocado, boysenberry, cabbage, cauliflower, celery, citrus, lettuce, potato, tamarillo and tomato crops as well as ornamentals for the control of various pest insects including aphids, caterpillars, moths, white butterflies, mealy bugs and scale insects.

Pesticides containing acephate have been registered for agricultural use in New Zealand since 1974. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). There are two products containing acephate that are currently registered for agricultural use in New Zealand: Orthene WSG and Lancer 750DF. There are also products available for home garden use containing acephate, such as McGregor’s Rose and Shrub Spray. From 1 July 2015, only approved handlers will be able to apply acephate.

ERMA notes that 2.5 tonnes of acephate were used in New Zealand in 2004, at an application rate of 4,500 grams of active ingredient per hectare. Acephate was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in strawberries, celery and lettuce.

### Forms and fate in the environment

Acephate degrades in aerobic soil with a half-life from less than two days to two weeks depending on soil type. This produces the intermediate degradation product methamidophos (qv), which is also an insecticidally active compound. Methamidophos is likewise rapidly metabolised by soil micro-organisms to carbon dioxide and microbial biomass (half-lifes of <10 days). Acephate does not photodegrade and hydrolyses only at high pHs. Soil mobility of acephate and methamidophos is expected to be high, however, studies of acephate applied to crops found that acephate and methamidophos were undetectable at 50 cm depths in silt loam, sand, and loam soils for the duration of the study (NPIC).

It is noted that acephate is highly soluble in water (835 g/L) and mobile. Despite the high solubility and mobility in water, acephate is considered a low risk of groundwater contamination because acephate and methamidophos do not persist in the environment.

NPIC (1994) quotes for acephate a soil half-life of three days, water solubility of 81.8 percent and a sorption coefficient (soil Koc) of 2. This resulted in a pesticide movement to groundwater rating of very low.

Octanol-Water Partition Coefficient (Kow): 0.13 at 25°C. Henry’s constant: 3.1 x 10-7 atm·m3/mol; 5.1 x 10-13 atm mole/m3. Soil Sorption Coefficient (Koc): 2; 2.7.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Acephate, like other organophosphates, causes neurotoxic effects at low concentrations following both acute and chronic exposure. The USEPA has classified acephate in Group C: a possible human carcinogen.

The RfD was calculated at 0.004 mg/kg/d (USEPA 1990). The aPAD/aRfD is 0.005 mg/kg/day and the cPAD/cRfD is 0.0012 mg/kg/day (NPIC). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0012 mg/kg/d, and an ARfD of 0.005 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for acephate is 0.05 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.003 mg/kg body weight, with a NOEL of 0.22 mg/kg bw from a two-year dietary rat study. The NOEL was based on inhibition of cholinesterase. The ADI incorporates a safety factor of 100.

Acephate was last evaluated by the JMPR in 2005 and 2003 when an ADI of  
0–0.03 mg/kg bw/day, an ARfD of 0.1 mg/kg bw/day were established. These values were reaffirmed in JMPR (2011), and include any methamidophos arising from use of acephate.

The ADI in New Zealand is 0.0012 mg/kg/d.

Acephate residues expected in food and drinking water do not pose risk concerns (USEPA 2001). Acephate residues have been found in New Zealand lettuce and celery at greater than the maximum residue limit (MRL): refer NZFSA: <http://www.nzfsa.govt.nz/>

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for acephate since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Acetochlor

CAS No. 34256-82-1. The IUPAC name for acetochlor is 2-chloro-N-ethoxymethyl-6′-ethylacet-o-toluidide. Also called 2-chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide (CAS name). Acetochlor is a racemic mixture of two thermally stable rotational isomers (rotamers) on the nitrogen atom in the structure.

### Maximum Acceptable Value

Not mentioned in the DWSNZ or the WHO Guidelines.

The USEPA concluded on 22 September 2009 that acetochlor is known or anticipated to occur in PWSs and may require regulation. Therefore they added acetochlor to their CCL 3 (Drinking Water Contaminant Candidate List 3). Also appearing on the list are the degradation products acetochlor ethanesulfonic acid (CAS No. 187022-11-3) and acetochlor oxanilic acid (CAS No. 184992-44-4) ( USEPA 2009).

EPA established an environmental exposure limit of 8 ng/L (0.008 µg/L) for acetochlor in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Acetochlor is a selective pre-emergent chloroacetanilide or amide [herbicide](http://en.wikipedia.org/wiki/Herbicide), commonly used with maize and rape, providing up to 10 weeks residual control of annual grasses and broadleaf weeds. Its mode of action is [elongase](http://en.wikipedia.org/w/index.php?title=Elongase&action=edit&redlink=1) [inhibition](http://en.wikipedia.org/wiki/Enzyme_inhibitor), and inhibition of [geranylgeranyl pyrophosphate](http://en.wikipedia.org/wiki/Geranylgeranyl_pyrophosphate) (GGPP) cyclisation enzymes, part of the [gibberellin](http://en.wikipedia.org/wiki/Gibberellin) pathway. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). ERMA notes that 62.9 tonnes of acetochlor were used in New Zealand in 2004, at an application rate of 2520 grams of active ingredient per hectare.

### Forms and fate in the environment

Acetochlor is adsorbed by soil colloids and leaches very little. Although acetochlor is not expected to leach through most agricultural soils, there is a potential for limited groundwater contamination in areas of highly permeable soils. Its solubility in water is about 200 mg/L. Its GUS score is 2.21, indicating intermediate leaching potential to groundwater.

The main method of degradation in topsoil is microbial breakdown, forming the major soil metabolites t-oxanilic acid (maximum 17 percent applied AR), and t-sulfonic acid (maximum 11.8 percent AR) which exhibited moderate to high persistence, and t‑sulfinylacetic acid (maximum 18 percent AR) which exhibited medium to high persistence. The minor soil metabolites s-sulfonic acid (maximum 9.8 percent AR) which exhibited moderate to medium persistence and t-norchloro acetochlor (maximum 3.3 percent AR) were also identified (EFSA 2011). See Appendix B in EFSA (2015) for a list of metabolites.

USGS (2006) give the following values: log Kow = 3.0; log Koc (where Koc is in mL/g) = 2.38; water solubility = 223 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -2.15; half-life in aerobic soil = 14 days; half-life in water = 2,300 days.

The degradation of acetochlor in soil maintained under aerobic conditions is rapid with four major degradates identified; tert-oxanilic acid, tert-hydroxy, tert-sulfonic acid and tert-sulfinylacetic acid. While parent acetochlor is degraded relatively quickly in soils the degradates formed are moderately persistent. In the laboratory studies, soil DT50 values for parent acetochlor ranged from 3.3 to 55 days while for field dissipation studies DT50 values ranged from 2.9 to 12.6 days. Acetochlor was stable to hydrolysis in aqueous solutions at pH 5, 7 and 9 (25°C) suggesting hydrolysis plays a negligible role in its degradation. Similarly negligible degradation was observed in an aqueous photolysis study suggesting photolysis is not a major route of degradation (JMPR 2015).

### Typical concentrations in drinking-water

Acetochlor was detected in five of 197 wells completed in alluvial aquifers in Iowa during 1995 to 1998. Detected concentrations ranged up to 0.0008 mg/L. The sulfonic and oxanilic acid metabolites of acetochlor were detected in 26 and 12 wells, respectively. Samples from monitoring wells in agricultural areas had the greatest number of detections.

Between 1998–2003, samples from eight water supplies in the US contained >0.03 mg/L acetochlor.

Five water utilities in the US reported detecting acetochlor in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.002 mg/L.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Actochlor was detected in three wells, from 0.063 to 0.091 µg/L, ie, up to 0.00009 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Acetochlor occurred in three wells, at 0.021 to 0.071 µg/L, ie, up to 0.000071 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2011).

### Health considerations

Acetochlor was classified by the USEPA in 1992 as a probable human [carcinogen](http://en.wikipedia.org/wiki/Carcinogen) (Group 2B); the September 2008 classification was “suggestive evidence of carcinogenic potential”. This classification is based on evidence of carcinogenicity from several sources. Laboratory animal tests found an increased incidence of cancer or tumours (benign or malignant) of the liver, thyroid, lung, uterus, ovaries, kidney, and nose. Certain tests also indicated that acetochlor is a mutagen, causing changes to cellular DNA. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Compared with a major alternative, alachlor, acetochlor is equally or less toxic to both humans and the environment. Acetochlor is also relatively less toxic than other herbicides of toxicological concern, including metolachlor and 2,4-D.

A three-month feeding study submitted by Monsanto with rats fed dosages of 0, 40, 100, and 300 mg/kg/day resulted in a no-observed-effect-level (NOEL) of 40 mg/kg/day based on loss of body weight and decreased food consumption at 100 mg/kg/day.

Acetochlor is not considered to be a material that causes developmental or reproductive toxicity. The lowest NOAEL for fetotoxicity was 21 mg/kg/day in a two-generation reproduction study and the lowest NOAEL for fetotoxicity in a developmental study was 150 mg/kg/day (USEPA 2000).

A NOEL of 10 mg/kg/d was based on a two-year study on rats; ADI = 0.01 mg/kg (EXTOXNET 1996).

The lowest NOAEL for chronic effects in dogs was 2 mg/kg/day and the lowest NOAEL for chronic effects in rats was 7.9 mg/kg/day. The USEPA established the Reference Dose (RfD) for acetochlor at 0.02 mg/kg/day based on the 2.0 mg/kg/day NOAEL in the ZENECA dog study and the application of a 100-fold safety factor (USEPA 2000). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.02 mg/kg/d, and an ARfD of 0.15 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for acetochlor is 1.50 mg/L.

The groundwater metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid, s‑sulfonic acid and t-norchloro acetochlor were considered toxicologically relevant taking into account the limited information available and the carcinogenic potential of the parent compound (EFSA 2011). EFSA quote an ADI of 0.0036 mg/kg bw/day using the LOAEL from the 78-week mouse study with a safety factor of 300, and an ARfD of 1.5 mg/kg bw, derived from the acute rat neurotoxicity study with the application of a safety factor of 100. These values also apply to the listed metabolites, plus N-oxamic acid. Reaffirmed in EFSA (2013 and 2015).

Acetochlor is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

The JMPR meeting established an ADI of 0–0.01 mg/kg bw on the basis of a NOAEL of 1.10 mg/kg bw per day in the 78-week dietary study in mice, based on slight anaemia and an increased incidence of bronchiolar hyperplasia and interstitial fibrosis in the kidney in males observed at 11.0 mg/kg bw per day. A safety factor of 100 was applied. An ARfD of 1 mg/kg bw was established on the basis of a NOAEL of 100 mg/kg bw per day in a study of developmental toxicity in rabbits, based on decreased feed consumption, decreased body weight (GDs 6–8) and the death of two dams observed at 300 mg/kg bw per day. A safety factor of 100 was applied. The meeting concluded that, on the basis of the weight of evidence, acetochlor was unlikely to be genotoxic in vivo (JMPR 2015).

### Derivation of Maximum Acceptable Value

No MAV.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for acetochlor is 0.009 mg/L; acetochlor ESA 0.3 mg/L; acetochlor OXA 0.1 mg/L; the acute limit (one day exposure) for acetochlor is 0.04 mg/L.

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# Acibenzolar

CAS No. 126448-41-7. The IUPAC name for acibenzolar is benzo[1,2,3]thiadiazole-7-carbothioic S-acid. The CAS name is 1,2,3-benzothiadiazole-7-carbothioic acid. Usually used as an ester or salt, particularly acibenzolar-S-methyl, CAS No. 135158-54-2: S‑methyl benzo[1,2,3]thiadiazole-7-carbothioate. Also called benzothiadiazole.

### Maximum Acceptable Value

Acibenzolar is not mentioned in the DWSNZ or the WHO Guidelines.

### Sources to water

Acibenzolar is a selective, systemic benzothiadiazole fungicide or plant activator. It induces host plant resistance which mimics the natural systemic activated resistance response found in most plant species; it has no direct effect on the target pests. The naturally occurring phenomenon of this defence response is called systemic activated resistance (SAR), also known as systemic acquired resistance or systemic induced resistance. It is used for the control of downy mildew on leafy vegetables, bacterial spot and bacterial speck on tomatoes. Acibenzolar-S-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Acibenzolar-S-methyl readily degrades under environmental conditions by abiotic and biotic processes. Degradation is rapid by photolysis in water and on soil at relevant environmental photoperiods and considerably less rapid hydrolytically at relevant environmental pHs (pH 6–9). The major degradates observed were benzo[1,2,3]thiadiazole-7-carboxylic acid (ie, acibenzolar or CGA 210007) in the hydrolysis and soil photolysis studies (up to 100 percent) with considerably lesser amounts found in the photolysis in water study (8.4 percent). CGA 210007 has low-high soil persistence, the DT50 reported from four to 106 days (EFSA 2014). The major degradate in the photolysis in water study was CO2 (>33 percent). Other degradates identified that may be of toxicological concern were CGA 323060 and 324041 (hydroxymetabolites from the photolysis on soil study). These were found in amounts not exceeding 0.5 percent.

The acid metabolite of acibenzolar-S-methyl (designated as CGA 210007) has a potential for leaching, which might require particular attention in vulnerable areas to ensure protection of groundwater. Water-sediment studies show acibenzolar-S-methyl is rapidly transformed to acibenzolar acid (CGA 210007) which exhibits high persistence under these conditions (geomean DT50 whole system >1 year) and it is found both in sediment (maximum 38 percent) and water (maximum 75 percent) phases.

In drinking water, the residues of concern are acibenzolar-S-methyl and its degradate CGA-210007. These residues are non-persistent to slightly persistent in the environment under aerobic aquatic conditions in and are unlikely to reach surface water or groundwater. Although acibenzolar would sorb to soils and sediments, degradation is the principal impediment to leaching. Acibenzolar would not be expected to accumulate in sediments due to the rapid metabolism under aerobic conditions.

In an anaerobic aquatic environment, acibenzolar-S-methyl is considered to be slightly to moderately persistent. The water solubility of acibenzolar-S-methyl is about 7.7 mg/L; Henry’s Law constant is 1.3 x 10-2 Pa m3 mol-1, partition coefficient is Log Pow: 3.1 at 25°C.

### Removal methods

Soil adsorption properties suggest that treatment processes that remove particulate matter should be effective at reducing the concentration of acibenzolar in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2014).

### Health considerations

Acibenzolar-S-methyl is rapidly and almost completely absorbed after oral administration. The active substance is widely distributed, the highest concentrations being found in the liver, kidney, blood and blood rich tissues. Acibenzolar-S-methyl is extensively metabolised, and rapidly excreted mainly via urine.

The USEPA (2000) concluded from the review of the supporting data that there are no risks of concern from the use of acibenzolar-S-methyl. There was no significant acute toxicity in a battery of acute toxicity studies and no dermal sensitivity was detected. It was calculated that the risk due to exposure to residues in food and water was below the Agency’s level of concern for all population subgroups, including infants and children. Risk from exposure of workers (applicators and other handlers) was also below the Agency’s level of concern. The Agency also concluded that its labelled uses were unlikely to represent a significant threat to non-target organisms or the environment.

Based on the aPAD of 0.0033 mg/kg/day for this exposure scenario/population subgroup (females 13–50 years), the maximum allowable exposure to acibenzolar-S-methyl from drinking water is 0.0004 mg/kg/day. Using HED default assumptions of 2 L/day adult drinking water consumption and 60 kg body weight for adult females, this results in an acute drinking water level of comparison (DWLOC) of 0.012 mg/L. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD and an ARfD of 0.082 mg/kg/d for acibenzolar-S-methyl. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for acibenzolar-methyl is 2.7 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for acibenzolar-S-methyl is 0.005 mg/kg body weight, with a LOEL of 5 mg/kg bw, based on a 12‑month chronic oral toxicity study in dogs. The ARfD is 0.01 mg/kg bw.

EC (2002) reports an ADI of 0.1 mg/kg/d based on 90‑day and 12‑month dog studies. They report a lowest relevant NOAEL (for long-term toxicity and carcinogenicity) of 8 mg/kg/d based on a two-year rat study.

EFSA (2012 and 2013) quote an ADI of 0.1 mg/kg/d for acibenzolar-S-methyl and state that no ARfD was established because of the low acute toxicity of the active substance (EFSA 2014) now states that the acceptable daily intake (ADI), the acceptable operator exposure level (AOEL) and the acute reference dose (ARfD) of acibenzolar-S-methyl are 0.03 mg/kg bw (per day), based on the LOAEL of 10 mg/kg bw per day from the developmental toxicity study in rat, applying an uncertainty factor (UF) of 300, 100 standard factor plus additional factor of 3 to account for the LOAEL basis. Acibenzolar acid (free and conjugated) that is included in the residue definition applicable in the current assessment is of similar toxicity as the parent active substance.

JPMR (2016) established an ADI of 0–0.08 mg/kg bw on the basis of the NOAEL of 7.77 mg/kg bw per day in a two-year study in rats for haemosiderosis in the spleen in males observed at 96.9 mg/kg bw per day. A safety factor of 100 was applied. The meeting established an ARfD of 0.5 mg/kg bw on the basis of the NOAEL of 50 mg/kg bw per day in a rat developmental toxicity study for decreased maternal feed consumption early during treatment and an equivocal increase in malformations observed at 200 mg/kg bw per day. A safety factor of 100 was applied.

### Derivation of Maximum Acceptable Value

No MAV.

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# Alachlor

CAS No. 15972-60-8. IUPAC name is 2-chloro-2′,6′-diethyl-N-methoxymethylacetanilide. CAS name is 2-chloro-N-(2,6-diethylphenyl)-N-methoxymethylacetamide. Earlier called 2-chloro-2’,6’-dimethyl-N-(methoxymethyl) acetanilide.

### Maximum Acceptable Value

Based on health considerations, the concentration of alachlor in drinking-water should not exceed 0.02 mg/L. Alachlor is included in the [plan of work](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en) of the rolling revision of the WHO *Guidelines for Drinking-water Quality*.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.002 mg/L.

The USEPA concluded on 22 September 2009 that the degradation products alachlor ethanesulfonic acid (alachlor ESA – CAS No. 142363-53-9) and alachlor oxanilic acid (alachlor OA – CAS No. 171262-17-2) are known or anticipated to occur in PWSs and may require regulation. Therefore they added them to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009a).

JMPR (1993) states that the maximum concentration of the impurity 2-chloro-2’,6’-diethylacetanilide (2-chloro-N-(2,6-diethylphenyl)acetamide) is 30 g/kg.

### Sources to water

Alachlor belongs to the acetanilide chemical group. It is used as a herbicide for selective pre- and post-emergence control of annual grasses and broadleaf weeds in barley, kumara, maize, onions, pumpkins, soyabeans, squash, and other crops.

Alachlor may enter source waters as a result of its application as a herbicide, used for pre‑ and post emergence control of most annual grasses and broad leaved weeds in various crops.

The total annual usage of alachlor in New Zealand in the late 1980s was 42,000 kg, 41,000 kg of which was used in the North Island. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 39.8 tonnes of alachlor were used in New Zealand in 2004, at an application rate of 3,360 grams of active ingredient per hectare.

### Forms and fate in the environment

Loss of alachlor from the soil is primarily by microbial degradation, with some volatilisation and photodegradation. The literature reports that its field half-life ranges from seven to 49 days, with 15 days being a recommended average value. It is metabolised rapidly in plants and does not bioaccumulate. Under certain conditions, alachlor can leach beyond the root zone into the groundwater. Many alachlor degradation products have been identified in soil. AWWARF (2008) compiled a risk index for pesticide degradates; four of the five highest risk compounds were all degradates of alachlor: 2,6-dimethyl-N-methoxymethyl-2-sulfo-acetanilide, alachlor oxanilic acid, 2,6-diethyl-N-methoxy-methoxanilic acid, and alachlor ethane sulfonic acid. Another metabolite is 2,6-diethylaniline.

NPIC (1994) quotes for alachlor a soil half-life of 15 days, water solubility of 240 mg/L and a sorption coefficient (soil Koc) of 170. This resulted in a pesticide movement to groundwater rating of moderate.

USGS (2006) give the following values: log Kow = 2.8; log Koc (where Koc is in mL/g) = 2.23; water solubility = 240 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -2.7; half-life in aerobic soil = 20.4 days; half-life in water = 640 days.

If released to soil, alachlor is expected to have high to low mobility based upon a Koc range of 120 to 2,138. Mobility decreases with an increase in organic carbon and clay content. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 8.32 x 10-9 atm-cu m/mole. Half-lifes of 2–3 weeks under aerobic conditions indicate that biodegradation is a moderately important environmental fate process in soil. When incorporated into soil samples, alachlor degraded 22 to 39 percent following eight-hour exposure to eight-hour sunlight, the rate of degradation being enhanced by low pH and low soil organic matter. If released into water, alachlor may adsorb to some suspended solids and sediment based upon the Koc range. Approximately 20 percent degradation after 30‑day incubation in lake water indicates that biodegradation is not expected to be an important environmental fate process in water. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. A BCF of 6 suggests bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyse under environmental condition. A 1 percent degradation in 135 minutes of alachlor in aqueous solution irradiated with light from 300 nm sunlamps suggests that photolysis in water is a slow environmental fate process (EAWAG accessed February 2015).

It has a water solubility of 240 mg/L and a sorption coefficient of 170 mL/g.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of alachlor (limit of detection = 0.0002 mg/L) (ESR 2001).

Alachlor has been found 12 times in groundwater in several areas of the North Island, ranging from 0.00002 to 0.0037 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Alachlor occurred at 0.1 µg/L (0.0001 mg/L).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Alachlor occurred at 0.02 to 0.25 µg/L, ie, up to 0.00025 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Alachlor occurred at 0.039 to 0.048 µg/L, ie, up to 0.000048 mg/L.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Alachlor was found in four wells, from 0.02 to 12 µg/L, ie, up to 0.012 mg/L or 60 percent of the MAV.

Alachlor was found in one bore during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.034 mg/L (ie, greater than the MAV). The bore was in the Manawatu region.

Alachlor has been detected in groundwater and surface water; it has also been detected in drinking-water at levels below 0.002 mg/L (WHO 2004).

Forty-one water utilities in the US reported detecting alachlor (Lasso) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.002 mg/L.

### Removal methods

Adsorption on to granular activated carbon can be used to remove alachlor from water (0.001 mg/L should be achievable), and significant reduction can also be achieved by ozonation.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Capillary Column Gas Chromatography with Mass Spectrometry (EPA 525).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 505).

2. Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector (EPA 507).

### Health considerations

Alachlor is absorbed through the gastrointestinal tract of rats and it is distributed mainly to the blood, spleen, liver, kidney and heart.

Long-term exposure studies in dogs and rats reported hepatotoxicity at all dose levels for both species. The rat study also reported highly significant levels of ocular lesions in the mid and high dose groups (>42 mg/kg body weight per day), identified as the uveal degeneration syndrome.

The International Agency for Research on Cancer has not evaluated alachlor. On the basis of available data, evidence for the genotoxicity of alachlor is considered to be equivocal. However, a metabolite of alachlor, 2,6-diethylaniline, has been shown to be mutagenic. Available data from two studies in rats indicate clearly that alachlor is carcinogenic, causing benign and malignant tumours of the nasal turbinate, malignant stomach tumours, and benign thyroid tumours. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. As at September 2008, the USEPA has classified alachlor as “not likely to be carcinogenic to humans at low doses”.

The USEPA (2009/2011) quotes a health advisory of 0.04 mg/L for alachlor, representing a 10-4 cancer risk.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.01 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.4 mg/L.

Alachlor is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

In view of the data on carcinogenicity, the MAV for alachlor was calculated by applying the linearised multistage model to data on the incidence of nasal tumours in rats. The MAV in drinking-water associated with an excess lifetime cancer risk of one per 100,000 (10-5) is a concentration of 0.02 mg/L.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for alachlor is 0.005 mg/L; alachlor ESA 0.07 mg/L; alachlor OXA 0.07 mg/L.

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# Aldicarb

CAS No. 116-06-3. The IUPAC name for aldicarb is (EZ)-2-methyl-2-(methylthio)propionaldehyde-O-methylcarbamoyloxime. CAS: 2-methyl-2-(methylthio)propanal O-[(methylamino)carbonyl]oxime.

### Maximum Acceptable Value

Based on health considerations, the concentration of aldicarb in drinking-water should not exceed 0.01 mg/L.

The maximum contaminant level or MCL for aldicarb (USEPA 2006/2009/2011) is 0.003 mg/L. The USEPA (2006/2009/2011) also has a MCL of 0.002 mg/L for aldicarb sulfone which is also called aldoxycarb (CAS No. 1646-88-4) and 0.004 mg/L for aldicarb sulfoxide (CAS No. 1646-87-3). USEPA (2006/2009/2011) states that “the MCL value for any combination of two or more of these three chemicals should not exceed 0.007 mg/L because of a similar mode of action”.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.007 mg/L for each, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The maximum acceptable concentration in Canada is 0.009 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.004 mg/L; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Aldicarb may enter source waters as a result of its application as a broad spectrum systemic oxime carbamate insecticide used to control nematodes in soil, and insects and mites on a wide variety of crops. Aldicarb sulfone and aldicarb sulfoxide are breakdown products. They have also been used as pesticides in their own right. Aldicarb should not contain more than 12.5 g/kg methyl isocyanate, 50 g/kg dimethylurea + trimethylbiuret, or 12.5 g/kg trimethylamine.

USEPA. 2007. states: in order to mitigate potential drinking water concerns … an increased well setback from 300 to 500 feet is required for wells not encased to a depth of 100 feet in vulnerable soils, and a shallow depth to groundwater (less than 25 feet).

As at 2009 aldicarb is not registered for use in New Zealand.

### Forms and fate in the environment

Aldicarb is oxidised fairly rapidly to the sulfoxide. In some soils, 48 percent of the parent compound was converted to the sulfoxide seven days after application. It is oxidised much more slowly to the sulfone. Hydrolysis of the carbamate ester groups, which inactivates the pesticide, is pH-dependent, with half-lifes in distilled water varying from a few minutes, at a pH of 12, to 560 days, at a pH of 6.0. Half-lifes in surface soils ranged from approximately 0.5 to 3 months and, in the saturated zone, from 0.4 to 36 months. Hydrolysis of aldicarb is somewhat slower than that of either the sulfoxide or the sulfone.. It is highly mobile in soil, particularly if sandy. The greatest leaching occurs in sandy soils with a low organic matter content, particularly where the water table is high. It is very persistent in groundwaters; the half-life for degradation to non‑toxic products ranges from a few weeks to several years. Drainage aquifers and local, shallow wells have been contaminated with aldicarb sulfoxide and sulfone. Levels have generally ranged between 1 and 50 µg/litre, but levels of approximately 500 µg/litre have been recorded (ICPS 1991).

NPIC (1994) quotes for aldicarb a soil half-life of 30 days, water solubility of 6,000 mg/L and a sorption coefficient (soil Koc) of 30. NPIC (1994) quotes for aldicarb sulfone a soil half-life of 20 days, water solubility of 10,000 mg/L and a sorption coefficient (soil Koc) of 10. This resulted in a pesticide movement to groundwater rating of high, for both.

The water solubility is 6,000 mg/L and the sorption coefficient is 30 mL/g.

### Typical concentrations in drinking-water

No data are available on the concentration of aldicarb in New Zealand drinking-water supplies.

Aldicarb has been found in Canadian waters at concentrations up to 0.028 mg/L, and in waters from the USA in concentrations ranging from <0.01 to 0.5 mg/L.

Nineteen water utilities in the US reported detecting aldicarb in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.45 mg/L. This result was something of an outlier – the next highest was 0.0047 mg/L.

Fifteen water utilities in the US reported detecting aldicarb sulfone in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.001 mg/L.

Twenty-eight water utilities in the US reported detecting aldicarb sulfoxide in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.004 mg/L.

Concentrations in well water as high as 500 μg/l have been measured; aldicarb sulfoxide and aldicarb sulfone residues are found in an approximately 1:1 ratio in groundwater (WHO 2017).

### Removal methods

Adsorption on to granular activated carbon can be used to remove aldicarb from water, and ozone should destroy the molecule. Air stripping may also be effective.

### Recommended analytical techniques

#### Referee method

Reverse Phase High Performance Liquid Chromatography (EPA 531.).

#### Some alternative methods

No alternative methods have been recommended for aldicarb because no methods meet the required criteria. See WHO (2003) for further information.

### Health considerations

Aldicarb is absorbed rapidly from the gastrointestinal tract, the respiratory tract and the skin. It is metabolised rapidly and excreted. Aldicarb does not accumulate in tissues, but it appears to cross the placental barrier. The principal toxic effect of aldicarb and its sulfoxide and sulfone metabolites is cholinesterase inhibition as measured in plasma, erythrocyte and brain.

Aldicarb is highly acutely toxic in animals and it is one of the most acutely toxic pesticides. Poisoning in humans has resulted from ingestion of contaminated cucumbers and melons, the latter at a dose as low as 0.0021 mg/kg body weight.

In humans, clinical symptoms of aldicarb intoxication include dizziness, weakness, diarrhoea, nausea, vomiting, abdominal pain, excessive perspiration, blurred vision, headache, muscular convulsions, temporary paralysis of the extremities, and dyspnea. Recovery is rapid, usually within six hours.

The only toxic effect observed consistently with both long-term and single-dose administration of aldicarb in studies conducted to date is the rapidly reversible inhibition of acetylcholinesterase activity. The toxic effects of aldicarb appear to be dependent on the method and vehicle of administration.

It is converted to the sulfoxide and sulfone. Aldicarb sulfoxide is a more potent inhibitor of acetylcholinesterase than aldicarb itself, whereas aldicarb sulfone is considerably less toxic than either aldicarb or the sulfoxide (WHO 2017).

The reference dose or RfD (USEPA 2006/2009/2011) is 0.001 mg/kg/d for each of aldicarb, aldicarb sulfone and aldicarb sulfoxide. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.035 mg/L for each of aldicarb, aldicarb sulfone and aldicarb sulfoxide.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.001 mg/kg body weight, with a NOEL of 0.01 mg/kg bw from an acute dietary study in human volunteers. The NOEL is based on cholinesterase inhibition in plasma and erythrocytes at 0.025 mg/kg bw. The ADI incorporates a safety factor of 10. The ARfD is 0.001 mg/kg bw.

JMPR (2006) quotes an ARfD of 0.003 mg/kg bw.

The International Agency for Research on Cancer has concluded that aldicarb is not classifiable as to its carcinogenicity to humans (Group 3). As at September 2008, the USEPA has classified aldicarb in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

WHO (2003) states:

In 1992, JMPR recommended an ADI of 0.003 mg/kg of body weight, based on a single oral dose study in human volunteers with a NOAEL of 0.025 mg/kg of body weight per day for depression of erythrocyte cholinesterase activity and an uncertainty factor of 10 (FAO/WHO 1993). The calculated guideline value would, therefore, be 0.009 mg/L, assuming an allocation of 10 percent of the ADI to drinking-water. Because this is very similar to the guideline value of 0.01 mg/L derived in the WHO second edition, the guideline value of 0.01 mg/L is retained.

WHO (2017) states the ADI is 0–0.003 mg/kg body weight based on cholinesterase depression in a single oral dose study in human volunteers.

The MAV for aldicarb in drinking-water was derived as follows:

0.4 mg/kg body weight/day x 70 kg x 0.1 = 0.014 mg/L (rounded to 0.01 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 0.4 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for intra- and interspecies variation. No allowance has been made for the short duration of the study in view of the extremely sensitive and rapidly reversible biological end-point used).

The WHO (2nd edition 1993) guideline value of 0.01 mg/L had been derived for aldicarb as follows:

A tolerable daily intake approach has been used for the derivation of the MAV for aldicarb in drinking-water. The No-observable-adverse-effects level (NOAEL) used for the MAV derivation is for acetylcholinesterase inhibition found in a 29‑day study in rats administered drinking-water containing a 1:1 ratio of aldicarb sulfoxide and aldicarb sulfone. This study is considered to be the most relevant to the derivation of a drinking-water guideline because the rats were administered a ratio of aldicarb metabolites similar to that normally found in drinking-water.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for aldicarb is 0.001 mg/L.

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# Aldrin/dieldrin

**Aldrin:** CAS No. 309-00-2. The IUPAC name for aldrin is (1R,4S,4aS,5S,8R,8aR)-1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalene (HHDN). The CAS name is (1R,4S,4aS,5S,8R,8aR)-rel-1,2,3,4,10,10-hexachloro-1,4,4a,5,8,8a-hexahydro-1,4:5,8-dimethanonaphthalene.

**Dieldrin:** CAS No. 60-57-1. The IUPAC name for dieldrin is (1R,4S,4aS,5R,6R,7S,8S,8aR)-1,2,3,4,10,10-hexachloro-1,4,4a,5,6,7,8,8a-octahydro-6,7-epoxy-1,4:5,8-dimethanonaphthalene (HEOD), or 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-endo-1,4-exo-5,8-dimethanonaphthalene. CAS name is (1aR,2R,2aS,3S,6R,6aR,7S,7aS)-rel-3,4,5,6,9,9-hexachloro-1a,2,2a,3,6,6a,7,7a-octahydro-2,7:3,6-dimethanonaphth[2,3-b]oxirene.

### Maximum Acceptable Value

Based on health considerations, the total concentration of aldrin and dieldrin in drinking-water should not exceed 0.00004 mg/L (0.04 g/L).

The maximum acceptable concentration for aldrin plus dieldrin in Canada is 0.0007 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0003 mg/L (for aldrin and dieldrin combined); minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Aldrin and dieldrin are “priority pollutants” under the US Clean Water Act.

Aldrin and dieldrin are two of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention. See <http://chm.pops.int/>

Aldrin and dieldrin appear on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

Dieldrin is listed as a “priority contaminant” in the Ministry for the Environment’s *Toxicological Intake Values for Priority Contaminants in Soil* (MfE 2011).

### Sources to water

Dieldrin is a stereoisomer of endrin and a metabolite of aldrin. Technical dieldrin contained 85 percent dieldrin and 15 percent insecticidally active related products.

Impurities of aldrin included octachlorocyclopentene (0.4 percent), hexachlorobutadiene (0.5 percent), toluene (0.6 percent), a complex mixture of compounds formed by polymerisation during the aldrin reaction (3.7 percent) and carbonyl compounds (2 percent) (taken from ICPS 1999).

The organochlorine pesticides, aldrin and dieldrin, may enter source waters as a result of their use as highly effective insecticides for soil dwelling pests and for protection of wooden structures against termites and borer. The use of aldrin and dieldrin has been restricted severely, or banned, in many countries since the early 1970s.

Aldrin and dieldrin are not currently used in New Zealand but they have been used in the past, for example in sheep dips. Their registration was cancelled in 1989.

MfE (2012) developed a national set of soil contaminant standards for 12 priority contaminants and five common land uses; levels range from 1.1 to 160 mg/kg depending on land use for dieldrin or aldrin separately, or to the sum of aldrin and dieldrin if both are involved.

NPIC (1994) quotes for aldrin a soil half-life of 365 days, water solubility of 0.027 mg/L and a sorption coefficient (soil Koc) of 5,000. This resulted in a pesticide movement to groundwater rating of very low.

For dieldrin a soil half-life of 1,000 days, water solubility of 0.2 mg/L and a sorption coefficient (soil Koc) of 12,000. This resulted in a pesticide movement to groundwater rating of extremely low. However, Hadfield and Smith (1999) found dieldrin could be widespread in shallow groundwater, about 5 m depth, and could slowly increase in concentration, seeping from old sheep dip sites.

USGS (2006) give the following values: log Kow = 5.20; log Koc (where Koc is in mL/g) = 4.08; water solubility = 0.17 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.0492; half-life in aerobic soil = NA days; half-life in water = 3830 days.

### Forms and fate in the environment

Aldrin, used as a soil insecticide, is the major source of dieldrin (up to 97 percent) in the environment. Aldrin and the reaction product dieldrin are rapidly adsorbed on soils, especially soils containing a high level of organic matter. Consequently, there is little penetration into the soil, and contamination of groundwater does not generally occur. The GUS score for dieldrin is -0.24, indicating that it should not leach to groundwater. Transport of both compounds takes place mainly through soil erosion (as wind drift) and sediment transport (surface run-off), but not through leaching (IPCS 1989).

The use of aldrin and dieldrin in agriculture leads to residues (mainly of dieldrin) in the soil that can persist for years, the estimated half-life being between four and seven years. In living animals and in most environmental conditions, aldrin is oxidised rapidly to dieldrin, which in the body is oxidised in the liver and eliminated.

The water solubilities for aldrin and dieldrin are 0.027 and 0.18 mg/L respectively.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, found aldrin + dieldrin in three zones at concentrations ranging from 0.00001 to 0.00003 mg/L (100 percent of the then MAV, and 540 people with >50 percent of the MAV), with the median concentration being “nd” (limit of detection = 0.00001 mg/L). The P2 programme in 2001 found dieldrin at >50 percent of its MAV in two zones in Northland and in one zone in Invercargill (ESR 2001).

Dieldrin has been found in Waikato groundwaters twice, at 0.00001 and 0.00018 mg/L (MAF 2006).

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Dieldrin was detected in one well at a concentration of 0.13 mg/m3 (µg/L) in November 2010, more than three times the MAV. The well was resampled seven months later and the concentration in the second sample was 0.14 mg/m3, ie, 0.00014 mg/L. This well was not used for drinking purposes but was used for irrigation and stock water purposes. An old sheep dip site was identified at the site located approximately 20–30 m upgradient from the well.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Despite not having been used since the mid-1960s, dieldrin was found in two wells, at 0.008 and 0.043 µg/L, ie, up to 0.000043 mg/L (MAV = 0.00004 mg/L).

Aldrin and dieldrin have occasionally been detected in large Australian water storages where the maximum concentration reported is less than 0.001 mg/L, but the frequency of detection has dropped markedly since 1980.

Nine water utilities in the US reported detecting aldrin in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.094 mg/L. This result is something of an outlier – the next highest was 0.00023 mg/L.

Nineteen water utilities in the US reported detecting aldrin in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.094 mg/L. This result is something of an outlier – the next highest was 0.00055 mg/L.

### Removal methods

Adsorption on to granular activated carbon can be used to remove aldrin/dieldrin from water. Approximately 50 percent removal can be attained through conventional treatment using alum. Destruction can be achieved through oxidation by ozone. Aldrin is completely broken down by chlorination; chlorination removes 85 percent of dieldrin.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6630C).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 505).

Aldrin and dieldrin are listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by any national drinking-water guidelines.

### Health considerations

Aldrin and dieldrin are absorbed by ingestion, inhalation and skin contact and tend to accumulate in adipose tissue. Aldrin and dieldrin can be metabolised from the adipose tissue compartment, causing an increase in blood level that results in toxic effects. The major metabolite is 9-hydroxy dieldrin.

Both aldrin and dieldrin are highly toxic to humans. The target organs are the central nervous system and the liver. Severe cases of both accidental and occupational poisoning, and a number of fatalities have been reported. The lethal dose of dieldrin is estimated to be approximately 10 mg/kg body weight per day. The majority of individuals intoxicated with aldrin and/or dieldrin usually recover, and irreversible effects of residual pathology have not been reported.

Analyses have shown that dieldrin occurs almost ubiquitously in human breast milk. Nevertheless, the concentration of this chemical in the blood and adipose tissue of suckling infants does not increase with age during the first six months, nor is the dieldrin level in their blood higher than that in the blood of bottle-fed babies. Under these circumstances, the benefits of natural breast feeding may still be regarded as outweighing the alternative methods of infant feeding (ICPS 1989).

The majority of studies on aldrin and dieldrin have not shown mutagenicity.

The International Agency for Research on Cancer has classified dieldrin in Group 3 (not classifiable as to its carcinogenicity to humans). All the available information on aldrin and dieldrin taken together, including studies on humans, support the view that for practical purposes these chemicals make very little contribution to the incidence of cancer in humans.

Aldrin was classified by the USEPA in 1987 in Group 2B: a probable human carcinogen; aldrin was not in their 24 September 2008 list. These chemicals appear on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. The USEPA (2009/2011) quotes a health advisory of 0.0002 mg/L for aldrin, and for dieldrin, representing a 10-4 cancer risk.

MfE (2011) states: Dieldrin is a threshold contaminant, with the liver being the critical target of chronic toxicity in several animal species. Most jurisdictions have adopted the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) value for ADI of 0.1 µg/kg bw/day, based on hepatotoxicity in rats, and this is recommended for use in New Zealand. No dermal absorption data is available for dieldrin; hence, it is recommended that an absorption factor of 0.1 is used. The dietary intake for a child aged 1–3 years was estimated to be 0.0036 µg/kg bw/day and for an adult, 0.0014 µg/kg bw/day, while intake from drinking water is negligible.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for aldrin of:

* 0.002 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.00003 mg/kg/day for chronic-duration oral exposure (>364 days).

As at July 2013 ATSDR quotes a minimal risk level (MRL) for dieldrin of:

* 0.0001 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.00005 mg/kg/day for chronic-duration oral exposure (>364 days).

The reference dose or RfD for aldrin (USEPA 2006/2009/2011) is 0.00003 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.001 mg/L.

The reference dose or RfD for dieldrin (USEPA 1990/2006/2009/2011) is 0.00005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.002 mg/L.

The Tolerable Daily Intake (TDI) adopted in Australia for both aldrin and for dieldrin is 0.0001 mg/kg body weight, based on a no-observed-effect level (NOEL) of 0.025 mg/kg bw/day from two-year dietary studies in rats and dogs. The NOEL is based on liver damage. The TDI incorporates a safety factor of 250.

Dieldrin is one of the Substances from the Carcinogenic Potency Database which are of particular concern even if ingested at doses at or below 0.0025 μg/kg body weight per day (EFSA 2016).

### Derivation of Maximum Acceptable Value

Due to the fact that dieldrin is considered to contribute very little, if any, to the incidence of cancer in humans, a tolerable daily intake approach has been used for the derivation of the MAV for aldrin/dieldrin in drinking-water.

In 1977, the Joint FAO/WHO Meetings on Pesticide Residues (JMPR) recommended an ADI of 0.1 μg/kg of body weight (0.0001 mg/kg) for combined total for aldrin and dieldrin. This was based on a no-observable-adverse-effect level of 1 mg/kg of diet in the dog and 0.5 mg/kg of diet in the rat, which are equivalent to 0.025 mg/kg of body weight per day in both species. JMPR applied an uncertainty factor of 250 based on concern about carcinogenicity observed in mice. WHO (2003/2011) has reaffirmed this ADI which has been used for the derivation of the MAV for aldrin/dieldrin.

The MAV for aldrin/dieldrin (ie, the sum of) in drinking-water was derived as follows:

0.025 mg/kg body weight/day x 70 kg x 0.01 = 0.000035 mg/L (rounded to 0.00004 mg/L)

2 L/day x 250

where:

* no-observable-adverse-effect level = 0.025 mg/kg body weight per day based on two studies on dogs and rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01. Such a low percentage of the ADI was considered inappropriate for Australia, where the use of these pesticides has been severely restricted, so they adopted 0.1, which led to a 0.0003 mg/L limit
* uncertainty factor = 250 (based on concern about carcinogenicity observed in mice).

In 1995 and 2000 the MAV was 0.00003 mg/L. The increase to 0.0004 mg/L was only the result of rounding.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for dieldrin is 0.0002 mg/L; the acute limit (one day exposure) is also 0.0002 mg/L.

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# Allethrin

Allethrin (CAS No. 584-79-2) is the ISO common name for a racemic mixture of four pairs of diastereoisomers, ie, eight stereoisomers. Esbiothrin (CAS No. 260359-57-5) is the name given by the manufacturer to a mixture of two stereoisomers, [1R,trans;R] and [1R,trans;S], of allethrin in an approximate ratio of 1:3. Bioallethrin consists of [1R,trans;1R] and [1R,trans;1S] isomers in an approximate ratio of 1:1. S-bioallethrin, also called esbiol (CAS No. 28434-00-6) consists of the [1R,trans;1S] isomer (IPCS 1989a, WHO 2004).

The IUPAC name for d-allethrin is (RS)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1R)-cis, trans-chrysanthemate (no CAS number).

The IUPAC name for bioallethrin is (RS)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1R, 3R)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate (no CAS number).

The IUPAC name for s-bioallethrin is (S)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1R,3R)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate.

The IUPAC name for esbiothrin is (RS)-3-allyl-2-methyl-4-oxocyclopent-2-enyl (1R, 3R)-2,2-dimethyl -3-(2-methylprop-1-enyl)cyclopropanecarboxylate.

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for esbiothrin in water (set by an approval under Part 5 of the HSNO Act) of 0.000089 mg/L (0.089 µg/L).

### Sources to water

It was estimated that several hundred tonnes of allethrin, d-allethrin, bioallethrin, esbiothrin, and S-bioallethrin were manufactured and used yearly throughout the world, mainly for the control of household insects. Formulations include concentrates, aerosol sprays, smoke coils, electric mats, and emulsifiable with or without synergists or other insecticides (IPCS 1989). Their main use suggests that water contamination should be negligible.

Many pyrethrins and pyrethroids appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). None of the allethrins are currently listed. Allethrin was the first synthetic pyrethroid to be synthesised (in 1949).

### Forms and fate in the environment

The photodegradation rate was measured of a thin film of allethrin on glass under a sun lamp. Approximately eight hours of exposure were needed for 90 percent degradation. s‑Bioallethrin was rapidly decomposed, when similarly exposed to sunlight (IPCS 1989).

Allethrin is one of the least persistent pyrethroids. Allethrin is the only residue of concern from use of esbiothrin and S-bioallethrin (PMEP 1999, USEPA 1999).

The water solubility of d-allethrin is 5 mg/L.

The water solubility of bioallethrin is 4.6 mg/L. It has an octanol/water partition coefficient of 48,000, or log Kow of 4.7. It is stable to hydrolysis under neutral or slightly acid conditions, but hydrolyses readily under basic conditions. In water, bioallethrin is quickly degraded by photolysis but cis-allethrin was not detected as a significant product.

The water solubility of s-bioallethrin is 4.6 mg/L. It is prone to photolysis, with a half-life of 19 hours in water exposed to natural sunlight during November–February at 37ºN.

The water solubility of esbiothrin is 4.6 mg/L. It has a high octanol-water partition coefficient and a low volatility. Due to the sensitivity of esbiothrin to light and significant hydrolysis rates at elevated pH, or biologically, there is a low risk of accumulation in soil and biota.

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Under recommended conditions of use, the exposure of the general population to the allethrins is negligible and is unlikely to present a hazard (IPCS 1989a).

The manufacturer is proposing a RfD of 0.226 mg/kg bw/day to evaluate chronic dietary risk for S-bioallethrin and esbiothrin. This RfD is based on the NOAEL from the esbiothrin rat chronic toxicity/oncogenicity study with a 100-fold safety factor to account for interspecies extrapolation and intraspecies variation. The S-bioallethrin NOAEL served as a worst-case scenario because it contains the largest amount of d‑trans of d isomer by weight (PMEP 1999).

USEPA (1999) established an chronic RfD for esbiothrin of 0.226 mg.kg/d. The Acceptable Daily Intake (ADI) adopted in Australia for esbiothrin is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg/d.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.008 mg/kg/d, and an ARfD of 0.03 mg/kg/d for d-allethrin and for s-bioallethrin. The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for s-bioallethrin (esbiol) and d‑allethrin are 0.30 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

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# Ametoctradin

CAS No. 865318-97-4. The IUPAC and CAS name for ametoctradin is 5-ethyl-6-octyl[1,2,4]triazolo[1,5-a]pyrimidin-7-amine. BASF markets Zampro in New Zealand, a mixture of ametoctradin and dimethomorph (qv).

### Maximum Acceptable Value

Ametoctradin is not mentioned in the DWSNZ or in the WHO Guidelines.

### Sources to water

The non-systemic fungicide ametoctradin is a mitochondrial respiration inhibitor and belongs to a new class of chemistry, the pyrimidylamines, or triazolopyrimidines. It is used in preventive spray applications against late blight and downy mildews in a wide range of speciality crops, particularly grapes and potatoes. Less than 10 percent of the applied active ingredient is taken up by the leaves after 1–7 days. The majority remains on the leaf surface where it is absorbed on/in the epicuticular wax layer. The vapour phase activity is minimal. These characteristics indicate that ametoctradin is non-systemic.

Ametoctradin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (se<http://pmep.cce.cornell.edu/profiles/extoxnet/24d-captan/ametryn-ext.html> and <http://extoxnet.orst.edu/pips/ghindex.html>).

### Forms and fate in the environment

The half-life of ametoctradin in soil is about 1.4–3.5 days at 20°C, and 6.3 days at 10°C (JMPR 2012). PMEP (2015) quotes an aerobic DT50 of 6.9 to 16.7 days in a range of North American soils; in anaerobic soils the DT50 was 182 days. The mobility of ametoctradin in soil is classified as low to immobile so the risk to groundwater is low (APVMA 2012). The major soil metabolites M650F03 and M650F04 show a moderate to high persistence (maximum DT50 = 130.8 days and 223 days, respectively).

It is hydrolytically stable in sterile aqueous buffer solutions at pH 4, 5, 7 and 9 for at least seven days at 50°C in the dark (estimated DT50 >1 year at 25ºC). The half-life for hydrolysis of ametoctradin in sterile water at 25°C is >1 year. Assuming 12 hours of daylight, the estimated single first-order DT50 for aqueous photolysis of ametoctradin is 76.8 days on a clear summer day at 50º N.

In aerobic water and sediment systems, the DT50s for the water column phase, sediment phase, and total system were 0.8 days, 2.1 days, and 1.8 days respectively. In anaerobic water and sediment systems, the DT50s for the water column phase, sediment phase, and total system were 1.6 days, 13.8 days, and 7.4 days respectively (PMEP 2015).

See JMPR (2012) for information about metabolites that have toxicological relevance. The main ones are ω-hetarylbutanoic acid and ω-hetarylhexanoic acid.

The octanol/water partition coefficient is log P (or log Kow) = 4.40. Water solubility is 0.15 mg/L at pH 7, 20°C; the degradates are much more soluble: see PMEP (2015). Two ametoctradin degradates (M650-F03 and M650-F04) represent a leaching concern for groundwater.

### Recommended analytical techniques

Residues of ametoctradin in drinking/groundwater and surface water can be monitored by HPLC-MS/MS with an LOQ of 0.05 μg/L (EFSA 2012).

### Health considerations

The impurities amitrole and o-xylene are considered relevant with maximum limits of 50 mg/kg and 2 g/kg respectively (EFSA 2012).

For all toxicological end-points, short-term, long-term and carcinogenicity, reproduction and developmental toxicity, and neurotoxicity, no adverse effects were observed up to the highest dose level tested, rounded overall to 1,000 mg/kg bw per day. The acceptable daily intake (ADI) of ametoctradin is 10 mg/kg bw per day, based on the overall NOAEL of 1,000 mg/kg bw per day observed in short-term, long-term, reproduction and developmental toxicity studies, and applying the standard assessment factor (AF) of 100. No acute reference dose (ARfD) is allocated as it was considered not necessary (EFSA 2012, 2014 and 2017; EU 2013).

Since no ADI and no ARfD is considered necessary, no long-term or short-term intake assessment is considered necessary (JMPR 2012).

Ametoctradin was not carcinogenic in the rat or mouse and was not mutagenic or genotoxic with and without metabolic activation in vitro, and was not genotoxic in vivo. Additionally, ametoctradin was not a reproductive toxicant in rats, a developmental toxicant in rats and rabbits, neurotoxic or immunotoxic in rats. Toxicological studies on three major metabolites (M650 F02, M650 F03 and M650 F04) indicated they were not mutagenic or genotoxic (APVMA 2012).

APVMA (2012) developed an ADI for ametoctradin of 10 mg/kg bw/day using a 100‑fold safety factor. An acute reference dose (ARfD) was not established or necessary since ametoctradin was considered unlikely to present an acute hazard to humans after single dose administration.

Ametoctradin did not exhibit toxic effects in neurotoxicity, immunotoxicity, subchronic, chronic, developmental and reproductive toxicity studies. The highest doses tested ranged between 848 mg/kg/day bw in a chronic feeding study in dogs, up to 1543 mg/kg/day in a chronic feeding/carcinogenicity study in mice. Ametoctradin was not genotoxic in a number of studies, nor was it carcinogenic in studies conducted with rats and mice (PMEP 2015). This publication reports that Health Canada derived an ADI of 8.5 mg/kg/day for ametoctradin based on the NOEL (848 mg/kg/day) from the one-year dog dietary study and an uncertainty factor of 100.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2012. *Public Release Summary on the Evaluation of the New Active Ametoctradin in the Product Zampro® Fungicide*. APVMA Product Number P63651. Australian Pesticides and Veterinary Medicines Authority [68 pp]. <http://www.apvma.gov.au/registration/assessment/docs/prs_ametoctradin.pdf>

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EU. 2013. *Review Report for the Active Substance* ametoctradin (BAS 650 F). *SANCO*/ 12977/2012 rev 2 [9 pp]. <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

JMPR. 2012. *Ametoctradin* (253) [152 pp]. <http://www.inchem.org/> or <http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation12/Ametoctradin.pdf> or <http://www.inchem.org/documents/jmpr/jmpmono/v2012pr01.pdf>

PMEP. 2015. *Registration of the New Active Ingredient Ametoctradin (Active Ingredient Code 119210) Contained in Orvego Fungicide (EPA Reg. No. 7969-301) and Zampro Fungicide (EPA Reg. No. 7969-302)* [22 pp]. <http://pmep.cce.cornell.edu/profiles/fung-nemat/aceticacid-etridiazole/ametoctradin/ametoctradin_reg_1215.pdf>

# Ametryn

CAS No. 834-12-8. The IUPAC name for ametryn is N2-ethyl-N4-isopropyl-6-methylthio-1,3,5-triazine-2,4-diamine. CAS name is N-ethyl-N′-(1-methylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine. Sometimes spelt ametryne.

### Maximum Acceptable Value

Ametryn is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*. The final report has not been published as at 2011.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L (previously 0.05 mg/L); minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.06 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

### Sources to water

Ametryn is a methylthiotriazine herbicide, used, for example, on citrus, maize and potatoes, pre- and post-emergent. It has also been used in areas, such as beside roads and railway lines. This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Ametryn does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Despite that, ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (as amended), as at 22 May 2008 lists “liquid containing 140–180 g/litre 2,4-D, 210–250 g/litre ametryn and  
0.5–1.5 g/litre bronopol”.

It is also listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It appears as: 1,3,5-triazine-2,4-diamine, N-ethyl-N’-(1-methylethyl)-6-(methylthio)-.

In a US study, ametryn was found in very few surface water samples. The maximum concentration found was 0.0001 mg/L.

### Forms and fate in the environment

Ametryn’s half-life in soils is 70 to 250 days, depending on the soil type and weather conditions. Loss from the soil is principally by microbial degradation. Ametryn moves both vertically and laterally in soil due to its high water solubility (185 to 200 mg/L). Because it is persistent, it may leach as a result of high rainfall, floods, and furrow irrigation.

NPIC (1994) quotes for ametryn a soil half-life of 60 days, water solubility of 185 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of moderate.

If released to soil, ametryne is expected to have high to low mobility based upon a Koc value range of 69 to 530. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 2.4 x 10-9 atm-cu m/mole. Microbial degradation half-lifes in soil range from 70 to 129 days. If released into water, ametryne is expected to adsorb to suspended solids and sediment based upon the Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 19 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyse under environmental conditions (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

In a study of groundwater contaminants in the US, ametryn was found in 4 percent of the groundwater samples. The maximum concentration found was 0.45 mg/L.

### Removal methods

Chlorination and ozonation have proved effective for reducing the concentration of ametryn in water. Conventional coagulation/flocculation has been shown to be reliable if used in conjunction with activated carbon.

### Health considerations

Studies have shown that ametryn is not mutagenic. As at September 2008, the USEPA considers that the data are inadequate for an assessment of human carcinogenic potential.

The chronic oral RfD has been calculated (USEPA 1989/2009/2011) to be 0.009 mg/kg/day based on liver toxicity in a rat study. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.3 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw from a reproduction study in rats. The ADI incorporates a safety factor of 100.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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WHO. 2009. *Chemical Hazards in Drinking-water:* Ametryn. <http://www.who.int/water_sanitation_health/gdwqrevision/ametryn/en/index.html>

# Aminoethoxyvinylglycine

CAS No. 49669-74-1. The IUPAC name for aminoethoxyvinylglycine is (E)-L-2-[2-(2-aminoethoxy)vinyl]glycine. The CAS name is (2S,3E)-2-amino-4-(2-aminoethoxy)-3-butenoic acid. Also called aviglycine or AVG. Usually sold as the hydrochloride salt: CAS No. 55720-26-8.

### Maximum Acceptable Value

Aminoethoxyvinylglycine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Aminoethoxyvinylglycine is a plant growth regulator, an inhibitor of ethylene biosynthesis thereby suppressing methionine synthesis, thus inhibiting conidial germination and mycelial growth. It is commonly used on fruits and ornamentals. Aviglycine HCl is an amino acid which has been generated through a fermentation of a soil micro-organism (Streptomyces).

Aviglycine hydrochloride appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Aviglycine HCl is highly unlikely to contaminate groundwater resources due to its high soil sorption, and short soil and water/sediment half-lifes. Study results show that aviglycine HCl is easily adsorbed to soils, principally on to clay particles. Half-lifes in soils vary between 1.7 and 4.7 days. Water-sediment studies have shown that aviglycine HCl will be readily adsorbed to sediment where it is mineralised and incorporated into the organic fraction of the sediment. Biodegradation occurs in both systems. The half-life of aviglycine HCl in the aqueous phase and total water/sediment system was calculated to be 1.5 and 4.3 days respectively (USEPA 2005).

APVMA (2001) states that AVG is stable to photolysis and hydrolysis. Calculated KOC values ranged from 561–7495 classifying AVG as having low mobility to immobile depending on soil type (600 < KOC < 7,500). Adsorption of AVG generally increased with increasing clay content.

Solubility in water is approximately 4,000 mg/L.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration in water.

### Health considerations

AVG is rapidly and extensively absorbed following oral administration and excreted primarily in the urine over two to three days. The acute oral and dermal toxicity of AVG is low.

Conflicting evidence for carcinogenicity has been reported for aviglycine HCl. Mutagenicity, immunotoxicology, endocrine, subchronic, and chronic feeding studies strongly suggest that aviglycine HCl does not induce cancer. Effects observed in the carcinogenicity study, such as a threshold-response and reduction in the number of animals with tumours, with benign tumours, and with malignant tumours also support non-carcinogenic conclusions. In contrast, increased incidence of benign testicular interstitial cell adenomas, benign adrenal pheochromocytoma, and adrenal medullary cell hyperplasia suggest that aviglycine HCl may induce cancer. These effects, however, were seen only at an excessively toxic dose and may have been mediated indirectly through generic toxic mechanisms such as glutathione depletion and resultant oxygen radical-induced cell damage, rather than by aviglycine HCl. Dosing with excessive aviglycine HCl, therefore, weakened support for carcinogenic activity. In the end, weight-of-evidence suggests that aviglycine HCl is non-carcinogenic. However, definitive statements of carcinogenicity cannot be made at the current time, because information meeting rigorous criteria for defining it as non-carcinogenic (such as a second cancer study in a different species and strong non-conflicting evidence) is absent. These studies are not typically required in the testing of biochemical pesticides. To account for this, an additional database uncertainty factor of 10x was integrated with other UFs (100x) (increasing the overall uncertainty factor to 1,000) and the NOAEL established in the carcinogenesis study (0.7 mg/kg/day) to conservatively account for this deficiency (RfD = 0.0007 mg/kg/day) (USEPA 2004).

Aviglycine HCl, therefore, was qualified as a non-endocrine disrupting compound.

In repeat-dose studies in rats, the primary effect of AVG were alterations in the microscopic structure of the liver and kidneys and a reduction in the activity of marker enzymes in the blood (AST and ALT). The reduction in AST and ALT activity is not an adverse effect in itself but is a useful measure of AVG exposure. APVMA (2001) stated that based on the NOEL of 0.2 mg/kg bw/day in the 90-day rat dietary study and a safety factor of 1,000 to reflect the lack of a chronic toxicity study, the Acceptable Daily Intake (ADI) for AVG is 0.0002 mg/kg bw/day.

A developmental NOAEL of 0.2 mg/kg/day was established in a rabbit study based on foetal effects at a dose of 0.4 mg/kg/day which was below the maternal LOAEL of 0.7 mg/kg/day. The maternal and developmental LOAELs were the same in the rat developmental study indicating no differences in susceptibility to aviglycine HCl toxicity (USEPA 2004).

USEPA (2005) developed a chronic reference dose (RfD) of 0.007 mg a.i./kg/day and an acute NOEL of 1.77 mg/kg bwt/day. The RfD is based on the NOAEL of 0.7 mg a.i./kg/day from the rat chronic toxicity study (52 week) and the rat carcinogenicity feeding study (104-week) with a 100-fold uncertainty factor to account for intra-species and inter-species variations. The acute NOEL is based on the rat oral developmental toxicity study.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2001. *Evaluation of the New Active Eminoethoxyvinylglycine (AVG) in the Product Retain Plant Growth Regulator*. Australia: National Registration Authority for Agricultural and Veterinary Chemicals [43 pp]. http://archive.apvma.gov.au/registration/assessment/docs/prs\_aminoethoxyvinylglycine.pdf

IUPAC. Accessed 2009. *Aviglycine-HCl* (reference ABG 3097). See: <http://sitem.herts.ac.uk/aeru/iupac/Reports/44.htm>

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# 1-Aminomethanamide dihydrogen tetraoxosulphate

CAS No. 21351-39-3. The IUPAC name for 1-aminomethanamide dihydrogen tetraoxoxsulphate is monocarbamide dihydrogen sulphate. The CAS name is uronium hydrogen sulfate. Also called urea sulfate, urea dihydrogen sulfate, sulfuric acid monourea, and AMADS.

### Maximum Acceptable Value

1-Aminomethanamide dihydrogen tetraoxoxsulphate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

1-Aminomethanamide dihydrogen tetraoxoxsulphate is used both as a herbicide and a desiccant on agricultural crops.

1-Aminomethanamide dihydrogen tetraoxoxsulphate does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it does appear in ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008; see <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides. It is applied to crops with chlorethephon. Has been used with glyphosate overseas.

1-Aminomethanamide dihydrogen tetraoxosulfate (AMADS) appears on the Australian Pesticides and Veterinary Medicines Authority (APVMA) list of active constituents not requiring evaluation. See <http://apvma.gov.au/node/4176#1> (as at August 2002, accessed December 2014).

### Forms and fate in the environment

The USEPA (2005) has determined that urea sulfate readily degrades to urea and sulfuric acid and/or sulfate ions in the environment, so environmental fate studies of the parent product are not needed.

Solubility in water is very high.

### Health considerations

The USEPA (2005) has determined that urea sulfate readily degrades to urea and sulfuric acid and/or sulfate ions in the human body, therefore chronic studies on the parent substance are not needed. The oral LD50 (for rats) is 350 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

IUPAC. Accessed 2009. *Urea Sulphate*. <http://sitem.herts.ac.uk/aeru/iupac/Reports/676.htm>

USEPA. 2005. *Tolerance Reassessment Eligibility Decision for Urea Sulfate* [14 pp]. <http://www.scribd.com/doc/1735611/Environmental-Protection-Agency-urea-sulfate-tred> or <http://www.epa.gov/oppsrrd1/REDs/urea_sulfate_tred.pdf>

# Aminopyralid

CAS No. 150114-71-9. The IUPAC name for aminopyralid is 4-amino-3,6-dichloropyridine-2-carboxylic acid or 4-amino-3,6-dichloropicolinic acid. The CAS name is 4-amino-3,6-dichloro-2-pyridinecarboxylic acid. Can also be marketed as the triisopropylammonium (TIPA) salt.

### Maximum Acceptable Value

Aminopyralid does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.06 mg/L (60 µg/L for aminopyralid in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Aminopyralid is a [picolinic acid](http://www.alanwood.net/pesticides/class_herbicides.html#picolinic_acid_herbicides) or pyridine systemic post-emergence broad-spectrum herbicide. It is a selective hormone-based auxin-type [herbicide](http://en.wikipedia.org/wiki/Herbicide) manufactured used for control of broadleaf weeds such as docks, thistles and nettles. Aminopyralid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The commercial product may contain up to 4 percent picloram.

### Forms and fate in the environment

Aminopyralid is persistent in manures, which if used to enrich soil, can damage vegetable plants such as tomatoes, potatoes and beans; for this reason aminopyralid use was suspended temporarily in the UK (HSE 2009).

Under aerobic conditions, degradation of aminopyralid in five different soils resulted in the production of CO2 and non-extractable residues. Half-lifes ranged from 32 to 533 days in five soils. For risk assessment purposes, the USEPA (2005) used a half-life of 103.5 days. Aminopyralid photolysed moderately slowly on a soil surface with a half-life of 72 days. Aminopyralid is weakly sorbed to soil, which along with its high solubility, suggests it could leach to groundwater. Two field dissipation studies indicate that aminopyralid is likely to be non-persistent and relatively immobile in the field. Half-lifes of 32 and 20 days were determined, with minimal leaching below the 15 to 30 cm soil depth. Henry’s Law constant at pH 7 is 9.61 x 10-12 Pa m3 mol-1 (EFSA 2013).

Solubility in water is very high, about 20 percent. In aquatic systems, the primary route of degradation is photolysis, where a laboratory experiment yielded a half-life of 0.6 days (corrected for natural sunlight conditions). In addition to CO2, oxamic and malonamic acid were identified as major degradates, along with a number of minor  
2–3 carbon chain length acid amides. Aminopyralid was stable to direct hydrolysis and in anaerobic sediment-water systems. In aerobic sediment-water systems, degradation proceeded slowly, with observed total system half-lifes of 462 to 990 days.

### Removal methods

GAC is likely to be effective.

### Health considerations

In a chronic neurotoxicity study in rats and in a rat developmental study, the NOAEL was equal to or greater than 1,000 mg/kg/day. In a developmental toxicity study in rabbits with aminopyralid, the NOAEL for maternal toxicity was 250 mg/kg/day. In a one-year chronic toxicity study in dogs, the NOAEL was 99 mg/kg/day for males and 93 mg/kg/day for females based on thickening of the stomach, slight lymphoid hyperplasia of the gastric mucosa, and slight chronic mucosal inflammation at the HDT. Aminopyralid was negative in all mutagenicity studies. Aminopyralid has been classified as “not likely” to be carcinogenic to humans (USEPA 2005).

The chronic RfD for aminopyralid is 0.5 mg/kg/day. This value is based on the NOAEL of 50 mg/kg/day in the rat combined chronic toxicity/carcinogenicity study with a 100‑fold uncertainty factor to account for interspecies extrapolation (10X) and intraspecies variability (10X). An additional safety factor to protect infants and children is not required, due to the toxicity properties of the material and the conservative nature of the exposure estimates (USEPA 2005). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.5 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for aminopyralid is 3.5 mg/L (no acute one-day value available).

The JMPR 2007 Meeting established an ADI of 0–0.9 mg/kg bw based on a NOAEL of 93.2 mg/kg bw per day identified on the basis of histological changes in the gastric mucosa at higher doses in a one-year study in dogs, and a safety factor of 100. The meeting concluded that it was not necessary to establish an ARfD for aminopyralid. The only end-point that might be suitable as a basis for establishing an ARfD for aminopyralid was uncoordinated gait in the studies of developmental toxicity in rabbits (FAO/WHO 2007).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.3 mg/kg body weight, with a NOEL of 26 mg/kg bw, and the ARfD is also 0.3 mg/kg.

The toxicological profile of aminopyralid was assessed in the framework of the peer review and the data were sufficient to propose an ADI of 0.26 mg/kg bw per day and an ARfD of 0.26 mg/kg bw. (EFSA 2013 and 2019). It is concluded that aminopyralid has no genotoxic potential relevant to humans. EC (2014) adopted the same values.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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HSE. 2009. Aminopyralid – new approvals. *Regulatory Update* 32/2009. Health and Safety Executive, Chemicals Regulation Directorate, Pesticides. See: <http://www.pesticides.gov.uk/garden.asp?id=2799>

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USEPA. 2005. *Pesticide Factsheet: Aminopyralid*. United States Office of Prevention, Pesticides Environmental Protection and Toxic Substances Agency [56 pp]. See: <http://www.epa.gov/opprd001/factsheets/>

USEPA. 2005. *Aminopyralid: Aggregate Human Health Risk Assessment* … [61 pp]. <http://www.epa.gov/opprd001/factsheets/>

USEPA. 2005. *Aminopyralid: Environmental fate and ecological effects risk assessment* [151 pp]. <http://www.epa.gov/opprd001/factsheets/>

# Amitraz

CAS No. 33089-61-1. The IUPAC name for amitraz is N,N′-[(methylimino)dimethylidyne]di-2,4-xylidine. Also called N-methylbis(2,4-xylyliminomethyl)amine. The CAS name is N′-(2,4-dimethylphenyl)-N-[[(2,4-dimethylphenyl)imino]methyl]-N-methylmethanimidamide.

### Maximum Acceptable Value

WHO (2004 and 2011) states that amitraz degrades rapidly in the environment and is not expected to occur at measurable concentrations in drinking-water supplies.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.009 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Amitraz is a triazapentadiene compound, a member of the amidine class. It is an [insecticide](http://en.wikipedia.org/wiki/Insecticide) and [acaricide](http://en.wikipedia.org/wiki/Acaricide) used to control [red spider mites](http://en.wikipedia.org/wiki/Red_spider_mite), [leaf miners](http://en.wikipedia.org/wiki/Leaf_miner), [scale insects](http://en.wikipedia.org/wiki/Scale_insect), and [aphids](http://en.wikipedia.org/wiki/Aphid). This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Amitraz is registered for use in New Zealand as impregnated honey strips for use in beehives to control the parasitic mite (Varroa destructor) on honey bees. Amitraz should not contain more than 3 g/kg of 2,4-dimethylaniline.

Dogs can be treated to control Rhipicephalus sanguineus (ticks) with a wide range of veterinary preparations, such as acaricide-impregnated collars, shampoos or oily pour-on or spot-on formulations, which permeate the entire hair coat after a small initial application. The acaricides commonly used for this purpose are amitraz, carbaryl, fipronil and permethrin.

### Forms and fate in the environment

Amitraz is broken down rapidly in soil containing oxygen. The half-life in soil, the amount of time needed for the chemical to degrade to half its original concentration, is less than one day. Degradation occurs more rapidly in acidic soils than in alkaline or neutral soils.

NPIC (1994) quotes for amitraz a soil half-life of two days, water solubility of 1 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of very low.

Solubility in water is approximately 1 mg/L.

### Health considerations

In a double-blind randomised cross-over study, six healthy male volunteers received sequential single oral doses of 0, 0.063, 0.13 mg/kg body weight of amitraz, two to three weeks apart. There were no clinically significant changes in vital signs or electrocardiographic parameters. The NOAEL was 0.13 mg/kg bw, being the highest dose tested.

The RfD was calculated at 0.0025 mg/kg/d (USEPA 1988). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.00125 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for amitraz is 0.013 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 0.25 mg/kg bw from a two-year study in dogs. The ADI incorporates a safety factor of 100.

JMPR (1998) established an ADI of 0–0.01 mg/kg bw on the basis of the NOAEL of 1.3 mg/kg bw per day in the study of reproductive toxicity in rats and a safety factor of 100. The meeting established an acute RfD of 0.01 mg/kg bw, on the basis of the NOAEL of 0.13 mg/kg bw per day in the study in humans and a safety factor of 10.

This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. The USEPA has classified (September2008) amitraz as having “suggestive evidence of carcinogenic potential”; and previously (since 1990) in Group C: a possible human carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Amitrole

CAS No. 61-82-5. Also known as amino-triazole, and sometimes spelt amitrol. The IUPAC and CAS name is 1H-1,2,4-triazol-3-ylamine.

### Maximum Acceptable Value

Amitrole is not mentioned in the DWSNZ or the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0009 mg/L (previously 0.01 mg/L); minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Amitrole is a non-selective systemic triazole herbicide which has been used since the 1950s. Its main use is for the control of the more difficult to control weeds by inhibiting chlorophyll formation and regrowth from buds.

Amitrol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The technical grade (solution) may contain ammonium thiocyanate which enhances its activity. EFSA (2014) states: the impurities N-(1H-[1,2,4]-triazol-3-yl)-formamide, 4H‑[1,2,4]-triazole-3,4-diamine and methanoic acid are considered toxicologically relevant based on their existing classification and structural alerts for mutagenicity and sensitisation.

### Forms and fate in the environment

Microbial breakdown of amitrole takes 2–3 weeks in warm, moist soil. In laboratory studies, the half-life of amitrole ranged from 2 to 26 days at ambient temperature in different soils; amitrole is degraded to NH3 and CO2, in addition to cyanamide and urea (JMPR 1998).

Although the parent compound leaches through some soils, degradation products are tightly bound to soil. Since amitrole is degraded rapidly in soil, the high potential of the herbicide to leach does not seem to occur in practice (IPCS 1994).

In aquatic environments, amitrole does not break down by hydrolysis or photolysis, volatilise, nor bioaccumulate in aquatic organisms. The biodegradation half-life for amitrole in water is about 40 days. It is highly soluble in water (about 28 percent). Degradation of amitrole in open waters may occur through oxidation by other chemicals. The main route of removal from waters may be through adsorption to sediment particles. Amitrole may persist in surface waters for longer than 200 days.

NPIC (1994) quotes for amitrole a soil half-life of 14 days, water solubility of 36 percent and a sorption coefficient (soil Koc) of 100. This resulted in a pesticide movement to groundwater rating of very moderate.

### Typical concentrations in drinking-water

Under practical conditions there is little risk that amitrole would reach the groundwater level.

### Removal methods

Amitrole has been shown to be effectively removed by ozonation, and the concentration may be reduced further by activated carbon. Any amitrole adsorbed to sediment particles may also be filtered out.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Amitrole is classified as USEPA toxicity class III – slightly toxic. All use of amitrole on food crops was cancelled by the USEPA in 1971 because it caused cancer in experimental animals. The USEPA had classified amitrole in 1992 in Group C: a possible human carcinogen, but in the September 2008 list it is considered not likely to be carcinogenic to humans at doses that do not alter rat thyroid hormone homeostasis. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

With particular regard to residues, the review (EU 2001) has established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is <3 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems.

In a study on apples, triazolylalanine was the major metabolite (22–24 percent), occurring in the free form and as conjugates. This compound is also produced by the metabolism of other triazole pesticides and was therefore reviewed by the 1989 JMPR, which concluded that residues of triazolylalanine do not present a toxicological hazard.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0003 mg/kg body weight, with a NOEL of 0.025 mg/kg bw from a one-year rat study. The ADI incorporates a safety factor of 100.

IARC (2001) concluded that there is inadequate evidence in humans for the carcinogenicity of amitrole, ie, not classifiable as to its carcinogenicity to humans (Group 3). In making its evaluation, the Working Group concluded that amitrole produces thyroid tumours in mice and rats by a non-genotoxic mechanism, which involves interference with the functioning of thyroid peroxidase, resulting in a reduction in circulating thyroid hormone concentrations and increased secretion of thyroid-stimulating hormone. Consequently, amitrole would not be expected to produce thyroid cancer in humans exposed to concentrations that do not alter thyroid hormone homeostasis. An additional consideration of the Working Group, based on the lack of genotoxicity of amitrole, was that the liver tumours in mice and benign pituitary tumours in rats were also produced by a non-genotoxic mechanism. Evidence from epidemiological studies and from toxicological studies in experimental animals provide compelling evidence that rodents are substantially more sensitive than humans to the development of thyroid tumours in response to thyroid hormone imbalance.

EFSA (2014) set an ADI of 0.001 mg/kg/d based on thyroid effects in the 90-day rat studies supported by the multigeneration study with rats, and applying an uncertainty factor (UF) of 100. The acute reference dose (ARfD) is 0.015 mg/kg bw, based on the recent rabbit teratogenicity study (study on maternotoxicity) and applying an UF of 200 due to the uncertainty related to the limited investigations of the developmental effects in the study (only external examinations).

Amitrol is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

No MAV.

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# Asulam

CAS No. 3337-71-1. Also known as asulox. The IUPAC name for asulam is methylsulfanilylcarbamate. Also called N-(4-aminophenyl)sulfonylcarbamic acid methyl ester. CAS name is methyl[(4-aminophenyl)sulfonyl]carbamate. Sometimes appears as asulam sodium.

### Maximum Acceptable Value

Asulam is not mentioned in DWSNZ or in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L: minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Asulam is a selective postemergent systemic carbamate herbicide used to control a variety of annual grasses and broadleaf weeds, often used to control bracken. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Asulam was approved in the UK (MAFF 1985) for the control of weeds on banks near water. The maximum permitted concentration in water is 1 mg/L. However, asulam is no longer approved as a plant protection product in accordance with Regulation (EC) No 1107/2009 (EU 2011).

### Forms and fate in the environment

Asulam is highly to very highly soluble (about 5,000 mg/L). It is stable in water without light, but unstable in water and on soil under light. Sulfanilamide and acetyl sulphanilamide are reported to be metabolites.

NPIC (1994) quotes for asulam sodium salt a soil half-life of seven days, water solubility of 55 percent and a sorption coefficient (soil Koc) of 40. This resulted in a pesticide movement to groundwater rating of moderate.

In soil laboratory incubations under aerobic conditions in the dark, asulam exhibited low to moderate persistence, forming the major (>10 percent AR) metabolite sulfanilamide (maximum 14 percent AR) which also exhibited low to moderate persistence. Asulam exhibited very high to high mobility in soil. Sulfanilamide exhibited high to medium soil mobility. It was concluded that the adsorption of asulam, asulam salts and sulfanilamide was not pH dependent. In laboratory incubations in dark aerobic natural sediment water systems, asulam exhibited medium persistence. The potential for groundwater exposure from the representative uses by asulam and its salts and sulfanilamide above the parametric drinking water limit of 0.1 μg/L was concluded to be low (EFSA 2018).

### Typical concentrations in drinking-water

It appears that asulam is highly mobile and has a strong potential to leach into groundwater or move off-site into surface water.

### Removal methods

Asulam’s high water solubility means coagulation and filtration processes are unlikely to be effective. Oxidation processes, mainly involving ozone are needed.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

An adequate LC–MS/MS method was available for the determination of residues of asulam and its metabolite sulfanilamide in water with a LOQ of 0.05 μg/L for each compound (EFSA 2018).

### Health considerations

Asulam is of relatively low acute toxicity. It is practically non-toxic by the oral and inhalation routes; technical asulam is in USEPA Toxicity Category IV (the lowest of four categories) for these effects.

The RfD was calculated at 0.05 mg/kg/d (USEPA 1995). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.36 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for asulam is 2.52 mg/L (no acute one day value available).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 40 mg/kg bw from a two-year rat study. The NOEL is based on effects on the thyroid and adrenal medulla. The ADI incorporates a safety factor of 2,000.

EFSA (2013/2018) reports an ADI of 0.36 mg/kg/d and an ARfD of 1 mg/kg bw. Asulam and asulam‐sodium are considered equivalent and unlikely to be genotoxic. The new in vitro chromosome aberration test can be considered acceptable and showed negative results. The substance showed no carcinogenic potential in rats and mice. The toxicological profile of the metabolite sulfanilamide appears to be qualitatively similar to asulam. An ADI of 0.005 mg/kg/d was established for sulfanilamide, and an ArfD of 0.03 mg/kg; the experts agreed that reference values of sulfanilamide also apply to metabolites malonyl sulfanilamide, 4‐acetylbenzene sulfonamide, sulfanilic acid and acetyl sulfanilamide. No conclusion could be drawn regarding asulam dimer 1 and 2 since the precise structure is unknown.

Asulam is carcinogenic in rats based on thyroid and adrenal tumours in males. As at September 2008 the USEPA has classified asulam as a Group C carcinogen: a possible human carcinogen for which there is limited animal evidence.

### Derivation of Maximum Acceptable Value

No MAV.

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# Atrazine

CAS No. 1912-24-9. The IUPAC name for atrazine is 6-chloro-N2-ethyl-N4-isopropyl-1,3,5-triazine-2,4-diamine. Also called 6-chloro-N-ethyl-N’-isopropyl-1,3,5-triazine-2,4-diamine, 2-chloro-4-ethylamino-6-isopropylamino-1,3,5-triazine or 2-chloro-4-(ethylamino)-6-(isopropylamino)-s-triazine. The CAS name is 6-chloro-N-ethyl-N’-(1-methylethyl)-1,3,5-triazine-2,4-diamine.

The chloro-s-triazine metabolites:

* The CAS number for deethyl-atrazine (DEA) is 6190-65-4.
* The CAS number for deisopropyl-atrazine is 1007-28-9.
* The CAS number for diaminochlorotriazine (also called didealkylatrazine or DACT) is 3397-62-4.

The CAS No. for hydroxyatrazine is 2163-68-0.

### Maximum Acceptable Value

Based on WHO (2017), the concentration of atrazine and its chloro-s-triazine metabolites (deethyl-atrazine, deisopropyl-atrazine and diaminochlorotriazine) in drinking-water should not exceed 0.1 mg/L. In 2011/17 the WHO added a GV of 0.2 mg/L for hydroxyatrazine.

The MAV for atrazine in DWSNZ (2008) is 0.002 mg/L.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.003 mg/L. The maximum acceptable concentration for atrazine plus its N-dealkylated metabolites in Canada is 0.005 mg/L.

The 2004 version of the *Australian Drinking Water Guidelines* stated that atrazine should not be detected in drinking water; if present in drinking water, atrazine would not be a health concern unless the concentration exceeded 0.04 mg/L. If it is detected, then remedial action should be taken to stop contamination. The practical limit of determination is 0.0001 mg/L. The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline value is based on long-term effects.

The technical product is usually up to about 95 percent pure; common impurities include symmetric triazines, such as simazine and propazine.

### Sources to water

Atrazine, a broad spectrum triazine pesticide, may enter source waters as the result of its use as a pre- and post-emergence selective systemic herbicide for the control of annual grass and broad leaved weeds in various crops. It is also used in forestry and for non-selective weed control in non-crop areas. The highest concentrations due to run-off are generally found during the six weeks to two months after application and lower to undetectable concentrations during the rest of the year.

Atrazine has been reported in groundwater supplies at concentrations up to 0.002 mg/L in an area in Australia where atrazine was used over a 10-year period to suppress weed growth in irrigation channels (at application rates of 2–4 kg per hectare per year). Atrazine has residual activity of up to one year.

Due to its persistence in soil and its transport to surface and groundwater drinking water sources, it is the most commonly detected pesticide in surface water sources in the United States and it is frequently detected in groundwater sources.

Atrazine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 49 tonnes of atrazine were used in New Zealand in 2004, at an application rate of 6,300 grams of active ingredient per hectare. Atrazine is formulated with many other pesticides, some of which also contain ethylene glycol and formaldehyde.

The total annual usage of atrazine in New Zealand in the late 1980s was 73,200 kg, mainly in the North Island. The highest usage of 11,100 kg was mainly on forestry in Taupo county which has an area of 393,000 ha. Atrazine is no longer used in Europe.

### Forms and fate in the environment

Atrazine can be degraded in surface water by photolysis and micro-organisms via N‑dealkylation and hydrolysis of the chloro substituent, with a half-life of about 12 weeks at pH 5 and 20°C; breakdown is negligible in neutral or somewhat alkaline waters, with a half-life of two years or more.. Hydrolysis and microbial degradation also take place in the soil with half-lifes ranging from 18 to 120 days. The recommended average soil half-life is 60 days. Degradation rates normally decrease with increasing depth and atrazine can be reasonably stable in groundwater. Atrazine’s degradation products in soil include several of the chloro-s-triazine metabolites commonly found in water; unsubstituted amino metabolites and triazine are formed later and may be mineralised completely.

Atrazine was considered to be a Priority A chemical for potential groundwater contamination by the USEPA and was ranked highest of 83 pesticides in the Agriculture Canada priority scheme for potential groundwater contaminants (Health Canada 1993). Its GUS score is 4.10, indicating that it will leach to groundwater.

Atrazine and its chloro-s-triazine metabolites: deethyl-atrazine (DEA), deisopropyl-atrazine (DIA) and diaminochlorotriazine (DACT) have been found in surface water and groundwater. The metabolite hydroxyatrazine is more commonly detected in groundwater than in surface water (WHO 2010).

Atrazine and its dealkylated metabolites are moderately to very mobile in soils but the hydroxytriazine metabolites show low mobility and long persistence in soil.

Degradation half-lifes of atrazine in soil ranged from 12 to 213 days over a wide geographical range of forestry sites in Australia; degradation rates were primarily dependent upon soil temperature (FHMG 2000). See WHO (2003) for a list of degradation products and WHO (2010) on their health effects.

The water solubility of atrazine is about 30 mg/L and the sorption coefficient is 100 mL/g. Atrazine was found in 4,123 of 10,942 surface water samples in the USA and in 343 of 3,208 groundwater samples. It has been found in the Mississippi River up to 0.02 mg/L.

NPIC (1994) quotes for atrazine a soil half-life of 60 days, water solubility of 33 mg/L and a sorption coefficient (soil Koc) of 100. This resulted in a pesticide movement to groundwater rating of high.

Health Canada (1993) states that its vapour pressure is 3 × 10-7 mm Hg (0.4 × 10-7 kPa) at 20°C, and its volatility is low, with a Henry’s Law constant of less than 10‑7 atm·m3/mol. Its log octanol-water partition coefficient is reported as 2.75, and it appears not to bioaccumulate to any great degree in the food chain.

USGS (2006) give the following values for atrazine: log Kow = 2.75; log Koc (where Koc is in mL/g) = 2.00; water solubility = 30 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -3.54; half-life in aerobic soil = 146 days; half-life in water = 742 days.

USGS (2006) give the following values for deethylatrazine: log Kow = 1.3; log Koc (where Koc is in mL/g) = 1.90; water solubility = 2,700 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -4.12; half-life in aerobic soil = 170 days; half-life in water = NA days.

If released to soil, atrazine is expected to have high to slight mobility based upon a Koc range of 54 to 1,164. Volatilisation half-lifes of atrazine in soil range from 111 to >1,000 days. Biodegradation of atrazine in soil is affected by the moisture content of the soil. The half-life of atrazine at 25°C in wet (and dry) Colorado loam soil, New York sandy loam soil, and Mississippi silt loam was determined to be 30 (90), 28 (55), and 35 (78) days, respectively. Temperature and pH also affect the biodegradation of atrazine in soil. Microbial degradation of atrazine in silty loam and sand samples occurred in alkaline soil with the primary metabolites of desethyl atrazine and deisopropylatrazine while chemical degradation of atrazine yielded hydroxyatrazine; in addition, atrazine degraded 3–4 times faster in soils at 25°C than at 10°C. In soils, hydrolysis of atrazine is favoured by low soil pH, high organic matter content, low moisture content, high temperature, and high clay content. If released into water, atrazine may adsorb to suspended solids and sediment in water based on the Koc value range. Atrazine was degraded by 23 percent in raw seawater after 96 hours. However, atrazine was found to be recalcitrant in natural groundwater after a period of 96 days. The half-life of atrazine in an anaerobic wetland sediment was determined to be 224 days with no additional carbon present; the only metabolite present during degradation was hydroxyatrazine. Volatilisation from water surfaces is not expected to be an important fate process based on a Henry’s Law constant of 2.6 x 10-9 atm-cu. A BCF range of <0.27 to 100 in fish suggests bioconcentration in aquatic organisms is low to moderate. Hydrolysis of atrazine follows first-order kinetics, producing hydroxyatrazine as the major transformation product. Atrazine may hydrolyse fairly rapidly in either acidic or basic environments, yet is fairly resistant to hydrolysis at neutral pHs. The rate of hydrolysis was found to increase drastically upon small additions of humic materials, indicating atrazine hydrolysis could be catalysed in natural waters. Atrazine may undergo photolysis in sunlit surface waters (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Atrazine was not detected (approximately <0.003 mg/L) in all of 230 samples from 212 drinking-water supplies sampled in New Zealand between 1988 and 1992. However, it has been found in groundwater in the Gisborne area (Close 1993). The well was sampled three times with levels of 0.037 mg/L, less than detection and 0.0021 mg/L (2.1 µg/L) being measured. Atrazine has also been found at low levels in several wells in the South Canterbury area and the Canterbury Regional Council is investigating the source of this atrazine.

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of atrazine (limit of detection = 0.0001 mg/L) (ESR 2001).

Atrazine has been found in 45 groundwater samples, in many parts of the country, ranging from 0.00001 to 0.037 mg/L (MAF 2006). The degradation products, desethyl atrazine and desisopropyl atrazine were found frequently too, from 0.00001 to 0.00026 mg/L.

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and 1 fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Atrazine occurred at 0.05 to 0.9 µg/L, ie, up to 0.0009 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Atrazine occurred at 0.01 to 0.08 µg/L. DEA occurred at 0.01 to 0.15 µg/L. DIA occurred at 0.02 to 0.26 µg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Atrazine occurred at 0.011 to 0.058 µg/L. DEA occurred at 0.029 to 0.15 µg/L. DIA occurred at 0.17 µg/L.

Atrazine was found in three bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.000011 to 0.00094 mg/L. The bores were in the Gisborne, Manawatu and Canterbury regions. Atrazine was found in one groundwater sample in the 2014 four-yearly New Zealand groundwater survey, the concentration was 0.000017 mg/L (Humphries and Close 2015) and 0.00008 mg/L of DEA was found in one sample.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Atrazine occurred in three wells, from 0.016 to 0.042 µg/L. DEA (desethyl atrazine) occurred in one well, at 0.023 µg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Atrazine occurred in one well, at 0.017 µg/L. DEA occurred in one well, at 0.08 µg/L. DET occurred in two wells, at 0.1 to 0.71 µg/L.

661 water utilities in the US reported detecting atrazine in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0083 mg/L.

Three water utilities in the US reported detecting the metabolite desethylatrazine in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00037 mg/L.

### Removal methods

Conventional coagulation, sedimentation, filtration processes are ineffective in reducing atrazine concentration in water. Membrane filtration using ultrafiltration techniques does not remove atrazine, but nanofiltration is more successful. Removal of atrazine can be achieved by adsorption on to granular activated carbon (0.0001 mg/L should be achievable), and by ion exchange, bank filtration, ozone oxidation, and ultraviolet irradiation (see WHO 2010). Powdered activated carbon is less effective than granular carbon filters, requiring a dose of up to 50 mg/L. Ozone oxidation can be effective (Health Canada 1993).

### Recommended analytical techniques

#### Referee method

Liquid-Solid Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (EPA 52).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector (EPA 507).

### Health considerations

Most of the total daily intake of atrazine would be supplied from contaminated water. Extensive surveys of food have failed to find any residues, and intake from this source is therefore considered negligible. No air monitoring reports were found; atrazine is unlikely to be found in air, except immediately after application to crops, because of its low volatility (Health Canada 1993).

Atrazine appears to be absorbed readily from the gastrointestinal tract. Following ingestion by rats, atrazine is retained mainly in red blood cells, liver, spleen and kidney. Most of the same metabolites found in soil can be found in degradation products in rats, with 2-chloro-4,6-diamino-1,3,5-triazine being the major urinary component.

The chronic reference dose or cRfD is 0.018 mg/kg/d and the acute reference dose or aRfD for atrazine (USEPA 2006) is 0.1 mg/kg/d. The PADs are 0.0018 and 0.01 mg/kg/d respectively; the additional 10-fold safety factor accounts for potential pre- and post-natal toxicity and the completeness of the data with respect to exposure and toxicity to infants and children.. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.7 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.01 mg/kg/d for hydroxyatrazine. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for hydroxyatrazine is 0.07 mg/L (no acute one-day value available).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes for the metabolite DACT a RfD of 0.018 mg/kg/d, and an ARfD of 0.10 mg/kg/d.

JMPR (2007) and FAO/WHO (2007) stated that drinking-water may contain metabolites of atrazine as well as atrazine itself. The chloro-s-triazine metabolites DEA, DIA and DACT share the same mode of action as atrazine and have a similar toxicological profile and hence the meeting decided to establish a group ADI and ARfD. Hydroxyatrazine, the plant and soil degradate, was not included because its mode of action and toxicological profile are different to those of atrazine and its chloro-s-triazine metabolites. The meeting established a group ADI of 0–0.02 mg/kg bw based on the NOAEL for atrazine of 1.8 mg/kg bw per day identified on the basis of LH surge suppression and subsequent disruption of the oestrous cycle seen at 3.6 mg/kg bw per day in a six-month study in rats, and using a safety factor of 100. The meeting considered that this NOAEL is protective for the consequences of neuroendocrine and other adverse effects caused by prolonged exposure to atrazine and its chloro-striazine metabolites. The meeting established a group ARfD of 0.1 mg/kg bw based on the NOAEL for atrazine of 12.5 mg/kg bw per day identified on the basis of impaired suckling-induced prolactin secretion in dams and subsequent alterations in development of the central nervous system and prolactin regulation in male offspring in a special four-day study in rats, and using a safety factor of 100. For hydroxyatrazine, the meeting established an ADI of 0–0.04 mg/kg bw based on the NOAEL of 1.0 mg/kg bw per day identified on the basis of kidney toxicity (caused by low solubility in water resulting in crystal formation and a subsequent inflammatory response) at 7.8 mg/kg bw per day in a 24-month study in rats, and using safety factor of 25. The meeting concluded that it was not necessary to establish an ARfD for hydroxyatrazine in view of its low acute toxicity, the absence of relevant developmental toxicity that could be a consequence of acute exposure, and the absence of any other toxicological effects that would be likely to be elicited by a single dose.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw from a two-year dietary rat study. The NOEL is based on an increased incidence of mammary tumours in female rats at the next highest dose (2.8 mg/kg bw/day). The ADI incorporates a safety factor of 100, and was established in 1990. Subsequently, in 1994, the Advisory Committee on Pesticides and Health concluded that the rat mammary tumours were not relevant to human health. However, it was considered that the NOEL of 0.5 mg/kg bw/day continued to be an appropriately conservative endpoint on which to base the ADI, as the tumours were considered to reflect a hormonal interaction considered relevant to humans. An ARfD is not necessary.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for atrazine of:

* 0.01 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.003 mg/kg/day for intermediate-duration oral exposure (15–364 days).

An ADI of 0.005 mg/kg bw per day and an ARfD of 0.025 mg/kg bw, have been derived (EFSA 2015).

Atrazine is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

An epidemiological study in northern Italy reported an increased relative risk of ovarian neoplasia (tumour formation) among women exposed to triazine herbicides. An 80 percent formulation of atrazine did not cause skin sensitisation upon repeated application to humans.

The weight of evidence from a variety of genotoxicity assays indicates that atrazine is not genotoxic, although it appears on some lists of endocrine disrupting compounds. There is evidence that atrazine can induce mammary tumours by hormonal changes in rats. It is highly probable that the mechanism for this process is non-genotoxic. No significant increase in neoplasia was observed in mice.

The International Agency for Research on Cancer concluded in 1999 that there is sufficient evidence in experimental animals for the carcinogenicity of atrazine, but there is inadequate evidence in humans for the carcinogenicity of atrazine (Group 3: not classifiable as to its carcinogenicity to humans); whereas in IARC (1991) it was considered possibly carcinogenic to humans (Group 2B). As at September 2008 the USEPA describes atrazine as “not likely to be carcinogenic to humans”.

Desethyl atrazine (DEA) and desisopropyl atrazine (DIA) are chlorinated metabolites of atrazine and are well recognised in the toxicology literature. DEA and DIA were specifically tested in male and female rats, with significant results. Female rats demonstrated reduced maternal weight gain when exposed to 25 mg/kg-day over days 6 to 10 of gestation. Male rats had significantly reduced prostate weight and seminal vesicles after DEA and DIA exposure at 25 and 50 mg/kg-day (respectively) on postnatal days 23–53 (TOXNET 2004). Deisopropyl desethylatrazine, azoxystrobin acid, hydroxyatrazine and 6-hydroxy-N-isopropyl-1,3,5-triazin-2-ylamine (DEHA) have also been reported.

The toxicity profiles and mode of action of the chloro-s-triazine metabolites are similar to those of atrazine; the potency of these metabolites with regard to their neuroendocrine-disrupting properties appeared to be similar to that of the parent compound. The metabolite hydroxyatrazine does not have the same mode of action or toxicity profile as atrazine and its chloro-s-triazine metabolites. The main effect of hydroxyatrazine was kidney toxicity (owing to its low solubility in water, resulting in crystal formation and a subsequent inflammatory response), and there was no evidence that hydroxyatrazine has neuroendocrine-disrupting properties. There was no evidence of carcinogenicity, and hydroxyatrazine did not show genotoxicity in an adequate range of tests in vitro and in vivo (from WHO 2017).

USEPA (2015) presented their weight of evidence analysis of potential interaction with estrogen, androgen and thyroid pathways; conclusions on the Tier 1 Screening Assays for the List 1 Chemicals. EDSP Tier 2 testing with mammals, fish, amphibians, or birds is not recommended for atrazine at this time because it is not expected to impact current EPA-established regulatory endpoints for human health or ecological risk assessment.

### Derivation of Maximum Acceptable Value

A MAV for atrazine and its chloro-s-triazine metabolites based on the WHO (2017) Guideline Value could be derived as follows:

1.8 mg/kg body weight/day x 70 kg x 0.2 = 0.126 mg/L (rounded to 0.1 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 1.8 mg/kg body weight per day identified on the basis of luteinising hormone surge suppression and subsequent disruption of the estrous cycle seen at 3.6 mg/kg body weight per day in a six-month study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.2
* uncertainty factor = 100.

A MAV for hydroxyatrazine based on the WHO (2017) Guideline Value could be derived as follows:

1.0 mg/kg body weight/day x 70 kg x 0.2 = 0.28 mg/L (rounded to 0.3 mg/L)

2 L/day x 25

where:

* no-observable-adverse-effect level = 1.0 mg/kg body weight per day identified on the basis of kidney toxicity at 7.8 mg/kg body weight per day in a 24-month study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.2
* uncertainty factor = 25, based on kinetic considerations.

The MAV (up to and including DWSNZ 2008) for atrazine in drinking-water was derived as follows:

A tolerable daily intake approach has been used for the derivation of the MAV for atrazine in drinking-water.

0.5 mg/kg body weight/day x 70 kg x 0.1 = 0.00175 mg/L (rounded to 0.002 mg/L)

2 L/day x 1,000

where:

* no-observable-adverse-effect level = 0.5 mg/kg body weight per day based on a carcinogenicity study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1; the Australian Guidelines use a factor of 0.5, and derive a limit of 0.04 mg/L
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 to reflect potential neoplasia).

From available monitoring data, it appears that the major metabolites of atrazine (desethylatrazine, desisopropylatrazine, diaminochlorotriazine, hydroxyatrazine) may constitute approximately 50 percent of the total atrazine-derived triazine compounds in some ground and surface water samples (Lerch et al 1998). This has been taken into account in deriving the guideline value.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for atrazine is 0.003 mg/L.

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# Azaconazole

CAS No. 60207-31-0. The IUPAC name for azaconazole is 1-{[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-yl]methyl}-1H-1,2,4-triazole. The CAS name is 1-[[2-(2,4-dichlorophenyl)-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole.

### Maximum Acceptable Value

Azaconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Azaconazole is conazole (triazole) fungicide, used against wood-rotting fungi, sapstain fungi and moulds. It is also used on fruit trees and tomatoes, and as a wound dressing on pruning cuts. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Azaconazole is sometimes sold mixed with other pesticides, such as imazalil (see datasheet).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Stable to aqueous hydrolysis and photolysis.

Water solubility is about 300 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Azaconazole was found to be non-carcinogenic in male and female mice but the doses may not have been sufficient to assess the carcinogenic potential. Azaconazole was found to be non-carcinogenic in Wistar rats. The USEPA considers most other conazoles to be Class B2 (probable human carcinogen) or Class C (possible human carcinogen).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.025 mg/kg body weight, with a NOEL of 2.5 mg/kg bw.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L. See datasheet for triazole metabolites for latest ADI and ARfD.

### Derivation of Maximum Acceptable Value

No MAV.

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# Azinphos methyl

CAS No. 86-50-0. Also called S-(3,4-dihydro-4-oxobenzo(d)(1,2,3-triazin-3-ylmethyl)O,O-dimethyl phosphorodithioate. IUPAC name is S-3,4-dihydro-4-oxo-1,2,3-benzotriazin-3-ylmethyl O,O-dimethyl phosphorodithioate. CAS name is O,O-dimethyl S-[(4-oxo-1,2,3-benzotriazin-3(4H)-yl)methyl] phosphorodithioate. Sometimes spelt azinfos-methyl. Often referred to by its main trade name: guthion.

Also sold as the ethyl product, azinphos-ethyl, CAS No. 2642-71-9.

### Maximum Acceptable Value (Provisional)

Based on health considerations, the concentration of azinphos methyl in drinking-water should not exceed 0.004 mg/L (4 μg/L). WHO (2004 and 2011) did not develop a guideline value.

The maximum acceptable concentration in Canada for azinphos methyl is 0.02 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.03 mg/L; excursions above this level even for a limited period are of concern, as the health-based guideline is based on short-term effects.

### Sources to water

Azinphos methyl is used as a broad spectrum, non-systemic organophosphorus triazine (or benzotriazine organothiophosphate insecticide) insecticide and acaricide (ticks) and is available as a wettable powder or suspension concentrate.

Azinphos methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](https://eatsafe.nzfsa.govt.nz/web/public/acvm-register%20and%20select%20entire%20register)). ERMA announced in 2009 that Cotnion would be allowed to be used on potato, stone fruit and strawberry only for the next five years. Azinphos methyl is applied aerially and by ground methods. As at 2011, ERMA is assessing whether this pesticide should continue to be approved for use in New Zealand. On 16 November 2006, the USEPA issued its final decision on azinphos-methyl to phase out the remaining uses by 30 September 2012 (USEPA 2009). All uses in Canada were phased out in 2012. Azinphos methyl not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2018.

In New Zealand, azinphos methyl is applied to grapes, kiwifruit, pipfruit, stonefruit and potatoes for the control of leaf-rollers, greedy scales, codling moths, bronze beetles, cherry sawflies, grass grub beetles, oriental fruit moths and potato tuber moths. Formulations containing azinphos methyl have been registered for use in New Zealand since 1965. Cotnion 200 Insecticide is the only azinphos product that is currently (2009) registered for agricultural use in New Zealand.

No information is available on the annual usage of specific active ingredients in New Zealand, although azinphos methyl is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Azinphos methyl is moderately soluble in water: about 30 mg/L at room temperature (Health Canada 1989/1996); azinphos-ethyl about 5 mg/L. Because it is hydrolysed easily, azinphos methyl is not considered a significant leacher (USEPA 1985, cited in Health Canada 1989–96). The half-life of azinphos methyl in laboratory and natural water systems was found to be 30–70 days at pH 5.1 to 8.4 (Weiss and Gakstatter 1977, cited in Health Canada 1989/1996). See also USEPA (2006).

Guthion does not evaporate very quickly from soil and water. It attaches strongly to soil surfaces and does not easily move into groundwater below the soil surface. Based on its low mobility in soil, guthion is expected to adsorb to suspended solids and sediment in the water column. Guthion applied at a nominal application rate of 20 μg/L to the surface of a 2 ha pond was not detected in sediment samples three hours post-application; however, guthion levels in sediment gradually increased to a maximum concentration of 62.7 μg/kg four days post-application. The levels gradually decreased to 11.9 μg/kg eight days post-application and then continued to decrease at a near constant rate to 2.05 μg/kg 50 days post-application. Sediment samples collected at days 92, 120, and 366 had no measurable levels of guthion (detection limits 0.20 μg/kg). Accounting for the total mass balance in the pond, the authors concluded that both the aqueous phase and the sediment compartment are important environmental sinks for guthion applied to the water surface. The half-life in river water is about 40 days (from ATSDR 2008, which also discusses breakdown products).

NPIC (1994) quotes for azinphos methyl a soil half-life of 10 days, water solubility of 29 mg/L and a sorption coefficient (soil Koc) of 1,000;. this resulted in a pesticide movement to groundwater rating of low. Health Canada (1989) quotes a log octanol-water partition coefficient of 2.69 and a vapour pressure higher than 5.1 x 10-2 Pa at 20°C.

There is no information available regarding the greatest source of exposure to azinphos methyl for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included azinphos methyl, so typical concentrations in New Zealand drinking-waters are unknown. No information is available about concentrations of azinphos methyl in groundwaters or surface waters.

Azinphos methyl was not found in a survey of drinking-water samples from four Canadian provinces (detection limits ranged from 0.002 to 1 μg/L).

### Removal methods

Specific information about the removal of azinphos methyl from water is unavailable. However, oxidation of triazines (azinphos methyl is a member of this chemical family) by ozone is reported to be effective (Chiron et al 2000). The water chemistry, in particular the alkalinity and pH, will affect the oxidation rate. Use of activated carbon following ozonisation should be considered to adsorb oxidation products.

Nanofiltration (membrane technology) in water with a low natural organic matter concentration is reported to remove approximately 50 percent of atrazine and simazine (Agbekodo et al 1996). The percentage is increased to 90–100 percent when 3.6 mg/L of natural organic matter is present. Similar results may be expected for azinphos methyl as it is from the same chemical family.

Adsorption on to activated carbon is expected to achieve some removal of azinphos methyl, although a guide to the efficiency of the process cannot be provided.

Treatment processes that remove particulate matter should reduce the concentration in water.

### Recommended analytical techniques

#### Referee method

Liquid/liquid extraction/gas chromatography-electron capture detector (EPA 8141A).

#### Some alternative methods

None recommended.

### Health considerations

Orally administered azinphos methyl has a biological half-life of eight to nine hours with 90 percent of the dose being eliminated within 48 hours in the urine or faeces.

Exposure can be from dietary risk, worker risk and drinking-water risk. With regards to drinking-water, acute risk is of most concern and chronic exposure does not appear to be of concern. However, surface and groundwater monitoring studies are needed to refine current models and monitoring estimates (USEPA 1999).

Azinphos methyl is absorbed from the gastrointestinal tract.

#### Acute poisoning

Potential symptoms of overexposure to azinphos methyl are miosis, aching eyes, blurred vision, lacrimation (weeping) and rhinorrhea (nasal discharge), headache, chest tightness, wheezing, laryngeal spasms, salivation, cyanosis (bluish cast to skin), anorexia, nausea, vomiting and diarrhoea, sweating, twitching, paralysis and convulsions, low blood pressure, cardiac irregularities (Merck & Co 1996).

The acute oral LD50 for male guinea pigs is 80 mg/kg (RSocC 1987) which suggests a relatively high oral toxicity compared with other pesticides.

USEPA (2006) states: Acute (1-day) dietary risk was estimated using an acute RfD of 0.003 mg/kg/day, based on a LOAEL of 1 mg/kg/day from an acute neurotoxicity study in rats. This LOAEL was selected based on inhibition of plasma, red blood cell, and brain cholinesterase observed following a single dose. No NOAEL was observed in this study. Consequently, an additional safety factor of 3x was applied in addition to the existing uncertainty factors for inter-species extrapolation (10x) and intra-species variability (10x), resulting in a total uncertainty factor of 300x for the acute dietary risk assessment. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.003 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for azinphos-methyl is 0.03 mg/L.

The ARfD adopted in Australia is 0.075 mg/kg body weight for azinphos methyl.

#### Chronic exposure

Azinphos methyl is an organophosphate pesticide. It has been determined that the organophosphates share a common mechanism of toxicity, the inhibition of cholinesterase levels (WHO 1985).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.025 mg/kg body weight for azinphos methyl, and 0.002 for azinphos ethyl, with a NOEL of 0.25 mg/kg bw for azinphos methyl, and 0.02 for azinphos ethyl. The NOEL for azinphos methyl was based on a short-term (28-day) oral study in humans. The NOEL is based on the absence of cholinesterase inhibition at this dose, which was the only dose tested. The ADI incorporates a safety factor of 10. The acute reference dose (ARfD) of 0.075 mg/kg bw for azinphos methyl was established in 2002, based on the absence of cholinesterase inhibition and clinical signs of toxicity at the highest dose tested of 0.75 mg/kg bw/day in a single oral dosing study in humans. The ARfD incorporates a safety factor of 10.

USEPA (2006) states: Chronic dietary risk was estimated using a chronic RfD of 0.0015 mg/kg/day, based on a NOAEL of 0.149 mg/kg/day established in a one-year chronic toxicity study in dogs. The LOAEL in this study was 0.688 mg/kg/day for males and 0.775 mg/kg/day for females, based on the above noted significant decreases in red blood cell cholinesterase activity in both sexes as well as an increased incidence of diarrhoea in males. A total uncertainty factor 100x was used for the chronic dietary risk assessment to account for inter-species extrapolation (10x) and intra-species variability (10x). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0015 mg/kg/d.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for guthion of:

* 0.01 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.003 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.003 mg/kg/day for chronic-duration oral exposure (>364 days).

JMPR (2007) established an ADI of 0–0.03 mg/kg bw per day based on a NOAEL of 0.29 mg/kg bw per day for the absence of inhibition of erythrocyte acetylcholinesterase activity in a 30-day study of toxicity in male volunteers and a safety factor of 10. The meeting established an ARfD of 0.1 mg/kg bw based on the NOAEL of 1 mg/kg bw and using a safety factor of 10 (FAO/WHO 2007).

There is a data gap for studies of the effect of azinphos methyl on metabolism, teratology, reproduction and mutagenicity.

The International Agency for Research on Cancer (IARC) has not classified azinphos methyl for its ability to cause cancer. As at September 2008 the USEPA describes azinphos methyl as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for azinphos methyl in drinking-water, as follows:

0.125 mg/kg body weight per day x 70 kg x 0.1 = 0.00438 mg/L (rounded to 0.004 mg/L)

2 L x 100

where:

* no observable adverse effect level = 0.125 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Azocyclotin

CAS No. 41083-11-8. The IUPAC name for azocyclotin is tri(cyclohexyl)-1H-1,2,4-triazol-1-yltin. The CAS name is 1-(tricyclohexylstannyl)-1H-1,2,4-triazole.

This datasheet also contains some information about a related product, cyhexatin: CAS No. 13121-70-5. Its IUPAC name is tricyclohexyltin hydroxide, and the CAS name is tricyclohexylhydroxystannane.

### Maximum Acceptable Value

Azocyclotin and cyhexatin do not have MAV in the DWSNZ, and are not mentioned in the WHO Guidelines.

### Sources to water

Azocyclotin is an organotin contact acaricide effective against phytophagous mites.

Azocyclotin does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it does appear in ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (as amended), as at 22 May 2008. Azocyclotin has been reported to have been used to control mites on orchids in Northland. Cyhexatin appears on neither list.

### Forms and fate in the environment

Azocyclotin aqueous buffer solutions were incubated for 10, 30, and 60 minutes under sterile conditions and an azocyclotin drinking water solution for 10 minutes in the dark at 20°C. Under the experimental conditions, azocyclotin was completely hydrolysed within 10 minutes. Two hydrolysis products were observed: tricyclohexyltin hydroxide (cyhexatin) and 1,2,4-triazole.

The metabolites of cyhexatin are dicyclohexyltin oxide, and monocyclohexyl stannoic acid (cyclohexyl stannoic acid).

Water solubility of azocyclotin is about 0.1 mg/L. Water solubility of cyhexatin is about 0.7 mg/L at pH 4, and <0.04 mg/L at pH 7 and higher.

NPIC (1994) quotes for cyhexatin a soil half-life of 50 days, water solubility of <1 mg/L and a sorption coefficient (soil Koc) of 4000. This resulted in a pesticide movement to groundwater rating of very low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See FAO (2005).

### Health considerations

The 2005 JMPR established a group ADI of 0 to 0.003 mg/kg bw for cyhexatin and azocyclotin based on the NOAEL of 0.34 mg/kg bw per day for retinal atrophy in a long-term study of toxicity/carcinogenicity with cyhexatin in rats and using a safety factor of 100. The meeting concluded that these uses of cyhexatin and/or that of azocyclotin resulting in long-term intake of residues of cyhexatin, as considered by the JMPR, are unlikely to present a public health concern. The 2005 JMPR established a group ARfD of 0.02 mg/kg bw for women of childbearing age for cyhexatin and azocyclotin. An ARfD for the rest of the population was considered unnecessary.

JMPR concluded that azocyclotin is unlikely to be genotoxic.

The Acceptable Daily Intake (ADI) adopted in Australia for azocyclotin is 0.003 mg/kg body weight, with a NOEL of 0.25 mg/kg; and 0.001 and 0.1 respectively for cyhexatin.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0025 mg/kg/d for cyhexatin, and an ARfD of 0.0067 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cyhexatin is 0.067 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

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# Azoxystrobin

CAS No. [131860-33-8](http://www.commonchemistry.org/ChemicalDetail.aspx?ref=131860-33-8). Its chemical name is methyl(E)-2-{2-[6-(2-yanophenoxy)pyrimidin-4-yloxy]phenyl}-3-methoxyacrylate.

### Maximum Acceptable Value

Azoxystrobin is not mentioned in the DWSNZ or the WHO Guidelines.

### Sources to water

Azoxystrobin, a methoxyacrylate compound, is one of the first of a new class of fungicides, the strobilurins (based on naturally occurring antifungal compounds in certain wood-decaying mushrooms), to be commercialised. It is now one of the leading proprietary fungicides in the world (mainly at the expense of triazole fungicides), but there are already serious resistance concerns. Azoxystrobin was first marketed in 1998 and is a systemic, broad-spectrum fungicide with activity against the four major groups of plant pathogenic fungi including Ascomcetes (eg, powdery mildews), Basidiomycetes (eg, rusts), Deutoromycetes (eg, rice blast) and Oomycetes (eg, downy mildew). It inhibits spore germination and mycelial growth. It has worldwide uses on cereals, vines, rice, citrus, potatoes and tomatoes.

Azoxystrobin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Azoxystrobin has been found above the maximum residue limit in olive oil (NZFSA).

### Forms and fate in the environment

Azoxystrobin is labelled as dangerous to fish and other aquatic life on the basis of toxicity of the product to algae. In addition, azoxystrobin partitioned into the sediment where it persisted with a half-life of greater than 100 days. Some degradation products had the potential to leach into groundwater under some conditions, and a ‘groundwater advisory’ was placed on the label. Volatilisation from the water surface is not expected to be an important fate process based on the estimated Henry’s Law constant.

EC (1998) reports very slow degradation rates, with residues being found after a year. See JMPR (2009) and EFSA (2013) for a list of metabolites.

JMPR quotes a soil mean half-life of 279 days, with 24–42 percent azoxystrobin remaining after 360 days. There was no significant degradation of azoxystrobin in the sterile treatment, which suggests that the aerobic degradation observed in the other treatments was due to microbial activity. Under anaerobic conditions, degradation of azoxystrobin was more rapid with a mean half-life of 181 days and 25–33 percent remaining after 360 days. At 25°C, there was no significant hydrolysis (<10 percent) at any pH.

If released to soil, azoxystrobin is expected to have moderate to low mobility based upon Log Koc values of 2.3 to 2.8. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant.

EFSA (2013) states that DT50 values of azoxystrobin range around 262 days.

Water solubility is about 6–10 mg/L.

### Removal methods

GAC is likely to be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Azoxystrobin is classified by the World Health Organization as ‘slightly hazardous’ (Class III). The USEPA review concludes azoxystrobin is ‘unlikely to be a carcinogen’ and is of low acute and chronic toxicity to humans, birds, mammals, and bees. Azoxystrobin was not teratogenic or mutagenic.

The lowest relevant NOAEL for short-term toxicity is reported by EC (1998) to be 10 mg/kg/d in a 90 day gavage test on dogs. An ADI of 0.1 mg/kg/d was reported.

The 2008/2012 JMPR meeting established an ADI of 0–0.2 mg/kg bw based on a NOAEL of 18.2 mg/kg bw per day in a two-year study of carcinogenicity in rats, identified on the basis of reduced body weights, food consumption and food efficiency, and bile-duct lesions seen at 34 mg/kg bw per day and above, and using a safety factor of 100. The meeting concluded that it was unnecessary to establish an ARfD for azoxystrobin because no toxicity could be attributable to a single exposure in the available database, including a study of developmental toxicity in rats and rabbits and a study of acute neurotoxicity in rats. FAO/WHO/JMPR (2013/2017) quote the same AfD/ARfD.

Due to the low acute toxicity of the active substance the setting of an ARfD was considered not necessary. The data were sufficient to derive an ADI value of 0.2 mg/kg bw/day (EFSA 2011 and 2013).

The No Observed Effect Level (NOEL/NOAEL) for azoxystrobin in the rat is 18 mg/kg bwt/day. The Reference Dose (RfD) for azoxystrobin should be based upon the NOAEL of 18 mg/kg bwt/day with an uncertainty factor of 100; RfD = 0.18 mg/kg bwt/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.18 mg/kg/d, and an ARfD of 0.67 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for azoxystrobin is 6.7 mg/L.

An ADI is quoted by NZFSA of 0.03 mg/kg. The Acceptable Daily Intake (ADI) adopted in Australia for azoxystrobin is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

### Derivation of Maximum Acceptable Value

No MAV.

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# Benalaxyl

CAS No. 71626-11-4. The IUPAC name for benalaxyl is methyl N-(phenylacetyl)-N-(2,6-xylyl)-DL-alaninate. The CAS name is methyl N-(2,6-dimethylphenyl)-N-(phenylacetyl)-DL-alaninate. The (−)-isomer of this substance has the ISO common name [benalaxyl-M.](http://www.alanwood.net/pesticides/benalaxyl-m.html)

### Maximum Acceptable Value

Benalaxyl does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Benalaxyl is a broad spectrum acylamino acid, acylalanine, or phenylamide anilide fungicide, commonly used for control of oomycetes, or water moulds, in grapes, potatoes and several vegetable crops. It is often used in conjunction with mancozeb.

Benalaxyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Benalaxyl should not contain more than 1 g/kg of 2,6-dimethylaniline.

### Forms and fate in the environment

The half-life of benalaxyl in aerobic soils is reported to range from 20 to 100 days. Anaerobic degradation followed the same pattern as observed under aerobic conditions although much slower. Benalaxyl, slightly mobile to immobile), is not expected to leach through or from soils. See JMPR (2009) for discussion on metabolites.

EFSA (2013) states: With regard to the groundwater metabolites (B-M1, racemate of BM-M7; B-M2, racemate of BM-M3; B-F7 (including R-isomer); R-isomer of B-F4; B-F8, racemate of BM-M2), considering the available toxicity data and taking into account the toxicological profile of benalaxyl-M, none of them is considered toxicologically relevant and the reference values of benalaxyl-M are considered applicable to them as well.

It was demonstrated in several degradation studies that benalaxyl is persistent in soil and that DT90 values exceed the trigger value of 100 days (DT90f ranges from 67 to 326 days) (EFSA 2013a).

Benalaxyl is fairly stable in water, tending to accumulate in the sediments. Water solubility is about 30 mg/L.

NPIC (1994) quotes for benalaxyl a soil half-life of 30 days, water solubility of 37 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2013), LOQ of 0.05 μg/L.

### Health considerations

IPCS (1987) stated that comprehensive short- and long-term dietary administration indicates that the toxicity of benalaxyl is low. The meeting concluded that although the hepatic enlargement observed in rodents was of questionable toxicological significance, it could be used to establish a no-effect level and to estimate an ADI: estimate of acceptable daily intake for man = 0.05 mg/kg bw.

The EC (2004) stated that benalaxyl shows no genotoxic or carcinogenic potential; they derived an ADI of 0.04 mg/kg bw based on a two-year rat study and an uncertainty factor of 100, and they considered that an acute reference dose (ARfD) was not needed. Reaffirmed by EFSA (2013) and EC (2013).

The 2005 and 2009 JMPR meeting established an ADI of 0–0.07 mg/kg bw based on a NOAEL of 6.5 mg/kg bw per day for atrophy of the seminiferous tubules occurring at 25 mg/kg bw per day in a one-year study in dogs and using a safety factor of 100. Benalaxyl has little acute toxicity and short-term dosing produced no significant general toxicity; however, a delay in ossification of cranial bones was observed at a dose of 50 mg/kg bw per day in the absence of maternal toxicity and of other markers of developmental delay in a study of developmental toxicity in rats. Although statistically significant, this is a marginal effect, but in the absence of data on historical controls, it was considered to be treatment-related. The meetings established a conservative ARfD of 0.1 mg/kg bw for benalaxyl for women of childbearing age on the basis of a NOAEL of 12.5 mg/kg bw per day in a study of developmental toxicity in rats, and a safety factor of 100. There is no concern regarding the acute toxicity of this compound for the rest of the population, including children.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight for benalaxyl, with a NOEL of 5 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

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# Bendiocarb

CAS No. 22781-23-3. IUPAC and CAS name for bendiocarb is 2,2-dimethyl-1,3-benzodioxol-4-yl methylcarbamate. Also called 2,3-isopropylidenedioxyphenyl methylcarbamate.

### Maximum Acceptable Value

Bendiocarb does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Bendiocarb is a broad spectrum carbamate insecticide, a fast acting anti-cholinesterase agent. All bendiocarb-containing products in the [US](http://en.wikipedia.org/wiki/United_States) were cancelled after its manufacturers voluntarily chose to pull their products off the market (due to its acute toxicity), rather than conduct additional safety studies required by the USEPA. In other countries, it is still used in homes, industrial plants, and food storage sites to control [mosquitoes](http://en.wikipedia.org/wiki/Mosquitoe), [flies](http://en.wikipedia.org/wiki/Fly), [wasps](http://en.wikipedia.org/wiki/Wasp), [ants](http://en.wikipedia.org/wiki/Ant), [fleas](http://en.wikipedia.org/wiki/Flea), [cockroaches](http://en.wikipedia.org/wiki/Cockroach), [silverfish](http://en.wikipedia.org/wiki/Silverfish), and [ticks](http://en.wikipedia.org/wiki/Tick) but can be used against a wide variety of insects as well as snails and slugs. It is one of 12 insecticides recommended by the [World Health Organization](http://en.wikipedia.org/wiki/World_Health_Organization) for use in [malaria](http://en.wikipedia.org/wiki/Malaria) control.

Bendiocarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Bendiocarb was first registered in the United States in 1980. Its registration was voluntarily cancelled in September 1999, and all products containing bendiocarb lost registration in December 2001 (NPIC).

### Forms and fate in the environment

Laboratory studies indicate a high degree of mobility; however, field studies indicate that parent bendiocarb generally degrades before leaching through the soil and the major degradate, if detected, is present at low concentrations and remains in upper soil layers. Although parent bendiocarb is sufficiently mobile, screening models indicate that it is not likely to move through the soil to groundwater.

Bendiocarb is degraded in soil to 2,2-dimethyl-1,3-benzodioxol-4-ol, a phenol that is much less likely to leach.

The half-life of bendiocarb in the soil depends on soil composition and pH, ranging from 3 to 21 days, with an average soil half-life of five days.

Water solubility is about 30–40 mg/L. The half-life varies in water with the pH conditions, in more acidic waters the half-time is longer, pH 5 half-life is 48 days, compared with 81 hours in water with pH 7.

NPIC (1994) quotes for bendiocarb a soil half-life of five days, water solubility of 40 mg/L and a sorption coefficient (soil Koc) of 570. This resulted in a pesticide movement to groundwater rating of very low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Subchronic and chronic toxicity studies demonstrate that bendiocarb inhibits cholinesterease activity in whole blood, plasma, and brain in rats, mice and dogs.

Bendiocarb is classified by the USEPA as a Group E chemical, showing no evidence of carcinogenicity in laboratory animals or in humans.

For the chronic dietary risk assessment, the endpoint selected was whole blood cholinesterase inhibition at the LOAEL of 0.25 mg/kg/day in a special 14-day oral toxicity study in rats; the NOAEL in this study was 0.125 mg/kg/day. Thus the reference dose (RfD) for the chronic dietary assessment is 0.00125 mg/kg/day (USEPA 1999).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.004 mg/kg body weight for bendiocarb, with a NOEL of 0.4 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

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# Benomyl and carbendazim

CAS No. 17804-35-2 (benomyl). IUPAC name is methyl 1-(butylcarbamoyl)benzimidazol-2-ylcarbamate. CAS name is methyl [1-[(butylamino)carbonyl]-1H-benzimidazol-2-yl]carbamate.

CAS No. 10605-21-7 (carbendazim). IUPAC name is methyl benzimidazol-2-ylcarbamate (MBC). CAS name methyl 1H-benzimidazol-2-ylcarbamate.

### Maximum Acceptable Value

Benomyl is not mentioned in the DWSNZ or the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.09 mg/L, and 0.09 mg/L for carbendazim; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects. Products containing benomyl were withdrawn in Australia due to health concerns in December 2006.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for carbendazim in water (set by an approval under Part 5 of the HSNO Act) of 0.00011 mg/L (0.11 µg/L).

### Sources to water

Benomyl degrades to carbendazim. Benomyl and carbendazim are closely related systemic, broad spectrum, systemic fungicides of the methyl benzimidazole carbamate family. Benomyl is used to control smut diseases in onions, maize and wheat seeds in New Zealand. Carbendazim is used to control specific diseases in a range of fruits, vegetables, cereals, ornamentals and the causal organism of facial eczema in New Zealand. There are also a number of substances containing carbendazim used as timber antisapstains that have been approved under HSNO.

Formulations containing benomyl have been registered for use in New Zealand since 1991 and formulations containing carbendazim from 1973. Benomyl appeared on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register); however, it is not listed in 2013 (but carbendazim is). ERMA notes that 6.4 tonnes of carbendazim were used in New Zealand in 2004, at an application rate of 1,500 grams of active ingredient per hectare. Benomyl/carbendazim should not contain more than 0.5 mg/kg of 3-hydroxy-2-aminophenazine or 2,3‑diaminophenazine. One commercial product was called benlate.

Carbendazim was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in bok choi and ginger.

All benomyl registrations were voluntarily cancelled by registrants, effective in January 2002. Carbendazim is not approved in the US. There are currently no products containing benomyl registered for use in Australia. Dustable powder formulations containing a combination of benomyl at or above 7 percent, carbofuran at or above 10 percent, thiram at or above 15 percent appear on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>. Since 2014 benomyl is no longer able to be manufactured in or imported into New Zealand.

### Forms and fate in the environment

Benomyl is not readily degradable. It binds strongly to soil and does not dissolve in water to any great extent. When applied to turf or soil, it is rapidly converted to its major metabolite, carbendazim, which is more persistent giving an overall half-life of up to 12 months. See datasheet for thiophanate-methyl for more information. The strong adsorption of carbendazim on soil and sediment particles reduces its exposure to terrestrial and aquatic organisms, and limits run-off and leaching.

Benomyl is degraded both by hydrolysis and elimination in aqueous solution, with faster degradation under alkaline conditions. The half-lifes of benomyl in pH 5, 7 and 9 buffered solutions were approximately 3.5 hours, 1.5 hours and <1 hour, respectively. Benomyl is mainly hydrolysed to carbendazim at pH 5, while at pH 9 3-butyl-1,3,5-triazino[1,2a]benzimidazole-2,4(1H,3H)-dione (STB) is the main transformation product (JMPR 1998).

Water solubility of benomyl is less than 3 mg/L. PMEP quotes 3.8 mg/L (pure compound) in 1989 *Chemical Profile*. Water solubility of carbendazim is about 8 mg/L at pH 7 and 25°C.

If released to soil, benomyl is expected to have slight mobility based upon a Koc of 2,000. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 4.93 x 10-12 atm-cu m/mole. Benomyl is not expected to volatilise from dry soils based upon its vapour pressure. Biodegradation is not expected to be a major environmental fate process since benomyl hydrolyses rapidly to methyl 2-benzimidazole carbamate (carbendazim; MBC) and butyl isocyanate in moist soil and water. The half-life of benomyl is 2 and 19 hours in water and soil, respectively. If released into water, benomyl is expected to adsorb to suspended solids and sediment based upon the Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. An estimated BCF of 9 suggests potential for bioconcentration in aquatic organisms is low (EAWAG accessed February 2015).

If released to soil, carbendazim is expected to have moderate mobility in soil based upon an experimental Koc value of 350. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 2.1 x 10-11 atm-cu m/mole. Carbendazim is not expected to volatilise from dry soil surfaces based upon its vapour pressure. Carbendazim is expected to biodegrade slowly under normal conditions; however, degradation will be enhanced in pretreated soils. If released into water, carbendazim is expected to adsorb very little to suspended solids and sediment based on the experimental Koc value. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. Experimental BCF values ranging from 0.6 to 3.5 suggests bioconcentration in aquatic organisms is low. Measured hydrolysis half-lifes for carbendazim at 22°C were greater than 35 days at pH 5-7 and 124 days at pH 9 (EAWAG accessed February 2015).

NPIC (1994) quotes for benomyl a soil half-life of 67 days, water solubility of 2 mg/L and a sorption coefficient (soil Koc) of 1,900. This resulted in a pesticide movement to groundwater rating of low.

NPIC (1994) quotes for carbendazim a soil half-life of 120 days, water solubility of 8 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

Binding strongly to soil reduces its bioavailability to terrestrial and aquatic organisms, as well as its ability to leach into groundwater.

### Removal methods

Treatment processes that remove particulate matter, and activated carbon, should reduce the concentration of benomyl and carbendazim in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The World Health Organization has set an Acceptable Daily Intake (ADI) value for benomyl and carbendazim of 0.1 and 0.01 mg/kg body weight respectively.

The oral RfD for benomyl was calculated at 0.05 mg/kg/d (USEPA 1989). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.17 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for benomyl is 1.70 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight for benomyl, and 0.03 for carbendazim. The NOEL for benomyl and for carbendazim is 2.5 mg/kg bw from a two-year dog study. The NOEL is based on an increase in testicular degeneration. The ADI incorporates a safety factor of 100. The ARfD for benomyl/carbendazim is 0.06 mg/kg bw, and 0.05 mg/kg bw for carbendazim based on a NOEL of 6.25mg/kg bw/day from three developmental studies, which showed an increase in micro-/anophthalmia. The ARfD incorporates a safety factor of 100.

As at September 2008 the USEPA has classified benomyl and carbendazim in Group C: possible human carcinogens. Benomyl appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

JMPR (2005) states that the residues of benomyl, carbendazim and thiophanate-methyl are all expressed as carbendazim, which has the lowest ADI (0–0.03 mg/kg bw/day).

Carbendazim residues have been found in New Zealand ginger at greater than the maximum residue limit (MRL): refer NZFSA: <http://www.nzfsa.govt.nz/>.

### Derivation of Maximum Acceptable Value

No MAV.

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# Bentazone

CAS No. 25057-89-0. The IUPAC name for bentazone is 3-isopropyl-(1H)-2,1,3-benzothiadiazin-4(3H)-one 2,2-dioxide. Sometimes called bendioxide and sometimes spelt bentazon. Also called 3-(1-methylethyl)-1H-2,1,3-benzothiadiazin-4(3H)-one-2,2-dioxide (CAS name). A trade name is basagran.

### Maximum Acceptable Value

WHO (2004/2011/2017) states that because bentazone occurs in drinking-water at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a health-based guideline value.

WHO (2017) includes a health-based value of 0.5 mg/L, and adds that an acute health-based value is unnecessary because no ARfD has been established.

In the DWSNZ (2005), the provisional MAV for bentazone in drinking-water had been 0.35 mg/L.

Technical bentazone is 92–96 percent pure. Its main impurities are N‑isopropylsulfamoyl anthranilic acid (reactant; 2.4 percent), sodium chloride (raw material; 1.0 percent) and anthranilic acid (reactant; 0.6 percent). Some 50 other compounds have been found as impurities at very low concentrations.

The USEPA (2006/2009/2011) established a lifetime health advisory for bentazon of 0.2 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Bentazone, a benzimidazole or benzothiadiazole compound, may enter source waters as a result of its application as a contact herbicide, used on winter and spring cereals for selective post-emergence control of many broadleaf weeds. It is absorbed at the leaves.

The total annual usage of bentazone in New Zealand in the late 1980s was 8,670 kg with the highest use being 4000 kg in Ashburton county. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The technical product is about 93–96 percent pure. The main impurities are anthranilic acid, and N-isopropylsulfamoyl anthranilic acid. The BASF product may contain 1,2‑dichloroethane (which is considered a relevant impurity) at a maximum content of 3 mg/kg (EFSA 2015).

### Forms and fate in the environment

Bentazone is mobile in a range of soil types and has been found in both surface and groundwaters overseas. The mechanism for degradation in soil is not known (photolysis may be the major process) but the metabolite, 2-amino-N-isopropyl benzamide has been found. Half-lifes under optimal conditions range from 1.5 to 15 weeks depending on soil type. At temperatures below 10°C half-lifes are greater than 20 weeks. The recommended average soil half-life is three weeks.

It has a low octanol-water partition coefficient so is very molile in soil. Bentazone will be expected to pass both through the soil profile and via cracks to the underlying aquifer. Once outside the zone of biological action, there is no abiotic mechanism for its degradation. Some contamination of the groundwater would be expected to occur under these circumstances. This potential has been confirmed by some reports of bentazone in groundwater. Its GUS score is 3.52, indicating that it will leach to groundwater.

EFSA (2015) reports that in soil laboratory incubations under aerobic conditions in the dark, bentazone exhibited low to moderate persistence, forming the metabolite N‑methyl-bentazone. In laboratory incubations in dark aerobic natural sediment water systems, bentazone exhibited high persistence, remaining in the water column and forming the major metabolite N-methyl-bentazone.

The water solubility is about 5,000 mg/L for the acid and 230,000 mg/L for the sodium salt, and the sorption coefficient is 34 mL/g. Bentazone is not very volatile and very resistant to hydrolysis.

NPIC (1994) quotes for bentazone sodium salt a soil half-life of 20 days, water solubility of 230 percent and a sorption coefficient (soil Koc) of 34. This resulted in a pesticide movement to groundwater rating of high.

USGS (2006) give the following values: log Kow = 2.80; log Koc (where Koc is in mL/g) = 1.54; water solubility = 500 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -3.7; half-life in aerobic soil = 35 days; half-life in water = >200 days.

JMPR (2013) reports a Henry’s Law constant of 2.1 x 10-9 kPa.m3.mol at 20°C; an octanol-water partition coefficient at 20°C of logP = 1.55 (pH 4), -0.94 (pH 7) and -1.32 (pH 9); water solubility of 3000 mg/L (pH 4), 7700 mg/L (pH 7) and 17,000 mg/L (pH 9); and hydrolysis: bentazone is hydrolytically stable at pH 5, 7 and 9.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of bentazone (limit of detection = 0.0001 mg/L) (ESR 2001).

Bentazone has been found three times in groundwaters in the Auckland area, ranging from 0.00002 to 0.0002 mg/L (MAF 2006).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Bentazone occurred at 0.015 to 0.18 µg/L, ie, up to 0.00018 mg/L.

Bentazone was found in four bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.0001 to 0.00016 mg/L. The bores were in the Auckland region.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Bentazone was found in four wells, from 0.1 to 0.24 µg/L, ie, up to 0.00024 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Bentazone occurred in four wells, at 0.11 to 0.17 µg/L, ie, up to 0.00017 mg/L.

Three water utilities in the US reported detecting bentazon (basagran) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.006 mg/L.

Concentrations up to 0.12 mg/L in groundwater and up to 0.014 mg/L in surface water have been measured (WHO 2017).

### Removal methods

Bentazone has been shown to be broken down by ozonation. Moderate removal can be achieved using powdered activated carbon adsorption but it requires a high dose; powdered activated carbon with a dosage of a few tens of milligrams per litre or more is required for 80 percent removal with a contact time of 0.5–2 hours (from WHO 2016). Its solubility suggests that conventional coagulation and filtration processes will not be effective.

### Recommended analytical techniques

Not necessary, no MAV since 2005.

#### Some alternative methods

1. Bentazone may be determined by extraction with dichloromethane followed by gas chromatography with electron capture detection. The detection limit in tap water and river water is about 0.00005 mg/L (WHO 2004).

2. High Performance Liquid Chromatography with a Photoiodide Array Ultraviolet Detector (EPA 555).

### Health considerations

In animal studies, bentazone was absorbed rapidly from the gastrointestinal tract and distributed via the bloodstream to various organs and tissues. Liver and kidneys exhibited the highest activity, but no penetration across the blood-brain barrier was observed. Up to ninety percent of the dose was excreted in the urine within 24 hours as unchanged bentazone.

The acute toxicity of bentazone appears to be moderate to low. Rats subjected to acute exposure exhibited poor muscle coordination, tremor and breathing difficulties.

No cases of human poisoning have been reported following bentazone exposure.

The reference dose or RfD (USEPA 1998 and 2006/2009/2011) is 0.03 mg/kg/d based on the NOAEL of 3.2 mg/kg bwt/day for blood clotting changes and evidences of blood in the intestinal tract of the male dog. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 1 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw. This NOEL is based on decreased bodyweight and significant changes in organ weights observed in a two-year rat study. The ADI incorporates a safety factor of 100. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

EC (2000) also has an ADI of 0.1 mg/kg/d, based on a 24-month rat feeding study, the ARfD (acute reference dose) was reported at 0.25 mg/kg. These values were confirmed in EFSA (2012), which also tabulates the main metabolites. These were modified by EFSA (2015) to an ADI of 0.09 mg/kg/d for blood, liver and kidney toxicity observed in the two-year study in rats and applying the standard uncertainty factor (UF) of 100. The ARfD (acute reference dose) became 1 mg/kg based on the NOAEL of 100 mg/kg bw per day for increased post implantation loss, reduced number of live foetuses and retarded foetal development observed in a developmental toxicity study in rats, 100 UF applied.

In 1991 JMPR allocated an ADI of 0–0.1 mg/kg bw on the basis of the NOAEL of 9 mg/kg bw per day in a long-term study in rats and a safety factor of 100. Further data were made available to the JMPR, including observations in humans and a 90-day study in rats fed with 6-hydroxybentazone, a metabolite of bentazone. Data from studies of genotoxicity with 6-hydroxybentazone were also supplied. It was concluded that 6-hydroxybentazone was less toxic than bentazone, and the ADI of 0–0.1 mg/kg bw was maintained. The 2004 meeting concluded that the establishment of an ARfD was unnecessary.

FAO/WHO (2012) states: The meeting established an ADI of 0–0.09 mg/kg bw derived from a NOAEL of 9 mg/kg bw per day from the two-year study of toxicity and carcinogenicity in rats, on the basis of prolonged blood coagulation and clinical chemistry changes indicative of effects on liver and kidney at 35 mg/kg bw per day. A safety factor of 100 was applied. This ADI was supported by the NOAEL of 13.1 mg/kg bw per day observed in the one-year study in dogs for anaemia, altered blood coagulation parameters, clinical signs and weight loss seen at the highest dose of 52.3 mg/kg bw per day; by the NOAEL of 14 mg/kg bw per day in the two-generation study in rats, on the basis of reduced parental feed consumption and body weight gain and reduced pup body weight resulting from parental toxicity at 59 mg/kg bw per day; and by the NOAEL of 12 mg/kg bw per day in a two-year toxicity and carcinogenicity study in mice, based on prolongation of prothrombin time and an increased incidence of testicular calcification at 47 mg/kg bw per day. The meeting reaffirmed its previous conclusion that no ARfD is necessary. JMPR (2013) and FAO/WHO (2013) reaffirm the ADI and ARfD.

JMPR (2016) established an ARfD of 0.5 mg/kg bw, based on a NOAEL of 50 mg/kg bw for decreased motor activity in males observed on day 0 in an acute neurotoxicity study in rats, using a safety factor of 100. There was no change to the ADI.

Long-term studies conducted in rats and mice do not indicate a carcinogenic potential, and a variety of in vitro and in vivo assays indicate that bentazone is not genotoxic. The USEPA had classified bentazone in Group E: evidence of non-carcinogenicity for humans. USEPA (1998) states that this chemical is characterised as not likely to cause cancer to humans.

Bentazone is not carcinogenic in rats or mice, and showed no evidence of genotoxicity in a range of in vitro and in vivo assays. Consistent observations in repeated-dose toxicity studies in mice, rats and dogs are effects on haematology and blood coagulation (eg, prolongation of prothrombin time and partial thromboplastin time) (WHO 2017).

### Derivation of Maximum Acceptable Value

WHO (2017) revised their health-based value. Allocating 20 percent of the upper bound of the JMPR ADI of 0.09 mg/kg bw to drinking-water and assuming that a 60 kg person consumes 2 L of drinking-water per day, an HBV of 0.5 mg/L (500 μg/L) can be derived for bentazone. The default allocation factor of 20 percent has been used on a precautionary basis, as the available food exposure data do not generally include information from developing countries, where exposure via this route may be higher. The HBV for bentazone is protective against health effects resulting from lifetime exposure to the pesticide from drinking-water. Small exceedances of the HBV for short periods would not normally constitute a health emergency.

In DWSNZ 2005, the provisional MAV for bentazone had been derived as follows: the Joint FAO/WHO Meetings on Pesticide Residues (JMPR) evaluated bentazone in 1991 and the ADI they established has been used as the basis for the derivation of the MAV for bentazone in drinking-water shown below. The no-observable-adverse-effect level used in the derivation is based upon haematological effects at higher doses, derived from a two-year dietary study in rats.

10 mg/kg body weight/day x 70 kg x 0.1 = 0.35 mg/L (rounded to 0.4 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 10 mg/kg body weight per day based upon haematological effects at higher doses, derived from a two-year dietary study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter and intra-species variation).

The WHO (1993) Guidelines established a health-based guideline value of 0.03 mg/L for bentazone. The proportion of tolerable daily intake allocated to drinking-water they had used was 0.1, and this was the basis adopted in the datasheet in the 1995 Guidelines and in deriving the MAV in the 1995 DWSNZ. This guideline value was amended to 0.3 mg/L in the addendum to the WHO Guidelines, published in 1998, based on new information on the environmental behaviour of bentazone and exposure from food.

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# Benzalkonium chloride

CAS No. 8001-54-5. Benzalkonium chloride is a mixture of alkylbenzyldimethylammonium chlorides (quaternary ammonium compounds), with the alkyl chain lengths usually C8 to C18. It appears under many trade names. In the literature the generic term alkyl dimethyl benzyl ammonium chloride is often used as a general term for benzalkonium chloride.

### Maximum Acceptable Value

Benzalkonium chloride does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.0013 mg/L (1.3 µg/L) for benzalkonium chloride in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Benzalkonium chloride is an unclassified algicide, biocide and fungicide which is thought to affect the cytoplasmic membrane that controls cell permeability. Benzalkonium chloride is also a detergent and quaternary ammonium compound with a broad range of antimicrobial activity. It was first introduced as a germicide in the 1910s and became more widely used in the 1940s. In the ophthalmic industry, it was first used in the 1940s as a means to preserve hard contact lens solutions. Since then, it has been used in nearly all classes of ophthalmic solutions, from antiglaucoma medicines to over-the-counter artificial tear solutions. Benzalkonium chloride is the most frequently used preservative in ophthalmic solutions today, and its concentration in glaucoma formulations ranges from 0.004 to 0.02 percent. It is also used as a spermicide, and an antiseptic for cleaning wounds. It is also recommended as a bactericide and fungicide in shrimp hatcheries and other aquaculture activities.

Benzalkonium chloride appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Benzalkonium chloride is available mixed with other compounds such as chlorothalonil, prochloraz, and copper sulphate.

Benzalkonium chloride is proposed for use as a fungicide for kiwifruit and olives. Application may be at a 17.5 to 23 g ai/ha up until the end of flowering; NZFSA (2008) proposes to exempt benzalkonium chloride when used as a fungicide for kiwifruit and olives.

### Forms and fate in the environment

Benzalkonium chloride is very soluble in water (one trade product is a 17 percent solution).

### Removal methods

Activated carbon has been reported to reduce the concentration of benzalkonium chloride in water.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

No ADI has been set for benzalkonium chloride; however it is used safely in many cleaning products and medicinal products such as eye drops and mouth washes. Trace amounts of benzalkonium may be consumed with no incident through accidental contamination of food and water with surface cleaners and dishwashing liquids. No dietary risk is expected through the use of benzalkonium on kiwifruit and olives (NZFSA 2008).

IPCS (1999) reports that no ADI has been proposed, and there are no data available on its carcinogenicity, teratogenicity and mutagenicity.

For the dietary risk assessment EFSA used the ADI and ARfD values derived by the BfR (ADI for both DDAC and BAC: 0.1 mg/kg bw per day, ARfD for both compounds: 0.1 mg/kg bw). These values are considered as indicative, since no full toxicological dossiers are available for the compounds. It is noted that in the framework of a previously submitted MRL application an indicative ARfD of 0.61 mg/kg was derived for DDAC (EFSA 2014).

Some lab tests have shown that at high concentrations, benzalkonium chloride is mutagenic to mammalian somatic cells and bacteria and/or yeast.

### Derivation of Maximum Acceptable Value

No MAV.

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# Benzovindiflupyr

CAS No. 1072957-71-1. The IUPAC name for benzovindiflupyr is N-[(1RS,4SR)-9-(dichloromethylene)-1,2,3,4-tetrahydro-1,4-methanonaphthalen-5-yl]-3-(difluoromethyl)-1-methylpyrazole-4-carboxamide. The CAS name is N-[9-(dichloromethylene)-1,2,3,4-tetrahydro-1,4-methanonaphthalen-5-yl]-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide. Also called solatenol.

### Maximum Acceptable Value

Benzovindiflupyr does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Benzovindiflupyr is an [amide](http://www.alanwood.net/pesticides/class_fungicides.html#amide_fungicides) or pyrazole fungicide used on cereals. Metabolite NOA449410 is common to other pyrazole carboxamide active substances such as fluxapyroxad, isopyrazam and sedaxane).

Benzovindiflupyr was approved for use in New Zealand by EPA in September 2016.

### Forms and fate in the environment

Benzovindiflupyr exhibited very high persistence in the five soil types tested. In one soil, metabolite SYN546206 reached levels >5 percent of the dose at the end of the study (365 days) and needs to be assessed with respect to potential groundwater contamination.

The degradation of benzovindiflupyr in soil seems to be enhanced by the activity of photosynthethising micro‑organisms. Under these conditions metabolite NOA449410 was observed at levels up to 11.8 percent AR. Degradation by microalgae produced NOA449410, SYN508272, a metabolite chromatographically consistent with SYN546039, and a number of other unidentified metabolites. A soil half-life of 1,000 days has been used, and 400–700 days in water/sediment systems. The degradation of benzovindiflupyr under anaerobic conditions was investigated in two experiments; practically no degradation occurred. Benzovindiflupyr is stable to hydrolysis in buffered solutions (pH 4, 5, 7 and 9), even when heated to 50°C.

Metabolite NOA449410 (in plants and soil), potentially leaches to groundwater according to environmental fate and behaviour models (EFSA 2015).

Water solubility of benzovindiflupyr is about 1 mg/L. Henry’s Law constant is 1.3 x 10-6 Pa/m3/mol. Partition coefficient = 4.3 at 25°C.

### Analytical methods

#### Referee method

No MAV.

#### Some alternative methods

HPLC-MS/MS methods exist for monitoring benzovindiflupyr in the environmental matrices with a LOQ of 1 µg/kg in soil, and 0.05 µg/L in surface water and drinking water.

### Health considerations

The target organ of benzovindiflupyr is the liver and general signs of toxicity as manifested by decreased body weight and body weight gain in all species tested, colon/rectum hyperplasia in mice and gastrointestinal tract effects in dogs. The relevant short-term no observed adverse effect level (NOAEL) is 7.6 mg/kg bw per day from the 90-day study in rats based on reduced body weight, body weight gain, food consumption and food utilisation, and liver toxicity that included increased weight, altered biochemical parameters and centrilobular hypertrophy. The relevant long-term NOAEL is 4.9 mg/kg bw per day from the two-year study in rats based on the same effects on the body weight and liver, and additionally hepatocyte pigmentation, vacuolation and eosinophilic foci, and follicular cell adenomas. Benzovindiflupyr did not present genotoxic potential. Benzovindiflupyr is not classified or proposed to be classified as carcinogenic or toxic for the reproduction category 2 in accordance with the provisions of Regulation (EC) No 1272/2008 (EFSA 2015).

The ADI of benzovindiflupyr is 0.05 mg/kg bw per day. The ARfD is 0.1 mg/kg bw. The ADI of metabolite NOA449410 is 0.25 mg/kg bw per day, based on the maternal and developmental NOAEL of 250 mg/kg bw per day, the highest dose tested in a developmental toxicity study in rabbits, while a dose-range finding study presented severe maternal toxicity at 500 mg/kg bw per day, 1,000 UF applied to account for the limited database available (no long-term, multigeneration or rat developmental toxicity study available); NOA449410 does not require the setting of an ARfD (EFSA 2015).

The USEPA established an acute RfD of 0.10 mg/kg/day and aPAD = 0.10 mg/kg/day. The chronic RfD (= PAD) = 0.082 mg/kg/day. The USEPA concluded that a nonlinear RfD approach was appropriate for assessing cancer risk to benzovindiflupyr; therefore, a separate dietary exposure assessment for the purpose of assessing cancer risk is unnecessary (USEPA 2015).

JMPR (2016) reports an ADI of 0–0.05 mg/kg bw, and an ARfD of 0.1 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Benzyladenine

CAS No. 1214-39-7. The IUPAC name for benzyladenine is: N6-benzyladenine or N‑benzyl-1H-purin-6-amine. The CAS name is N-(phenylmethyl)-1H-purin-6-amine. Called N6-benzyladenine, 6-benzyladenine, 6-benzylaminopurine or BAP as well.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for benzyladenine in drinking-water. WHO (2004 and 2011) does not mention benzyladenine.

### Sources to water

Benzyladenine is a synthetic plant growth regulator, or a cytokinin, which enhances the growth and development of plants. In January 1990, the USEPA classified it as a biochemical pesticide because it resembles natural plant growth regulators and uses a non-toxic mode of action.

Benzyladenine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

N6-Benzyladenine is slightly toxic to aquatic organisms, and consequently is not permitted to be used in or near bodies of water (USEPA 2001). Soil metabolism studies indicate that it has a half-life of seven to nine weeks (USEPA 1994).

Water solubility is about 70 mg/L at pH 7 to 9. Residues reaching surface waters from field run-off should quickly absorb to sediment particles and be partitioned from the water column; detections in groundwater are not expected. Together, these data indicate that residues are not expected in drinking water (USEPA 2004).

In soil, 6-benzyladenine exhibits very low persistence and did not show any metabolite needing further consideration. 6-Benzyladenine is stable to hydrolysis; however, in water/sediment systems it is degraded relatively rapidly. According to the FOCUS GW models available (using worst case input parameters), it is not expected that 6‑benzyladenine will contaminate groundwater above the limit of 0.1 μg/L when used according to the representative uses proposed (EFSA 2010).

### Typical concentrations in drinking-water

Absorbing to sediment particles suggests that filtration techniques may reduce the concentration of benzyladenine in water.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

In a subchronic toxicity study using rats, N6-benzyladenine caused decreased food consumption, decreased body weight gain, increased blood urea nitrogen, and minimal changes in kidney tissue. N6-Benzyladenine showed some maternal and developmental adverse effects when it was given to pregnant rats. To minimise exposure to workers who handle large amounts of N6-benzyladenine, the USEPA requires that all such workers wear specified personal protective equipment (USEPA 2001).

Although N6-benzyladenine has two food crop-related uses (on fruit-bearing apple trees and spinach grown for seed), it is exempt from the requirement of a tolerance because it is a biochemical pesticide used at a rate of less than 20 grams of active ingredient per acre. Therefore, the Agency will revoke the existing tolerance and establish an exemption from the requirement of a tolerance for the currently registered uses of this pesticidal compounds on apples and spinach. The potential for dietary exposure is negligible (USEPA 1994).

USEPA (1994a) established a NOEL/LOEL for developmental toxicity of 50/175 mg/kg/d based on significantly decreased foetal body weight, increased incidence of hydrocephalus, and unossified sternebrae, incompletely ossified phalanges, and maligned sternebrae in a rat study.

The Acceptable Daily Intake (ADI) adopted for benzyladenine in Australia is 0.02 mg/kg body weight, with a NOEL of 30 mg/kg bw.

EC (2011) set an ADI of 0.01 mg/kg/d.

No Acceptable Daily Intake (ADI) or Acute Reference Dose (ARfD) values were considered necessary since no consumer exposure was expected for the representative uses, also based on the indication in the residue assessment that 6-benzyladenine was a naturally occurring compound. 6-Benzyladenine has no genotoxic concern based on the results from in vitro and in vivo mutagenicity studies (EFSA 2010).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Bifenthrin

CAS No. 82657-04-3. The IUPAC name for bifenthrin is: 2-methylbiphenyl-3-ylmethyl (1RS,3RS)-3-[(Z)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate; or alternatively:

2-methylbiphenyl-3-ylmethyl (1RS)-cis-3-[(Z)-2-chloro-3,3,3-trifluoroprop-1-enyl]-2,2-dimethylcyclopropanecarboxylate. The CAS name is (2-methyl[1,1′-biphenyl]-3-yl)methyl (1R,3R)-rel-3-[(1Z)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethylcyclopropanecarboxylate.

Eight stereoisomers are possible: the active ingredient contains at least 97 percent cis isomers. Bifenthrin is a mixture of the E- and the Z-isomer with a Z/E-ratio of 99.67 percent Z-bifenthrin: 0.33 percent E-bifenthrin and can be present as a cis-isomer and a trans-isomer. The ratio of cis- to trans- isomers is typically 98.65 : 1.35 (specification = 97 percent cis minimum: 3 percent trans maximum).

### Maximum Acceptable Value

There are insufficient data to determine a MAV for bifenthrin in drinking-water. WHO (2004 and 2011) does not mention bifenthrin.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for bifenthrin in water (set by an approval under Part 5 of the HSNO Act) of 0.05 ng/L (0.00005 µg/L).

### Sources to water

Bifenthrin is a Type I synthetic pyrethroid ester insecticide or acaricide that occurs in the (Z)-1R-cis-acid and (Z)-1S-cis-acid forms. It is used to control worms, various insects (mainly in in turf, also in timber), and mites. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Bifenthrin was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in tomatoes.

### Forms and fate in the environment

Bifenthrin has high persistence in soil (half-life varying from about seven days to eight months) and consequently it is one of the longest residual insecticides currently registered on the market today. Water solubility is less than 0.1 mg/L. See JMPR (2010) for discussion on metabolites. The trifluoroacetic acid metabolite is common in a wide range of pesticides which contain the trifluoromethyl group (fluazinam, saflufenacil, etc).

In soil under aerobic conditions bifenthrin exhibits moderate to high persistence (aerobic half-life from 97 to 250 days, depending on soil type) forming the major soil metabolite TFP acid (accounting for up to 11.6 percent of applied radioactivity (AR)) which exhibits low to moderate persistence and the minor non-transient metabolite 4’‑OH bifenthrin (accounting for up to 8.3 percent AR) which exhibits moderate persistence. Bifenthrin exhibits low mobility in soil, but TFP acid exhibits very high to medium mobility.

Bifenthrin was stable under sterile aqueous hydrolysis conditions at 25°C at pH 5, 7 and 9 (half-life >2 months); EFSA. 2011. Bifenthrin has a low potential to contaminate groundwater. Octanol-Water Partition Coefficient (Kow): 1.0 x 106. Henry’s constant: 7.2 x 10-3 atm·m3/mol. Soil Sorption Coefficient (Koc): 1.3 to 3.0 x 105.

NPIC (1994) quotes for bifenthrin a soil half-life of 26 days, water solubility of 0.1 mg/L and a sorption coefficient (soil Koc) of 240,000. This resulted in a pesticide movement to groundwater rating of extremely low.

EFSA (2011) discusses the potential for contamination of groundwater by the major soil metabolite TFP acid.

### Removal methods

Treatment processes that remove particulate matter should remove most of the bifenthrin.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

IPCS quote an estimate of acceptable daily intake (ADI) for humans of 0–0.02 mg/kg bw. The ADI was allocated on the basis of the NOAEL of 1.5 mg/kg bw/day in the one-year study in dogs using a 100-fold safety factor. This result was supported by the same NOAEL in the rat teratology study, although in the latter study gavage, rather than dietary administration, was used.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw. An ARfD was deemed unnecessary.

The JMPR 2009 meeting established an ADI of 0–0.01 mg/kg bw on the basis of a NOAEL of 1.0 mg/kg bw per day in a study of developmental toxicity in rats (gavage) based on the increased incidence of tremors in dams during days 10–19 of gestation and increased fetal and litter incidences of hydroureter without hydronephrosis seen at the LOAEL of 2.0 mg/kg bw per day, and using a safety factor of 100. This ADI was supported by a threshold dose of 1.3 mg/kg bw in males in a study of acute toxicity in rats treated by gavage and using a safety factor of 100, as well as several other studies, including a one-year study of toxicity in dogs, a two-year combined study of toxicity and carcinogenicity in rats and a 90-day study of neurotoxicity in rats, all with NOAELs in the range of 1.5–2.9 mg/kg bw per day. The meeting established an acute reference dose (ARfD) of 0.01 mg/kg bw based on a threshold dose of 1.3 mg/kg bw for motor activity in a study of acute toxicity in rats treated by gavage and using a safety factor of 100. Although this study was conducted with males only, it was considered appropriate, as there was no evidence of sex-specific differences among the data on bifenthrin. This ARfD was supported by the study of developmental toxicity in rats treated by gavage in which the NOAEL of 1.0 mg/kg bw per day was based on the increased fetal and litter incidences of hydroureter without hydronephrosis seen at the LOAEL of 2.0 mg/kg bw per day and which thereby was also protective for developmental effects.

The EFSA (2011 and 2015) states that the ADI is 0.015 mg/kg bw/day based on the one-year dog study with a SF of 100, supported by the developmental study in rats. The ARfD is 0.03 mg/kg bw based on the 90-day neurotoxicity study with a SF of 100.

USEPA (2003)states that the acute RfD = 0.033 mg/kg/day, and the chronic RfD = 0.004 mg/kg/day; the RfDs also = the PADs. In 1988 the RfD had been 0.015 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.031 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for bifenthrin is 0.31 mg/L.

In 1992 the USEPA (reaffirmed September 2008) characterised bifenthrin in Group C (a possible human carcinogen) primarily on the basis of a mouse study. For the purpose of risk characterisation, the reference dose (RfD) approach should be used for quantification of human cancer risk.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for bifenthrin since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

Bifenthrin residues have been found in New Zealand tomatoes, refer <http://www.nzfsa.govt.nz/science/research-projects/food-residues-surveillance-programme/results>.

### Derivation of Maximum Acceptable Value

No MAV.

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# Bitertanol

CAS No. 55179-31-2. The IUPAC name for bitertanol is: (1RS,2RS;1RS,2SR)-1-(biphenyl-4-yloxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)butan-2-ol; it comprises 20:80 ratio of (1RS,2RS)- and (1RS,2SR)-isomers. The CAS name is β-([1,1′-biphenyl]-4-yloxy)-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for bitertanol in drinking-water. WHO (2004 and 2011) does not mention bitertanol.

### Sources to water

Bitertanol is a broad spectrum triazole fungicide used on fruits, vegetables and cereals. This substance does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 but appears on ERMA’s list of pesticides commonly used in sports turf management (see <http://www.ermanz.govt.nz/resources/publications/word/ER-CG-16-supp.doc>). Bitertanol is registered in Australia for use on several types of beans (APVMA 2002). In New Zealand it is used in an aerosol to control black spot in home gardens. The use of bitertanol is no longer authorised within the EU (EFSA 2016).

### Forms and fate in the environment

In adsorption/desorption studies bitertanol was shown to be strongly adsorbed (low mobility or leaching) to three soils in the decreasing order of: sand, loam and silty clay. The half-life in a range of soils was 10 to 39 days; degradation was slower in anaerobic conditions. 1H-1,2,4-triazol-1-ylacetic acid (CAS No. 4314-22-1 ) is a predominant metabolite, which is more likely to leach to groundwater than the parent compound.

No apparent degradation was observed after 30 days in sterile aqueous solutions at a wide range of pH and temperatures. Water solubility is about 4 mg/L.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

In the available toxicity studies on bitertanol, there was no estrogen, androgen, and/or thyroid-mediated toxicity. A potential hormonal effect was seen in a subchronic dog study, but not in chronic dog studies. The hormonal effect in the chronic dog studies suggests that the effect was specific to the dogs tested in the subchronic study, and not as a result of bitertanol exposure. However, the reason for the difference in hormonal effect between the dog studies is unknown (USEPA 2005).

The Acceptable Daily Intake (ADI) for humans (INCHEM) is 0 to 0.003 mg/kg body weight. This was based on studies showing that dogs were more susceptible than rats; dog feeding studies of one and two years’ duration showed the formation of cataracts, conjunctivitis and mild hepatotoxicity, with a no-observed-adverse-effect level equivalent to 0.25 mg/kg bw/day. JPMR (1998) revised the this data and allocated an ADI of 0–0.01 mg/kg.

The Acceptable Daily Intake (ADI) adopted in Australia for bitertanol is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

EFSA (2011 and 2016) refers to a RfD of 0.003 mg/kg bw and an ARfD of 0.01 mg/kg bw; the setting of an ARfD was considered not necessary by JMPR in 1998.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0021 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for bitertanol is 1.65 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Bixafen

CAS No. 581809-46-3. The IUPAC name for bixafen is: N-(3′,4′-dichloro-5-fluorobiphenyl-2-yl)-3-(difluoromethyl)-1-methylpyrazole-4-carboxamide. The CAS name is N-(3′,4′-dichloro-5-fluoro[1,1′-biphenyl]-2-yl)-3-(difluoromethyl)-1-methyl-1H-pyrazole-4-carboxamide.

### Maximum Acceptable Value

There is no MAV in the DWSNZ for bixafen in drinking-water. WHO (2011) does not mention bixafen.

### Sources to water

Bixafen is an anilide or pyrazole-carboxamide fungicide. Bixafen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2015 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Bixafen exhibited very high persistence in soil studies; mineralisation in both aerobic and anaerobic conditions was negligible after 120 days. Bixafen has a soil half-life measured in years. Metabolite M44 has a soil half-life of 25 days. Bixafen exhibits slight mobility in soil; M44 exhibits high to very high mobility. Bixafen was hydrolytically stable when tested at 50°C and pH 4, 7 and 9. Aqueous photolysis is unlikely to be a significant route of degradation of bixafen in natural surface waters, as no significant degradation of bixafen was observed in either the light (after eight days continuous irradiation) or dark. Bixafen dissipated from the water phase mainly by partitioning on to sediment with 7.1-17.4 percent AR remaining in water and levels in sediment peaking at 73.8–88.3 percent AR after 118 days. Default DT50 values of 1,000 days have been assumed for degradation in both the water and sediment phases of natural surface water systems (EFSA 2012).

Water solubility is about 0.5 mg/L for pH 5 to 9. Partition coefficient = Log Pow = 3.3 at 40°C. Henry’s Law constant = 3.89 x 10-5 Pa m3 mol-1. JMPR (2013).

### Removal methods

Treatment processes that remove particulate matter from water should reduce the concentration of bixafen.

### Analytical methods

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2012).

### Health considerations

Bixafen is rapidly and extensively absorbed after oral administration; bixafen does not bioaccumulate in the body and is rapidly eliminated mainly in bile but also in urine. In the available studies, bixafen showed a low acute toxicity profile, and the target organs after repeated exposure were the liver and the thyroid. In long-term toxicity studies, there was no evidence of a carcinogenic potential for bixafen. The Acceptable Daily Intake (ADI) for bixafen is 0.02 mg/kg bw per day based on the two-year rat study, and the Acute Reference Dose (ARfD) is 0.2 mg/kg bw based on early effects in the rat developmental. Both reference values were derived with an uncertainty factor of 100 (EFSA 2012).

JMPR (2013/2016) reports the same values.

APVMA adopted an ADI of 0.02 mg/kg/d for Australia (<https://apvma.gov.au/>). The ARfD is 0.2 mg/kg.

For the metabolite M44 (also a groundwater metabolite) no conclusion can be drawn on its toxicological profile based on the data available in the bixafen dossier. However, it can be highlighted that it is a common metabolite for fluxapyroxad and isopyrazam, where toxicological data are available. For fluxapyroxad, this metabolite was considered not toxicologically relevant for groundwater, and an ADI of 0.30 mg/kg bw/d was derived (no ARfD was allocated) (EFSA 2012).

### Derivation of Maximum Acceptable Value

No MAV.

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# Boscalid

CAS No. 188425-85-6. The IUPAC name for boscalid is 2-chloro-N-(4′-chlorobiphenyl-2-yl)nicotinamide. The CAS name is 2-chloro-N-(4′-chloro[1,1′-biphenyl]-2-yl)-3-pyridinecarboxamide. Previously called nicobifen.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for boscalid in drinking-water. WHO (2004 and 2011) does not mention boscalid.

### Sources to water

Boscalid is described as an anilide or pyridine or carboxamide fungicide, commonly used for the control of botrytis in grapes.

Boscalid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

It is often sold mixed with other pesticides, eg, pyraclostrobin.

### Forms and fate in the environment

Boscalid is persistent and has low mobility in soil; boscalid concentrations declined to half of their initial values in 28 days to 208 days. However, boscalid may move to surface water through spraydrift and run-off of soil and suspended sediments. The degree of surface water contamination is mitigated by the relatively low seasonal application rates. The primary degradation pathway is aerobic soil metabolism, which proceeds slowly and results in the formation of intermediates which are relatively rapidly transformed into CO2 or bound soil residues. The majority of the apparent degradation of the compound is actually due to its transformation to bound residues. The compound is not transformed to any significant extent in either aerobic or anaerobic aquatic systems, but is relatively rapidly transferred (dissipation half-lifes of <2 weeks) from the water phase to the sediment phase, sorbing to the sediment.

EFSA (2014) quotes a DT90 of >1 year.

See JMPR (2006) for discussion on metabolites.

Water solubility is about 5 mg/L.

### Removal methods

Being strongly adsorbed to soil suggests treatment systems that remove particulate matter should remove boscalid.

### Analytical methods

#### Referee method

A referee method cannot be selected for boscalid because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

USEPA (2004) estimated the cPAD (chronic population adjusted dose) and cRfD at 0.218 mg.kg/d. As there were no toxic effects attributable to a single dose, an endpoint of concern was not identified to quantitate acute-dietary risk. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.218 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for boscalid is 1.53 mg/L (no acute one-day value available).

Boscalid was evaluated for the first time for toxicology and residues by the JMPR in 2006, developing a maximum ADI of 0.04 mg/kg bw. The 2006 JMPR decided that an ARfD was unnecessary.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.06 mg/kg body weight. The NOEL is 6 mg/kg bw, and the ARfD is 3 mg/kg bw. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

EFSA (2014) report an ADI of 0.04 mg/kg/d; an ARfD was deemed not necessary.

The USEPA determined that boscalid produced suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential. Boscalid was tested in five mutagenicity studies and was found to be negative in all of them.

### Derivation of Maximum Acceptable Value

No MAV.

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# Brodifacoum

CAS No. 56073-10-0. The IUPAC name for brodifacoum is: 3-[(1RS,3RS;1RS,3SR)-3-(4′-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxycoumarin. CAS name 3‑[3-(4′-bromo[1,1′-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzopyran-2-one. Also called super-warfarin, or bromfenacoum. Talon is a trade name common in New Zealand.

Brodifacoum exists as cis and trans isomers that may be separated by chromatography and identified by nuclear magnetic resonance spectroscopy. The commercially available preparation contains variable proportions of cis/trans isomers such as 50:50 and 70:30. There is no significant difference in activity between the two isomers (ICPS 1999).

### Maximum Acceptable Value

There are insufficient data to determine a MAV for brodifacoum in drinking-water.

WHO (2004 and 2011) does not mention brodifacoum.

### Sources to water

Brodifacoum, a bromylated hydroxycoumarin derivative, is an anticoagulant rodenticide, is stable in the solid form, and it does not lose activity after 30 days in direct sunlight. It is very effective against rats and mice, including warfarin-resistant strains. It is used in agriculture and urban rodent control as ready-to-use baits of low concentration (usually 0.005 percent brodifacoum).

Brodifacoum appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Brodifacoum does not enter the atmosphere, because of its low volatility. Brodifacoum is not taken up by plants. It is not expected to contaminate groundwater. The rate of degradation is relatively slow and depends on soil type. Brodifacoum appears to bind rapidly in the soil with very slow desorption and without leaching; in leaching studies, only 2 percent of brodifacoum added to the soil leached more than 2 cm from its source in four soil types tested. Brodifacoum degraded with a half-life of 157 days in sandy clay loam soil incubated in the dark at 21°C. No brodifacoum was found in soil or water after a pest eradication programme in Northland (Ogilvie et al 1997). This will have been due to brodifacoum’s overall low water-solubility, especially at acidic and neutral pH, and the adsorption of brodifacoum to organic particles.

The solubility of brodifacoum in water is less than 10 mg/L at 20°C and pH 7. It is a weak acid which does not form water-soluble salts.

### Typical concentrations in drinking-water

No information is available on concentrations in air, water, and soil. Being slightly soluble in water, its use cannot be a significant source of water contamination.

### Removal methods

Being strongly adsorbed to soil suggests treatment systems that remove particulate matter should remove brodifacoum from water.

### Analytical methods

#### Referee method

A referee method cannot be selected for brodifacoum because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for the above reason. However, the following information may be useful:

Analytical methods for the determination of brodifacoum include liquid chromatography with fluorescence detection and high-performance liquid chromatography, with detection limits of 0.001 mg/L and 0.002 mg/kg, respectively.

### Health considerations

Brodifacoum is absorbed through the gastrointestinal tract, skin, and respiratory system. The major route of elimination in different species after oral administration is through the faeces. The liver is the main organ of accumulation and storage. Brodifacoum has been found mainly as an unchanged compound. After a single oral dose to rats, liver concentrations remained high and relatively constant for 96 hours. Elimination from the liver is slow and biphasic with an initial rapid phase lasting from two to eight days after dosing and a slower terminal phase with an elimination half-life of 130 days. In accidentally poisoned patients, the plasma half-life was found to be approximately 16–36 days.

However, concerns have been raised over the persistence of brodifacoum in New Zealand’s natural ecosystems. Of particular concern is the contamination of wild game, such as feral pig, which eat the baits and also poisoned possum carcasses that might be contaminated with brodifacoum residues. Contaminated pigs could be a threat to human health if they were hunted and eaten. Therefore the Department of Conservation has undertaken to reduce and restrict the use of brodifacoum on the mainland (DoC 2005).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0000005 mg/kg body weight, one of the lowest on their list. The NOEL is 0.001 mg/kg bw.

### Derivation of Maximum Acceptable Value

There are insufficient data to determine a MAV for brodifacoum in drinking-water.

Exposure of the general population to brodifacoum through air, drinking-water, or food is unlikely and does not constitute a significant health hazard. Poisoning incidents may occur in cases of massive intentional or unintentional ingestion, or prolonged skin contact during manufacture and formulation.

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# Bromacil

[CAS No: 314-40-9](http://www.google.co.nz/aclk?sa=l&ai=BUXIITJQPSc7zCYOytQOiuaTVCaaWn3ni7t6zCbjqx4MCgLUYEAIYAigCOABQkPf-o_z_____AWCr7LGF4BigAfzewu8DyAEBgAIBqQL2ntT3e6GDPsgCiP-yCNkDFaYqTOd-xHc&num=2&sig=AGiWqtwhSk6ccFHDArxYLxMYhqbCNHA4HQ&q=http://www.synpartner.com/cgi/search-en.cgi%3Ff%3Dproduct_en%2Bcompany_en_1_%26t%3Dproduct_en%26w%3Dproduct_en%26terms%3Dbromacil%26imageField2.x%3D14%26imageField2.y%3D10). IUPAC name is (RS)-5-bromo-3-sec-butyl-6-methyluracil. Also called 5-bromo-6-methyl-3-(1-methylpropyl)-2,4(1H,3H)pyrimidinedione (CAS name).

### Maximum Acceptable Value (Provisional)

Based on health considerations, the concentration of bromacil in drinking-water should not exceed 0.4 mg/L (400 μg/L).

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.07 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Bromacil, a substituted uracil, is used as a broad spectrum herbicide to control weeds, and is available as a wettable powder. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Registered formulations are of three types: Chemagro Terminex-A (which also contains amitrole and diuron); Hyvar X; and Krovar I DF, which also contains diuron.

Bromacil is applied mainly by sprayers including boom, hand-held, knapsack, compressed air, tank-type, and power sprayers. Bromacil is also applied using aerosol, shaker, or sprinkler cans.

No information is available on the annual usage of specific active ingredients in New Zealand, although bromacil is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Bromacil is sometimes found above the default maximum residue limit in New Zealand vegetables, eg, asparagus (NZFSA).

### Forms and fate in the environment

Bromacil is a uracil compound that is very soluble in water: 815 mg/L (Hort Research 2000), and has a mobility (as Koc) of 32, which suggests a moderate level of adsorption to organic soil.

Bromacil is stable to hydrolysis under normal environmental conditions. The primary routes of dissipation appear to be photolysis in water under alkaline conditions and microbial degradation in anaerobic soil. Bromacil’s persistence is demonstrated by half-lifes of 124 to 155 days in the field dissipation studies (USEPA 1996). There is little information available on the breakdown rate of bromacil in water, although a two-month half-life is suggested for this herbicide in clean river water which is low in sediment.

NPIC (1994) quotes for bromacil acid a soil half-life of 60 days, water solubility of 700 mg/L and a sorption coefficient (soil Koc) of 32. This resulted in a pesticide movement to groundwater rating of very high. Its GUS score is 5.78, indicating that it will leach to groundwater.

USGS (2006) give the following values: log Kow = 2.11; log Koc (where Koc is in mL/g) = 1.86; water solubility = 815 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -4.89; half-life in aerobic soil = 275 days; half-life in water = >30 days.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included bromacil, so typical concentrations in New Zealand drinking-waters are unknown.

Bromacil has been found 14 times in groundwaters in the Waikato, Wellington and Southland areas, ranging from 0.00002 to 0.0064 mg/L (MAF 2006).

Bromacil has been detected on one occasion at one location in groundwater monitoring conducted by Environment Canterbury in and close to the Level Plain area in South Canterbury (Close et al 2001). In the Waikato region, bromacil has been detected in groundwater at four sites at concentrations of 0.00002–0.0064 mg/L (Hadfield and Smith 1999). Bromacil has been detected in groundwater in the Edendale area (Southland) at concentrations ranging between 0.00009 and 0.00024 mg/L (Hughes 2000).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Bromacil occurred at 0.56 µg/L, ie, 0.00056 mg/L.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Bromacil was detected in one well at a concentration of 0.057 µg/L, ie, 0.000057 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Bromacil occurred in one well, at 3.4 µg/L, ie, 0.0034 mg/L.

Thirteen water utilities in the US reported detecting bromacil in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0015 mg/L.

### Removal methods

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of bromacil, although a guide to the efficiency of the process cannot be provided.

Some newer advanced oxidation treatment processes show promise.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Health considerations

There is no information available regarding the greatest source of exposure to bromacil for New Zealanders (ie, dermal contact, inhalation, diet: food, water). Based on international studies, people may be exposed to residues of bromacil through diet because it is applied to citrus crops.

A number of studies show that uracils, the class of compounds to which bromacil belongs, are absorbed into the body from the gut and excreted primarily in the urine (EXTOXNET 1996).

#### Acute poisoning

In studies using laboratory animals, bromacil is slightly toxic by the oral, dermal, and inhalation routes and has been placed in Toxicity Category IV (the lowest of four categories) for these effects. The herbicide is irritating to the skin, eyes and respiratory tract. When as little as 100 mg/kg of the herbicide was fed to dogs, it caused vomiting, watering of the mouth, muscular weakness, excitability, diarrhoea, and dilation of the pupils of the eyes. Rats that were fed single doses of bromacil experienced initial weight loss, paleness, exhaustion, and rapid breathing (Occupational Health Services Inc 1991, cited in PMEP 2001). Within four hours of being given 250 mg/kg of this, or a related material (isocil), sheep became bloated and walked with stilted gaits (Gosselin et al 1984, cited in PMEP 2001).

The acute oral LD50 for rats is 5,200 mg/kg (RSocC 1987) which suggests a relatively low oral toxicity compared with other pesticides.

#### Chronic exposure

In a chronic feeding study using beagle dogs, bromacil reduced body weight gain. In another chronic study using rats, effects in addition to reduced body weight gain included (1) increased incidence of thyroid cysts in the high dose males (2) enlargement of the thymus in high dose females; and (3) dose-related incidence of thyroid tumours in the males.

Bromacil demonstrates some evidence of causing developmental toxicity effects in rats and rabbits. These effects are likely to be due to maternal toxicity from exposure to bromacil rather than from specific developmental toxicity of bromacil. Therefore the USEPA does not consider bromacil a developmental toxicant (USEPA 1996).

The reference dose or RfD (USEPA 2006/2009/2011) is 0.1 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 3.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw from a long-term (two-year dietary) study. The NOEL is based on decreased bodyweight and increased relative thyroid weight in rats. The ADI incorporates a safety factor of 100.

The International Agency for Research on Cancer has not classified bromacil, but since January 1993 the USEPA has classified it as a Group C possible carcinogen based on increases in incidence of liver tumours in male mice, and positive trends in thyroid tumours in male rats, and, to a lesser extent, structural activity relationship to similar compounds. The lithium salt appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

The MAV is provisional because it was developed by the MoH in-house rather than by WHO. A tolerable daily intake approach has been used for the derivation of the MAV for bromacil in drinking-water, as follows:

10 mg/kg body weight per day x 70 kg x 0.1 = 0.35 mg/L (rounded to 0.4 mg/L)

2 L x 100

where:

* no-observable-adverse-effect level = 10 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Bromadiolone

CAS No. 28772-56-7. The IUPAC name for bromadiolone is 3-[(1RS,3RS;1RS,3SR)-3-(4′-bromobiphenyl-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxycoumarin. The CAS name is 3-[3-(4′-bromo[1,1′-biphenyl]-4-yl)-3-hydroxy-1-phenylpropyl]-4-hydroxy-2H-1-benzopyran-2-one. It is sometimes called broprodifacoum. It is a mixture of two diastereoisomers.

### Maximum Acceptable Value

Bromadiolone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Bromadiolone is a coumarin anticoagulant (vitamin K antagonist) rodenticide that is effective against rats and mice, including those resistant to first generation anticoagulants. It is used in the form of ready-to-use baits of low concentration usually containing 0.005 percent bromadiolone. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Bromadiolone is sometimes sold mixed with sulphaquinoxaline (qv) which also appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines.

Bromadiolone is slightly soluble in water and, in the form of bait-formulations, it is unlikely to be a source of water contamination.

### Forms and fate in the environment

Bromadiolone is unlikely to enter the atmosphere, because of its low volatility. Parent bromadiolone is not persistent to aerobic soil metabolism (half-life about 14 days although may be less than a day in light) and can generally be considered immobile except in soils of low organic matter and clay, such as sand. Although the parent compound is not persistent, two of the major degradates identified in the aerobic soil metabolism study are persistent, being detected after six to nine months. Bromadiolone is not expected to leach to groundwater.

Water solubility is about 15 to 20 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of bromadiolone in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Bromadiolone is very toxic for all mammalians. A single dose may cause death in rodent species; about 1 to 2 mg/kg for rats, mice and rabbits. The anticoagulant effect can be successfully countered by vitamin K1 administration (IPCS 1996).

Based upon the clinical and haematological findings in dog studies, the LOEL for subchronic toxicity of bromadiolone was 0.015 mg/kg; NOEL 0.01 mg/kg (USEPA 1998).

The Acceptable Daily Intake (ADI) adopted in Australia for bromadiolone is 0.000002 mg/kg body weight, with a NOEL of 0.004 mg/kg bw.

The toxicological assessment of bromadiolone was peer reviewed under Commission Regulation (EC) No 33/2008; however, an allocation of toxicological reference values for dietary exposure was not considered necessary because a direct application of bromadiolone on edible crops is not intended. Nevertheless, during the peer review, values for an acute and subchronic/chronic acute reference dose (AOEL) of 0.0023 μg/kg bodyweight (bw) and of 0.0012 μg/kg bw per day, respectively were set (EFSA 2010/2017).

### Derivation of Maximum Acceptable Value

No MAV.

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# Bromopropylate

CAS No. 18181-80-1. The IUPAC name for bromopropylate is isopropyl 4,4′-dibromobenzilate. The CAS name is 1-methylethyl-4-bromo-α-(4-bromophenyl)-α-hydroxybenzeneacetate. Also called isopropyl dibromobenzilate.

### Maximum Acceptable Value

Bromopropylate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Bromopropylate is a non-systemic contact bridged diphenyl (benzilate) acaricide (miticide). This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

In water, bromopropylate was found to have a half-life of 20 to 40 days. Bromopropylate and its metabolites were concluded to have low mobility in sandy loam, silty loam and sandy soils on the basis of leaching studies. The half-life in silty loam and sandy loam soils was about 45 days. Breakdown products include 4,4‑dibromobenzophenone and 4,4-dibromobenzilic acid, with 4,4-dibromobenzhydrol forming in anaerobic conditions.

Water solubility is less than 0.5 mg/L, or 0.1 mg/L in Wikipedia. Log Kow = 5.40. Henry’s Law constant = 4.6 x 10-7 atm cu m/mol at 25°C.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

FAO and IPCS (1973) quote an earlier ADI of 0.008 mg/kg bw.

JPMR established an ADI of 0.03 mg/kg bw (IPCS 1993) based on the NOAEL of 2.7 mg/kg bw/day in the one-year study in dogs, using a 100-fold safety factor. An ARfD was not derived since this was not common practice in 1993.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight for bromopropylate, with a NOEL of 2.8 mg/kg.

EFSA (2010) still uses the 1993 ADI of 0.03 mg/kg/d. Since the relevant toxicological studies are not available to EFSA, EFSA is not in a position to derive a proposal for an ARfD. EFSA therefore proposes to use the ADI as a surrogate to assess also the acute effects in the short-term intake assessment.

### Derivation of Maximum Acceptable Value

No MAV.

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# Bromoxynil

CAS No. 1689-84-5. The IUPAC and CAS name for bromoxynil is 3,5-dibromo-4-hydroxybenzonitrile. It may appear as its octanoate ester, CAS No. 1689-99-2, or other esters or salts.

### Maximum Acceptable Value

Bromoxynil does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The maximum acceptable concentration for bromoxynil in drinking water in Canada is 0.005 mg/L (5 µg/L).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.01 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Bromoxynil is a selective nitrile herbicide that is used for post-emergent control of annual broadleaf weeds, often used in cereal crops. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Bromoxynil has a low persistence in soil. In sandy soil, the half-life is about 10 days. Degradation in clay is slower, with half of the bromoxynil degraded to its metabolites in about a two-week period at 25°C. The persistence of the compound is also slightly longer in peat field soils than in the sandy soils. The evidence suggests that, while bromoxynil is broken down by some soil bacteria, it may inhibit the action of other bacteria that promote the formation of nitrite by nitrification. Soil metabolites include 3,5-dibromo-4-hydroxy-benzamide and 3,5-dibromo-4-hydroxybenzoic acid, which have maximum DT90 values of 18 days and <2 days, respectively (EFSA 2012).

Bromoxynil in aqueous solutions photolyses in sunlight to form 3-bromo-hydroxybenzonitrile (MBBP) and 4-hydroxybenzonitrile, and therefore may be susceptible to direct photolysis by sunlight. If released to soil, bromoxynil is expected to have moderate mobility based upon a reported Koc of 302. The pKa of bromoxynil is 3.86, indicating that this compound will exist almost entirely in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilisation from moist soil is not expected because the compound exists as an anion and anions do not volatilise. Bromoxynil may not volatilise from dry soil surfaces based upon its vapour pressure. Bromoxynil is rapidly biodegraded by soil micro‑organisms; the major biodegradation products in soil are 3,5-dibromo-4-hydroxybenzoic acid and 3,5-dibromo-4-hydroxybenzamide indicating that biodegradation is an important environmental fate process in soil. If released into water, bromoxynil is not expected to adsorb to suspended solids and sediment based upon the estimated Koc. Biodegradation data in water were not available. The pKa indicates bromoxynil will exist almost entirely in the anion form at pH values of 5 to 9 and therefore volatilisation from water surfaces is not expected to be an important fate process. An estimated BCF of 28 suggests the potential for bioconcentration in aquatic organisms is low. In the moist soil environment, bromoxynil is degraded by hydrolysis and debromination to less-toxic substances such as hydroxybenzoic acid suggesting that hydrolysis may be an important environmental fate process under environmental conditions (pH 5 to 9). Photolysis in sunlit surface waters is expected to be an important environmental fate process for bromoxynil; when buffered bromoxynil solutions were filtered to remove radiation below 300 nm, more than 80 percent and 60 percent of the bromoxynil degraded at pH 7.0 and 4.5, respectively (EAWAG accessed February 2015).

Its solubility in water is high at 130 mg/L at 25°C, and its vapour pressure is low, 1.0 x 10-3Pa at 20°C. Various esters are sold, eg, the heptanoate and octanoate; these are much less soluble.

NPIC (1994) quotes for bromoxynil butyrate ester a soil half-life of seven days, water solubility of 27 mg/L and a sorption coefficient (soil Koc) of 1079. This resulted in a pesticide movement to groundwater rating of very low. However, bromoxynil was ranked high with respect to potential for groundwater contamination in an Agriculture Canada survey, Health Canada (1989). The potential for groundwater exposure from all representative uses by bromoxynil octanoate and its metabolites bromoxynil, 3,5‑dibromo-4-hydroxybenzamide and 3,5-dibromo-4-hydroxybenzoic acid above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios (EFSA 2017).

### Typical concentrations in drinking-water

Traces (0.00001 mg/L) of bromoxynil were detected in two of 48 municipal water samples in Manitoba (detection limit 0.00001 mg/L). However, the USEPA (1998) states that the potential for groundwater contamination from bromoxynil octanoate is low; it does not exhibit the mobility or persistence characteristics of pesticides that are normally found in groundwater.

### Removal methods

Due to bromoxynil’s low persistence in soil and fairly high solubility, oxidation processes will be needed to reduce its concentration in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

With regard to residues, the review (EU 2004) established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is <2 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet and taking into account cereals only. Additional intake from water and products of animal origin are not expected to give rise to intake problems. Estimates of acute dietary exposure of adults and toddlers revealed that the Acute Reference Dose (ARfD) would not be exceeded (<7 percent).

The RfD for bromoxynil and bromoxynil octanoate was calculated at 0.02 mg/kg/d (USEPA 1988). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.015 mg/kg/d, and an ARfD of 0.04 mg/kg/d for bromoxynil and bromoxynil octanoate. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for bromoxynil and bromoxynil octanoate is 1.32 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.003 mg/kg body weight, with a NOEL of 0.3 mg/kg bw from a 12-month dietary study in dogs. The ADI incorporates a safety factor of 100.

Rapid conversion of the ester forms of the chemical (heptanoate and octanoate) permit the risk assessment to be based on exposure to the phenol. The Reference Dose (RfD) for bromoxynil phenol is 0.015 mg/kg/day based on the threshold NOEL/LOEL of 1.5 mg/kg/day in a 12‑month-chronic oral toxicity study in dogs (USEPA 1998).

As at September 2008 the USEPA has classified bromoxynil in Group C: a possible human carcinogen. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

EFSA (2012) states that the ADI and the ARfD were established at 0.01 mg/kg bw per day and 0.04 mg/kg bw respectively. EFSA (2017) now reports an ADI of 0.003 mg/kg/d and an ARfD of 0.013 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

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# Bupirimate

CAS No. 41483-43-6 (some references quote 58694-46-5). The IUPAC name for bupirimate is 5-butyl-2-ethylamino-6-methylpyrimidin-4-yl dimethylsulfamate. The CAS name is 5-butyl-2-(ethylamino)-6-methyl-4-pyrimidinyl dimethylsulfamate. A trade name is Nimrod.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for bupirimate, WHO do not mention bupirimate in their Guidelines.

### Sources to water

Bupirimate, a systemic pyrimidine fungicide, used on pip-fruit and cucurbit crops for the control of powdery mildew. It acts by interfering with nucleic acid synthesis, mainly by inhibiting sporulation.

Bupirimate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Bupirimate dissipates relatively rapidly from the water phase by partition to the sediment, and is moderately persistent in the whole water/sediment system. Bupirimate is persistent in soil with DT50 (half-life) 35 to 90 days. 165 d). Ethirimol is stable to hydrolysis at pH 5, 7, and 9. Aqueous photolysis is rapid. Another major metabolite is de-ethylated bupirimate (5-butyl-2-amino-6-methylpyrimidin-4-yl dimethyl sulphamate).

Solubility in water:

* 102 mg/L at 20°C (pH 4)
* 13 mg/L at 20°C (pH 7)
* 22.6 mg/L at 20°C (pH 9).

### Typical concentrations in drinking-water

Bupirimate is not expected to leach to groundwater.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

Direct injection into HPLC-MS/MS; EFSA (2010).

### Health considerations

The Acceptable Daily Intake (ADI) for bupirimate adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw.

IUPAC quotes an ADI of 0.05 mg/kg bw, and an acute reference dose (ARfD) of 0.05 mg/kg/d. NZFSA also quote an ADI of 0.05 mg/kg bw.

The Acceptable Daily Intake (ADI) of bupirimate is 0.05 mg/kg bw/day based on the two-year dog study, with a Safety Factor (SF) of 100. Based on the toxicological profile of bupirimate no ARfD was deemed necessary. For ethirimol, the ADI is 0.035 mg/kg bw/day, based on the two-year rat study and applying a SF of 100. Again, no ARfD was needed (EFSA 2010/2014).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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IUPAC. Accessed 2009. *Bupirimate* (Ref: PP 588). See: [http://sitem.herts.ac.uk/aeru/iupac/Reports/99.htm#none](http://sitem.herts.ac.uk/aeru/iupac/Reports/99.htm%23none)

# Buprofezin

CAS No. 953030-84-7. The IUPAC name for buprofezin is (Z)-2-tert-butylimino-3-isopropyl-5-phenyl-1,3,5-thiadiazinan-4-one. The CAS name is (Z)-2-[(1,1-dimethylethyl)imino]tetrahydro-3-(1-methylethyl)-5-phenyl-4H-1,3,5-thiadiazin-4-one. The name buprofezin was originally approved for a mixture of (E)- and (Z)-isomers [69327-76-0], but in 2008 the sponsor determined that the substance contains only the (Z)-isomer and requested that the definition be changed.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for buprofezin, WHO do not mention buprofezin in their Guidelines.

### Sources to water

Buprofezin, a thiadiazine insecticide, is used to control red scale and white louse scale, jassids (leafhoppers) as well as longtailed mealybugs, citrus mealybugs and citrophilous mealybugs in citrus crops. It is used in New Zealand to control mealy bugs on grapes. Buprofezin exerts its insecticidal effect through inhibition of chitin synthesis, a key component of insect body armour.

Buprofezin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Buprofezin was one of the agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes in lettuce.

In Japan the average annual environmental guideline for buprofezin in public waters is 0.01 mg/L.

### Forms and fate in the environment

Buprofezin has low to slight soil mobility and did not show any significant leaching in soil with a low organic matter content. There were no mobile degradation products seen in any significant quality and buprofezin is classified as an unlikely leacher. A field dissipation study in a rice paddy showed that buprofezin residues in the aquatic systems rapidly dissipated.

Buprofezin was stable in pH 7 and 9 aqueous buffer solutions. The half-life was estimated to be 51 days in a pH 5 buffer solution. Buprofezin, aged under aerobic conditions for 30 days, was not mobile in columns of loamy sand soil, and was slightly mobile in columns of sandy loam soil leached with distilled water. The half-life in aerobic soil was 37 to 101 days.

EFSA (2015) states that buprofezin was shown to significantly degrade to metabolites BF25 (up to 43 percent applied radioactivity (AR)), BF12 (up to 31 percent AR) and to aniline (up to 19 percent AR) under standard hydrolysis conditions.

Solubility in water: 0.38 mg/L at 25°C.

### Typical concentrations in drinking-water

Not likely to be found in groundwater.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See APVMA (2001).

### Health considerations

Specific studies indicated that buprofezin does not damage genetic material. Additionally, long-term exposure studies in mice, rats and dogs indicated that buprofezin does not cause cancer. There were no effects on reproductive behaviour or performance in rats and at doses which were not toxic to the mother, there were no developmental effects on the rat or rabbit foetus.

The lowest overall NOELs for buprofezin were 1 mg/kg bw/day established in a two-year rat study, based on increased kidney and heart weights and thickening and hyperplasia of thyroidal epithelial cells, and 0.9 mg/kg bw/day in a two generation reproduction study in rats, based on maternotoxicity and foetotoxicty at the next highest dose. A safety factor of 100 is considered appropriate for the ADI, due to the extensive, good quality toxicology database for buprofezin. This results in an ADI of 0.01 mg/kg bw/day, APVMA (2001). The Acceptable Daily Intake (ADI) adopted in Australia is also 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

USEPA (2001) quotes an acute RfD of 2.0 mg/kg/d, and a chronic RfD of 0.01 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0033 mg/kg/d, and an ARfD of 2.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for buprofezin is 66 mg/L.

On the basis of an adequate range of suitably conducted tests of genotoxicity both in vitro and in vivo, there is no evidence that buprofezin is genotoxic. The toxicological database on the carcinogenicity and genotoxicity of buprofezin is sufficient for setting reference values (EFSA 2007). As at September 2008 the USEPA considered there was suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.

The 2008/2012/2014/2016 JMPR Meetings established an ADI of 0–0.009 mg/kg bw based on a NOAEL of 0.9 mg/kg bw per day in the two-year study in rats, identified on the basis of increases in the incidence of thyroid F-cell hypertrophy at 8.71 mg/kg bw per day. A safety factor of 100 was applied. The difference between the current ADI and the previous ADI of 0.01 mg/kg bw per day is due to rounding of the figures; both ADIs were based on the same NOAEL from the same study. The meeting established an ARfD of 0.5 mg/kg bw based on a NOAEL of 50 mg/kg bw identified on the basis of ataxia at 300 mg/kg bw per day in a 13-week feeding study in dogs. A safety factor of 100 was applied. This ARfD would also be protective against the finding of enlarged aortic arches in rabbit fetuses, although this effect is unlikely to be the result of a single dose (FAO/WHO 2008). FAO/WHO (2013) and EFSA (2015) reaffirmed the ADI and ARfD values.

### Derivation of Maximum Acceptable Value

No MAV.

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# Captan

CAS No. 133-06-2. The IUPAC name for captan is N-(trichloromethylthio)cyclohex-4-ene-1,2-dicarboximide. The CAS name is 3a,4,7,7a-tetrahydro-2-[(trichloromethyl)thio]-1H-isoindole-1,3(2H)-dione. Has also been called 3a,4,7,7a-tetrahydro-N-(trichloromethanesulphenyl) phthalimide and N-trichloromethylmercapto-4-cyclohexenel,2-dicarboximide.

Captan is also a common name for [ethanethiol](http://en.wikipedia.org/wiki/Ethanethiol) or ethyl mercaptan, used as an odourant for [natural gas](http://en.wikipedia.org/wiki/Natural_gas) and liquid[;](http://en.wikipedia.org/wiki/Propane) this is not the same chemical.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for captan, WHO do not mention captan in their Guidelines.

The USEPA concluded on 22 September 2009 that captan is known or anticipated to occur in PWSs and may require regulation. Therefore they added captan to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Captan is a general use, non-systemic, broad spectrum phthalimide, or cyclic imide, or sulfenimide, [fungicide](http://en.wikipedia.org/wiki/Fungicides). Though it can be applied on its own, captan is often added as a component of other pesticide mixtures. It is used to control diseases on a number of [fruits](http://en.wikipedia.org/wiki/Fruits) and [vegetables](http://en.wikipedia.org/wiki/Vegetables) as well as [ornamental plants](http://en.wikipedia.org/wiki/Ornamental_plant) and nursery seedlings. It also improves the outward appearance of many fruits, making them appear brighter. Captan is used by home and agricultural growers and is often applied during apple production. It can also be used for seed treatment, as a pre-plant application to the soil, and for post-harvest application. Other uses include as an agent therapeutic agent against fungal infections of the skin.

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 46.6 tonnes of captan were used in New Zealand in 2004, at an application rate of 5760 grams of active ingredient per hectare. Captan was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in lettuce and strawberries.

Captan was phased out of general use as a pesticide in the United States in 1989.

Technical captan is usually 90 to 95 percent pure. Tetrahydrophthalimide (4‑cyclohexene-1,2-dicarboximide) is the main impurity.

### Forms and fate in the environment

Under aerobic aquatic conditions, the half-life of captan is from less than 1 day to 10 days depending on soil type. The calculated half-life of tetrahydrophthalimide (the major metabolite of captan) is up from 7 to 20 days. Captan is not very mobile, solubility in water is about 3 mg/L. Tetrahydrophthalimide has the potential to reach groundwater, but is not expected to be persistent.

Under aerobic aquatic conditions, the half-life of captan is less than one day. The calculated half-life of THPI is seven days (NPIC).

NPIC (1994) quotes for captan a soil half-life of 2.5 days, water solubility of 5.1 mg/L and a sorption coefficient (soil Koc) of 200. This resulted in a pesticide movement to groundwater rating of very low.

### Removal methods

Oxidation processes show promise, but chlorine needs to used at very high dosage; ozone and newer advanced oxidation processes are probably more realistic.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Technical grade captan is low in toxicity when ingested by both rats and mice with oral LD50 values of >9,000 mg/kg and >7,000 mg/kg, respectively.

In 1984, JMPR established an ADI of 0–0.1 mg/kg bw based on a NOAEL of 12.5 mg/kg bw per day in studies of reproductive toxicity in rats and monkeys. This ADI was confirmed by JMPR in 1995. In 2004, the meeting established an ARfD of 0.3 mg/kg bw, for women of childbearing age only, based on a NOAEL of 30 mg/kg bw per day for increased incidences of intrauterine deaths and malformations at 100 mg/kg bw per day in the study in rabbits and a safety factor of 100. The meeting concluded that the database was insufficient, particularly with regard to information about the possible developmental effects of the metabolite 1,2,3,6-tetrahydrophthalimide (THPI), to establish the mode of action by which the increased incidences of intra-uterine deaths and foetuses with malformations were induced.

The oral RfD was calculated at 0.13 mg/kg/d (USEPA 1989). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.13 mg/kg/d, and an ARfD of 0.10 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for captan is 3.30 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw from a short-term (developmental toxicity) study in rabbits. The NOEL is based on decreased bodyweight and food consumption in dams and associated foetotoxicity at 30 mg/kg bw/day and above. The ADI incorporates a safety factor of 100. The ARfD is 0.1 mg/kg bw based on a NOEL of 10 mg/kg bw/day from a developmental study in rabbits. The ARfD incorporates a safety factor of 100. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EC (2008) derived an ADI (acceptable daily intake) and ARfD (acute reference dose) of 0.1 mg/kg/d. The EC review established that for the active substance notified by the main data submitters the manufacturing impurities perchloromethylmercaptan, folpet and carbon tetrachloride are of toxicological concern and must not exceed maximum levels of 5 g/kg, 10 g/kg and 0.1 g/kg respectively in the technical material.

EFSA (2011, 2013 and 2014) quotes an ADI of 0.1 mg/kg/d and an ARfD of 0.3 mg/kg bw, as the “sum of captan and tetrahydrophthalimide (THPI), expressed as captan”.

Captan was tested for carcinogenicity in mice and rats by administration in the diet. It was carcinogenic to one strain of mice, inducing duodenal tumours (adenocarcinoma and adenomatous polyp). No evidence of carcinogenicity was found in rats, and the available data are insufficient to evaluate the carcinogenicity of captan to humans, ie, Group 3 (IARC 1983). This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

In 1998 the USEPA assigned captan a carcinogenicity classification of B2, a probable human carcinogen, but changed this in 2004 to “likely carcinogen at prolonged high-level exposures, but not likely at dose levels that do not cause cytotoxity and regenerative cell hyperplasma”. The USEPA has also determined that there is no risk concern from the consumption of captan residues in drinking water. Tetrahydrophthalimide has about four times the toxicity in mammals, but is considered non-carcinogenic.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for captan since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Carbaryl

CAS No. 63-25-2. The IUPAC name for carbaryl is 1-naphthyl methylcarbamate. The CAS name is 1-naphthalenyl methylcarbamate. Sevin is a common trade name.

### Maximum Acceptable Value

No MAV. WHO (2006) states that carbaryl does not appear to be found in drinking at significant concentrations and so it is not considered necessary to propose a guideline value. WHO (2017) states that carbaryl occurs in drinking-water at concentrations well below those of health concern.

A health-based value of 0.05 mg/L has been established in WHO (2017).

The maximum acceptable concentration in Canada is 0.09 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.03 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Carbaryl is a broad spectrum carbamate insecticide, molluscicide and acaricide that is used to control insect pests in crops, trees and ornamental plants. It is used in New Zealand to control over 100 different pests on fruit trees, vegetables, ornamentals, lawns and to control wasp nests. It is also used as a veterinary medicine in combination with other actives.

Formulations containing carbaryl have been registered for use in New Zealand since 1963. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 16 tonnes of carbaryl were used in New Zealand in 2004, at an application rate of 7,200 grams of active ingredient per hectare. From 1 July 2015, only approved handlers will be able to apply carbaryl.

Carbaryl was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL apricots and strawberries.

Carbaryl should not contain more than 0.05 percent of 2-naphthol or 2-naphthyl methylcarbamate.

### Forms and fate in the environment

Carbaryl is hydrolysed in water, the rate depending on temperature and pH (half-life of 3.2 hours at pH 9 and 12.1 days at pH 7, 1600 days at pH 5 ), although at low concentrations it may be hydrolysed within hours under favourable conditions, particularly summer light. It adsorbs to soils with a high organic content but adsorption is much lower in sandy soils. At usual rates of application it rapidly dissipates, with a half-life of 1 month or less. A major metabolite is 1-naphthol.

Water solubility is about 40 mg/L at 30°C, its vapour pressure at 26°C is less than 0.7 Pa. The log octanol-water partition coefficient is reported to range from 2.31 to 2.86; therefore, carbaryl is not likely to bioaccumulate significantly. Carbaryl is moderately mobile in soils so may be found in groundwater (Health Canada 1991).

If released to soil, carbaryl is expected to have moderate mobility based upon measured Koc values of 230, 370, and 390. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 2.8 x 10-9 atm-cu m/mole. Carbaryl is not expected to volatilise from dry soil surfaces based upon its vapour pressure. Carbaryl is expected to photolyse slowly on surface soil at a rate dependent on the water content. Average biodegradation half-life of 10 days in four different soils suggests that biodegradation is an important environmental fate process in soil. If released into water, carbaryl is expected to adsorb to suspended solids and sediment based upon the Koc values. Carbaryl’s half-lifes in aquatic environments have been reported as 1.7 days in river water and 5.8 days in mountain streams. In raw seawater, carbaryl was biodegraded to undetectable levels within 96 hrs. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. BCF values of 34, 30, and 9 suggest bioconcentration in aquatic organisms is low. At 20°C, hydrolysis half-lifes of carbaryl in water are 10.5 days, 1.8 days, 2.5 hours, and 15 min at pH values of 7, 8, 9, and 10, respectively. In neutral and alkaline soils, carbaryl is expected to hydrolyse rapidly. In acidic soils, hydrolysis is expected to occur more slowly (EAWAG accessed February 2015).

NPIC (1994) quotes for carbaryl a soil half-life of 10 days, water solubility of 120 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of low.

USGS (2006) give the following values: log Kow = 2.36; log Koc (where Koc is in mL/g) = 2.36; water solubility = 120 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -4.35; half-life in aerobic soil = 17 days; half-life in water = 11 days.

### Typical concentrations in drinking-water

Carbaryl has not often been reported in drinking water, however, it could occur following overspraying or spillage into surface water. Exposure through drinking-water is, therefore considered to be low unless in exceptional circumstances. For example, carbaryl was not detected in 199 samples of treated municipal and private water supplies from all 10 Canadian provinces in 1985.

Seventeen water utilities in the US reported detecting carbaryl in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0009 mg/L.

### Removal methods

Available data indicate that granular activated carbon (GAC) adsorption, ozonation and coagulation treatment will remove carbaryl from water. The percentage removal efficiency ranges from 43 to 99 percent. A carbaryl concentration below 0.05 mg/L should be achievable by conventional drinking water treatment.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

WHO (2008) summarises a range a suitable methods.

### Health considerations

Carbaryl acts through inhibition of brain cholinesterase, and this is also its primary mode of toxicity.

The major route of carbaryl intake for the general population is food but residues are considered to be relatively low. However, NZFSA have found carbaryl in a high proportion of nectarines.

The oral reference dose or RfD (USEPA 1989/2006/2009/2011) is 0.01 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.4 mg/L.

The latest JMPR toxicological evaluation was carried out in 2001 when an ADI of  
0–0.008 mg/kg bw and ARfD of 0.2 mg/kg bw were established. This was based on a lowest-observed adverse-effect level (LOAEL) of 15 mg/kg body weight per day and application of a safety factor of 2,000 (10 for interspecies variation, 10 for intraspecies variation and 20 to reflect the occurrence of the rare and malignant tumour for which a no-effect level could not be identified). A health-based value of 0.05 mg/L (rounded value) can be determined from the JMPR ADI of 0–0.008 mg/kg body weight, assuming a 60 kg adult drinking two litres of water per day and allowing 20 percent of the upper limit of the ADI from drinking-water (WHO 2011).

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand is 0.008 mg/kg body weight, with a LOEL of 16 mg/kg bw observed in a two-year dietary study in mice. The ADI incorporates a safety factor of 2,000 and was established in 2002. There is an additional factor of 5 is for the inadequate database and an additional factor of 4 for the seriousness of the carcinogenic response. The ARfD is 0.01 mg/kg bw based on a no-observed-effective level (NOEL) of 1 mg/kg bw/day from a medium-term (13-week) and neurotoxicity study in rats, where there were behavioural indications of autonomic neurotoxicity and brain, plasma and erythrocyte cholinesterase depression. The ARfD incorporates a safety factor of 100.

Carbaryl is considered to be a non-genotoxic carcinogen in mice, in which it causes vascular tumours in males. IARC has placed carbaryl in Group 3: no evidence of human carcinogenicity. In February 2002 the USEPA classified carbaryl as likely to be carcinogenic to humans (USEPA 2008); previously it had been classified in Group C: a possible human carcinogen. The USEPA (2009/2011) quotes a health advisory of 4 mg/L for carbaryl, representing a 10-4 cancer risk.

The metabolite 1-naphthol is approved for use in oxidative hair dye formulations at a maximum concentration of 2.0 percent on the human head (EC 2008), so presumably is not particularly hazardous.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for carbaryl since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

A health-based value of 50 μg/l (rounded value) can be determined from the JMPR ADI of 0–0.008 mg/kg body weight, assuming a 60 kg adult drinking two litres of water per day and allowing 20 percent of the upper limit of the ADI from drinking water (WHO 2017).

WHO (2008) states that the ADI is 0.008 mg/kg body weight. (The Acceptable Daily Intake (ADI) adopted in Australia is also 0.008 mg/kg body weight, with a LOEL of 16 mg/kg bw.) A health-based value assuming a 60 kg adult drinking two litres of water per day and allowing 20 percent of the ADI from drinking water would be 0.05 mg/L (rounded value), or 0.06 mg/L for a 70 kg body weight (WHO 2017).

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# Carbofuran

CAS No. 1563-66-2. The IUPAC name for carbofuran is 2,3-dihydro-2,2-dimethylbenzofuran-7-yl-methylcarbamate. CAS name is 2,3-dihydro-2,2-dimethyl-7-benzofuranyl methylcarbamate.

### Maximum Acceptable Value

Based on health considerations, the concentration of carbofuran in drinking-water should not exceed 0.008 mg/L (8 g/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.04 mg/L. The maximum acceptable concentration in Canada for carbofuran is 0.09 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.01 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The USEPA (2009) concluded on 22 September that [3-hydroxycarbofuran](http://en.wikipedia.org/wiki/1,1,1,2-Tetrachloroethane) (a degradation product) is known or anticipated to occur in PWSs and may require regulation. Therefore they have added [it](http://en.wikipedia.org/wiki/1,1,1,2-Tetrachloroethane) to their CCL 3 (Drinking Water Contaminant Candidate List 3).

### Sources to water

Carbofuran, an N-methyl carbamate pesticide, may enter source waters as a result of its use on crops and seeds as a broad spectrum systemic acaricide, insecticide and nematocide. Carbofuran is also the predominant metabolite of carbosulfan (qv), in both soil and water.

The total annual usage of carbofuran in New Zealand in the late 1980s was 1180 kg, all of it in the North Island. Carbofuran does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). Nor does it appear in ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008.

However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). Since 2014 carbofuran is no longer able to be manufactured in or imported into New Zealand.

### Forms and fate in the environment

Carbofuran can dissipate from water by direct photolysis and photo-oxidation. It undergoes chemical and microbial degradation mainly through hydroxylation and hydrolysis. Carbofuran is primarily metabolised into three phenolic carbamate metabolites and into 3-hydroxy carbofuran. The trio of phenolic metabolites is not deemed to be of toxicological significance. For risk assessment purposes, 3‑hydroxycarbofuran is considered to be of equal toxicity as parent carbofuran (USEPA.2007). Carbofuran is mobile in soils and sediments. It has a half-life in soil ranging from 1 to 37 weeks; the recommended average half-life is seven weeks. Hydrolysis half-lives in water at 25°C of 690, 8.2 and 1.0 weeks have been reported for pH levels of 6.0, 7.0 and 8.0, respectively.

The water solubility is 350 mg/L (700 mg/L in Agrochemicals Handbook) and the sorption coefficient is 22 mL/g.

Health Canada (1991) states that carbofuran has a vapour pressure of 2.7 x 10-3 Pa at 33°C; its solubility in water is 700 mg/L at 25°C. Its log octanol-water partition coefficient is reported to range from 1.60 to 2.32, therefore, carbofuran is not likely to bioaccumulate significantly.

If released to soil, carbofuran is expected to have very high to high mobility based upon Koc values of 7.3 to 123. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 4.5 x 10-10 atm-cu m/mole. Carbofuran is not expected to volatilise from dry soil surfaces based upon its vapour pressure. The half-life of carbofuran in soil has been reported as 11-75 days. Experimental data indicate that carbofuran degrades faster in soil that has previously been treated with carbofuran or other pesticides. If released into water, carbofuran is not expected to adsorb to suspended solids and sediment based upon the Koc values. Carbofuran dissipation from paddy water was rapid with an estimated half-life of three days and a 95 percent removal time of 13 days; dissipation was due to both hydrolysis and biodegradation. The aqueous hydrolysis half-life at 27°C was found to be 5.1 weeks at pH 7.0 and 1.2 hours at pH 10. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. A BCF of 117 using Tilapia nilotica suggests bioconcentration in aquatic organisms is high. The half-lifes for degradation of carbofuran in river, lake, and seawater following irradiation with sunlight were approximately 2, 6, and 12 hours, respectively; it was not reported whether the degradation was due to direct photolysis, indirect photooxidation or other processes (EAWAG accessed February 2015).

NPIC (1994) quotes for carbofuran a soil half-life of 50 days, water solubility of 351 mg/L and a sorption coefficient (soil Koc) of 22. This resulted in a pesticide movement to groundwater rating of very high.

USGS (2006) give the following values: log Kow = 2.32; log Koc (where Koc is in mL/g) = 2.02; water solubility = 351 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -4.30; half-life in aerobic soil = 11 days; half-life in water = 289 days.

### Typical concentrations in drinking-water

No data are available on the concentration of carbofuran in New Zealand drinking-water supplies.

Studies from the USA have found groundwater concentrations of carbofuran up to 0.03 mg/L. Typical detectable concentrations were in the 0.001 to 0.005 mg/L range. Nineteen water utilities in the US reported detecting carbofuran in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0025 mg/L.

Carbofuran was detected only once (at 0.003 mg/L) in 678 samples from surveys of Canadian municipal and private water supplies conducted from 1971 to 1986.

### Removal methods

Carbofuran has been found to decompose at high pH levels, such as during high pH softening. Hydrolysis products are produced. Alum coagulation does not remove carbofuran from water, but granular activated carbon should be able to control its concentration down to g/L levels. The newer advanced oxidation processes are effective. Reverse osmosis is expected to be effective in removing carbofuran from water.

### Recommended analytical techniques

#### Referee method

Reverse Phase High Performance Liquid Chromatography (EPA 531.).

#### Some alternative methods

Separation by HPLC, hydrolysis with sodium hydroxide, extraction of the resulting methylamine with o-phthalaldehyde and fluorescence detection of the derivative (detection limit 0.0009 mg/L). The concentration of carbofuran may also be quantified by acidification of the sample, extraction with dichloromethane and separation by gas chromatography with a nitrogen–phosphorus detector (detection limit 0.0001 mg/L).

### Health considerations

Residues in treated crops are generally very low or not detectable. The physicochemical properties of carbofuran and the few data on occurrence indicate that drinking-water from both groundwater and surface water sources is potentially the major route of exposure (WHO 2017).

Animal studies indicate that carbofuran is absorbed rapidly and metabolised by hydroxylation and/or oxidation reactions. Elimination of carbofuran is rapid, via urine.

Symptoms of carbofuran poisoning in humans resemble parathion intoxication except for diminished intensity and duration, particularly of the central nervous system. Carbofuran is highly toxic after a single oral dose. In a case of acute intoxication in a woman with a total dose of 60 mg carbofuran, slight cholinesterase inhibition was found, but the patient recovered completely within 72 hours.

Several cases of adverse effects have been reported in individuals involved in the application and formulation of carbofuran. Symptoms included mild and reversible symptoms of acetylcholinesterase depression, such as malaise, hypersalivation, and vomiting. Symptoms following more severe poisoning included chest tightness, muscular twitching, convulsions and coma.

Human volunteers administered 0.1 mg /kg body weight carbofuran orally showed symptoms of acetyl-cholinesterase depression, including salivation, diaphoresis (sweating), abdominal pain, drowsiness, dizziness, anxiety and vomiting. No symptoms were observed in volunteers administered 0.05 mg/kg body weight.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.00006 mg/kg/d. The risk assessment for carbofuran is based on BMD values, rather than No Observed Adverse Effect Level (NOAEL) or LOAEL values (USEPA 2007). The BMDL10 of 0.03 mg/kg/day for inhibition of ChE in the brain of PND11 male pups was selected for derivation of the acute RfD. A chronic RfD was not selected because the acute RfD is considered protective of chronic exposures, given that carbofuran-induced inhibition of ChE activity is reversible (within 24 hours). The oral RfD had previously been 0.005 mg/kg/d (USEPA 1987).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.003 mg/kg body weight, with a NOEL of 0.33 mg/kg bw from a one-year dietary study in dogs. This NOEL is based on inhibition of brain cholinesterase and histopathological effects. The ADI incorporates a safety factor of 100.

A periodic review of the toxicology of carbofuran was carried out by the 1996 JMPR. An ADI of 0–0.002 mg/kg bw was established. In 2002, an ARfD of 0.009 mg/kg bw was established. The 2008 JMPR evaluated newly submitted studies on acute toxicity and re-examined relevant data which had been considered by previous meetings. The 2008 meeting established an ARfD of 0.001 mg/kg bw. The meeting noted that this ARfD was lower than the current ADI of 0–0.002 mg/kg bw. The meeting concluded that the ADI and ARfD for carbofuran should be based on the same NOAEL and revised the ADI to 0–0.001 mg/kg bw (FAO/WHO 2008, 2013 and JMPR 2012).

EFSA (2014) quotes an ADI of 0.00015 mg/kg bw/d and an ARfD of 0.00015 mg/kg bw.

The International Agency for Research on Cancer has not evaluated carbofuran. As at September 2008, the USEPA has classified carbofuran as “not likely to be carcinogenic to humans”. Carbofuran does not have mutagenic activity.

Carbofuran is highly toxic after acute oral administration. The main systemic effect of carbofuran poisoning in short-term and long-term toxicity studies appears to be cholinesterase inhibition. No evidence of teratogenicity has been found in reproductive toxicity studies. On the basis of available studies, carbofuran does not appear to be carcinogenic or genotoxic (WHO 2011).

USEPA (2015) found that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for carbofuran since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

In the 1996 JMPR re-evaluation, an ADI of 0.002 mg/kg of body weight was determined based on a NOAEL of 0.22 mg/kg of body weight per day in a short-term (four-week) study of acute (reversible) effects in the dog, the most sensitive species, using an uncertainty factor of 100. This four-week study was conducted as an adjunct to a 13-week study in which inhibition of erythrocyte acetylcholinesterase activity was observed at the lowest dose. Use of a four-week study was considered appropriate because the NOAEL is based on a reversible acute effect. This NOAEL will also be protective for chronic effects (FAO/WHO 1997).

The MAV for carbofuran in drinking-water was derived as follows:

0.22 mg/kg body weight/day x 70 kg x 0.1 = 0.0077 mg/L (rounded to 0.008 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 0.22 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100.

In the 1995 datasheet and 1995 DWSNZ, the MAV had been derived as follows:

0.05 mg/kg body weight/day x 70 kg x 0.1 = 0.006 mg/L (rounded to 0.008 mg/L)

2 L/day x 30

where:

* no-observable-adverse-effect level = 0.05 mg/kg body weight per day based on inhibition of acetylcholinesterase
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 30 (10 for intra-species variation and 3 for the steep dose-response curve.

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# Carbosulfan

CAS No. 55285-14-8. The IUPAC name for carbosulfan is 2,3-dihydro-2,2-dimethylbenzofuran-7-yl (dibutylaminothio)methylcarbamate. The CAS name is 2,3‑dihydro-2,2-dimethyl-7-benzofuranyl [(dibutylamino)thio]methylcarbamate.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for carbosulfan, and WHO does not mention carbosulfan in their Guidelines.

### Sources to water

Carbosulfan is called a broad spectrum benzofuranyl methylcarbamate insecticide, or a carbamate nematicide. Carbosulfan is closely related to its main metabolite carbofuran, a major pesticide in its own right (qv). Carbosulfan is used to control soil and foliar pests in a variety of commodities. It may be applied to soil or foliage and is said to be effective through direct contact or stomach ingestion. Foliar pests may be controlled by soil applications via systemic action, although most of the systemic activities is not due to carbosulfan per se. It is also registered for seed treatment.

Carbosulfan does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals – likewise re Pesticides). Since 2014 carbosulfan is no longer able to be manufactured in or imported into New Zealand.

### Forms and fate in the environment

The fate of carbosulfan has been investigated in plants, animals, soil, water and light and in storage under a variety of conditions. In general, carbosulfan, carbofuran, 3‑hydroxycarbofuran and 3-ketocarbofuran are the principle carbamate residues in plants with relative amounts varying from crop to crop and with time. Phenolics and dibutylamine contribute an analytically significant part of the total residue. Carbofuran was shown to be the major residue in aged soil. Soil studies have confirmed the low potential for carbosulfan leaching but substantial degradation to and elution of its metabolites, primarily carbofuran.

The water solubility of carbosulfan is about 0.3 mg/L (JMPR 2003 quoted 3 mg/L). The hydrolysis rate of carbosulfan in water in the dark, buffered at pH 5, 7 and 9 and unbuffered, has been investigated. Half-lifes were 0.2, 11.4 and 18.2 hours at pH 5, 7 and 9 respectively. Carbofuran was the main product from carbosulfan at pH 5 and 7.

### Typical concentrations in drinking-water

Thirty water utilities in the US reported detecting 3-hydroxycarbofuran in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.005 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The estimate of acceptable daily intake for man is 0–0.01 mg/kg bw (IPCS 1986). The long-term intake ADI was still 0.01 mg/kg in 2003 (FAO 2003). The levels in the diet causing no toxicological effect were:

* mice: 1.3 mg/kg b.w./day
* rats: 1.0 mg/kg b.w./day
* dogs: 1.25 mg/kg b.w./day.

Carbosulfan is a cholinesterase inhibitor.

The oral RfD was calculated at 0.01 mg/kg/d (USEPA 1988).

The Acceptable Daily Intake (ADI) adopted in Australia for carbosulfan is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg.

JMPR (2003) states that the carbofuran residue is defined as carbofuran + 3‑hydroxycarbofuran, for compliance with MRLs, and carbofuran + 3‑hydroxycarbofuran + conjugated 3-hydroxycarbofuran, for dietary risk assessment. The ADI for carbosulfan is 0–0.01 mg/kg body weight/day, and the acute RfD for carbosulfan is 0.02 mg/kg.

EFSA (2014) quotes an ADI of 0.005 mg/kg bw/d and an ARfD of 0.005 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# Carboxin

CAS No. 5234-68-4. The IUPAC name for carboxin is 5,6-dihydro-2-methyl-1,4-oxathiine-3-carboxanilide. The CAS name is 5,6-dihydro-2-methyl-N-phenyl-1,4-oxathiin-3-carboxamide.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for carboxin, and WHO does not mention carboxin in their Guidelines.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.7 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.3 mg/L; excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Carboxin, a systemic anilide fungicide, is often used in combination with other fungicides such as thiram or captan, often as a seed treatment on corn and wheat.

Carboxin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Carboxin is rapidly degraded to carboxin sulfoxide in soil. It has a low persistence, with a half-life of about three days in soil. In one study after seven days, 95 percent of the parent was gone and the sulfoxide, a breakdown product, represented 31 to 45 percent of the amount applied. Minor products formed were carboxin sulfone, hydroxy carboxin, and CO2. Carboxin does not readily adsorb to soil. Both parent and sulfoxide are very mobile and could possibly leach to groundwater.

The water solubility of carboxin is about 170 mg/L. In water, carboxin oxidises to the sulfoxide and sulfone within seven days. This happens both under ultraviolet light and in the dark. Blue-green algae like Anabaena and Nostoc degrade the pesticide extensively. Other algae can also break down carboxin, but not to the same extent.

NPIC (1994) quotes for carboxin a soil half-life of three days, water solubility of 195 mg/L and a sorption coefficient (soil Koc) of 260. This resulted in a pesticide movement to groundwater rating of very low.

However, EFSA (2017) considers carboxin has a field DT90 was greater than 100 days, indicating that carboxin is persistent in the soil.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Beagle dogs showed no effects at the highest dose tested, 15 mg/kg for two years. Carboxin does not appear to cause cancer, and does not appear to be teratogenic.

The USEPA (2004) human heath risk assessment indicates no risks of concern. No toxicological endpoint attributable to a single oral dose was identified. Therefore, no acute dietary risk assessment was performed. Chronic risks from food are below the Agency’s level of concern. Chronic dietary exposure from drinking water from ground water or surface water sources are low and not of concern. Carboxin is classified as “not likely to be carcinogenic to humans”.

The reference dose or RfD (USEPA 1989/2006/2009/2011) is 0.1 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 3.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for carboxin is 0.08 mg/kg body weight, with a NOEL of 8.5 mg/kg from a long-term (two-year) dietary study. The NOEL is based on liver effects in mice. The ADI incorporates a safety factor of 100.

EFSA (2017) report an ADI of 0.008 mg/kg/d and that an ARfD is not necessary.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Carfentrazone-ethyl

CAS No. 128639-02-1. The IUPAC name for carfentrazone-ethyl is ethyl (RS)-2-chloro-3-{2-chloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorophenyl}propionate. The CAS name is ethyl α,2-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]-4-fluorobenzenepropanoate. Carfentrazone-ethyl is a derivative of [carfentrazone](http://www.alanwood.net/pesticides/carfentrazone.html), CAS No. 128621-72-7.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for carfentrazone-ethyl, and WHO does not mention it in their Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Carfentrazone-ethyl is a post-emergence triazolone (triazolinone) herbicide, commonly used on cereals to control broadleaf weeds. This chemical controls weeds through the process of membrane disruption which is initiated by the inhibition of the enzyme protoporphyrinogen oxidase. In plants, this inhibition interferes with the chlorophyll biosynthetic pathway. Carfentrazone-ethyl is also used for desuckering grapevines.

Carfentrazone-ethyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Carfentrazone-ethyl breaks down rapidly in the environment very low to medium persistence, while its degradates (the main one is carfentrazone-ethyl chloropropionic acid) are persistent in aquatic and terrestrial environments. Because of its low application rate, carfentrazone-ethyl residues are expected to occur at low levels in surface water and groundwater.

Carfentrazone-ethyl is immobile in loamy sand, sandy clay loam and silt loam soils, and breaks down in two to five days. Its half-life in water is about eight days.

The potential for groundwater exposure from the representative uses by carfentrazone-ethyl and its metabolites F8426-propionic acid and 3-hydroxymethyl-F8426-propionic acid above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all the relevant FOCUS groundwater scenarios (EFSA 2016).

The water solubility of carfentrazone-ethyl is about 12 mg/L at 20°C, and about 22 mg/L at 25°C.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In mammals, the inhibition of the enzyme protoporphyrinogen oxidase interferes with the heme biosynthetic pathway and results in alterations in haematological profiles and/or in increased urinary porphyrin levels and hepatotoxicity following long-term dosing. Repeat-dose studies indicate that the primary targets for carfentrazone-ethyl toxicity are the liver, kidney, and the red blood cell forming system.

The USEPA (2004) established a RfD for carfentrazone-ethyl of 0.03 mg/kg/day based on a two–year chronic toxicity/carcinogenicity study in rats with a threshold NOAEL of 3 mg/kg/day and an uncertainty factor of 100. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.03 mg/kg/d, and an ARfD of 5.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for carfentrazone-ethyl is 50 mg/L.

The lowest overall NOEL for carfentrazone-ethyl was 3 mg/kg bw/day. This NOEL was established in the two-year rat study, based on pigment deposition, red fluorescence and histopathological changes in the liver of rats at the next highest dose. A safety factor of 100 is considered appropriate for the ADI, due to the extensive, high quality toxicology database for carfentrazone-ethyl. This results in an ADI of 0.03 mg/kg bw/day (NRAAVC 2000).

The Acceptable Daily Intake (ADI) adopted in Australia for carfentrazone-ethyl is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg from a long-term (two-year) study in rats. The NOEL is based on red fluorescence seen in the female liver at the next highest dose of 12 mg/kg bw/day. The ADI incorporates a safety factor of 100.

EFSA (2012) stated that the toxicological profile of carfentrazone-ethyl was already evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI being established at 0.03 mg/kg bw per d. An ARfD was not deemed necessary. Reaffirmed 2016.

Carfentrazone-ethyl is proposed to be classified as carcinogenic category 2 and not as toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008 (EFSA 2016). Specific reference values (ADIs) were set on the basis of the 28‑day toxicity study in rats where the top dose level tested is the NOAEL, ie, ADIs of 0.0054, 0.0014, 0.00036, 0.0085 and 0.012 mg/kg bw per day for F8426-benzoic acid, F8426-propionic acid, F8426-α-sulfo-deschloropropionic acid, methoxy-F8426-despropionate and F8426-dicarboxylic acid, respectively. An UF of 1,000 was applied to derive the ADIs. A specific ADI of 0.01 mg/kg bw per day was set for metabolite 3‑hydroxymethyl-F8426-benzoic acon the basis of the 28-day toxicity study in rats where the top dose level tested, ie, 10 mg/kg bw per day is the NOAEL.

Carfentrazone-ethyl is not carcinogenic, neurotoxic or mutagenic and is not a developmental or reproductive toxicant (USEPA 1998).

USEPA (2004) state: Using the Guidelines for Carcinogen Risk Assessment, carfentrazone-ethyl should be classified as Group E for carcinogenicity – no evidence of carcinogenicity – based on the results of carcinogenicity studies in two species. There was no evidence of carcinogenicity in an 18-month feeding study in mice and a two–year feeding study in rats at the dosage levels tested. The doses tested are adequate for identifying a cancer risk. Thus, a cancer risk assessment is not necessary.

### Derivation of Maximum Acceptable Value

No MAV.

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# Chloralose

CAS No. 15879-93-3. The IUPAC name for chloralose is (R)-1,2-O-(2,2,2-trichloroethylidene)-α-D-glucofuranose. The CAS name is 1,2-O-[(1R)-2,2,2-trichloroethylidene]-α-D-glucofuranose. Sometimes called glucochloralose, alpha-chloralose, alpha-D-glucochloralose, alpha-D-glucofuranose, α-dextrochloralose and chloroalosane.

The commercial product comprises about 85 percent α-chloralose and 15 percent β‑chloralose; only the α-form is hypnotic/toxic. A trade name is pestoff.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for chloralose, and WHO does not mention it in their Guidelines.

### Sources to water

Chloralose, a [chlorinated](http://en.wikipedia.org/wiki/Chlorine) [acetal](http://en.wikipedia.org/wiki/Acetal) derivative of [glucose](http://en.wikipedia.org/wiki/Glucose), is used in various baits as a bird repellent and a rodenticide. It is also used (since 1893) in neuroscience and veterinary medicine as an [anaesthetic](http://en.wikipedia.org/wiki/Anesthetic) (hypnotic) and [sedative](http://en.wikipedia.org/wiki/Sedative). To kill animals the bait usually contains 10–15 percent chloralose; for anaesthetic purposes the baits usually contain <2 percent. It is generally used in urban or indoor situations.

Chloralose appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Nelson (1994) discusses its use in New Zealand. O’Hare et al (2007) discuss its use in the US.

### Forms and fate in the environment

Chloralose metabolises to glucose and chloral hydrate (trichloroacetaldehyde, qv) which can then break down to trichloroethanol.

Chloralose remains potent in baits for at least a month. The solubility and mobility are believed to be moderate, and environmental persistence is believed to be low. Bioaccumulation in plants and animal tissue is believed to be low. The alpha isomer is stable in sunlight.

The water solubility of chloralose is quite high in hot water, 4,400 mg/L in cold water. The octanol-water partition coefficient at pH 7, 20oC is 1.02. It is non-volatile.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

This toxin metabolises in the body to chloral, which in turn is converted largely to trichloroethanol which anesthetises the cortical centres of the brain; retarding metabolic processes, reducing blood pressure, lowering the body temperature, and rendering the dosed animal immobile and in coma-like state. The hypothermic effect is more marked on smaller animals due to their greater body surface to volume ratio. Recovery is possible for sub-lethally dosed animals, but over-dosage results in death. In humans there are reports that chloralose is not metabolised in the body but excreted mainly unchanged, and the features of over-dosage include generalised convulsions and coma (NSW Government 2013).

Due to its usage pattern and application, health risks due to chloralose are thought to be limited to the applicator. The chance of chloralose being found in drinking-water or source water is considered to be very limited.

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlorantraniliprole

CAS No. 500008-45-7. The IUPAC name for chlorantraniliprole is 3-bromo-4′-chloro-1-(3-chloro-2-pyridyl)-2′-methyl-6′-(methylcarbamoyl)pyrazole-5-carboxanilide. The CAS name is 3-bromo-N-[4-chloro-2-methyl-6-[(methylamino)carbonyl]phenyl]-1-(3-chloro-2-pyridinyl)-1H-pyrazole-5-carboxamide.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for chlorantraniliprole, and WHO does not mention it in their Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 6 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The following impurities which are of toxicological, ecotoxicological and/or environmental concern must not exceed a certain threshold in the material as technically manufactured (EC (2013):

* acetonitrile ≤3 g/kg
* 3-picoline ≤3 g/kg
* methanesulfonic acid ≤2 g/kg.

### Sources to water

Chlorantraniliprole is described as a selective anthranilic diamide or [pyrazole insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#pyrazole_insecticides), or ryanodine receptor agonist, first registered in 2008, which works by interrupting normal muscle contraction after ingestion by larvae. Despite its structural similarity to some of the phenylpyrazole insecticides, this substance has a different mode of action, which it shares with [cyantraniliprole](http://www.alanwood.net/pesticides/cyantraniliprole.html) (qv), and with [flubendiamide](http://www.alanwood.net/pesticides/flubendiamide.html), which appears not to be used in New Zealand.

Chlorantraniliprole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Often used on brassicas in New Zealand.

The impurities acetonitrile, 3-picoline and methanesulfonic acid are relevant impurities from the toxicological point of view, although at the level found in the technical specification they are considered to be of no concern (EFSA 2013).

### Forms and fate in the environment

Chlorantraniliprole may be characterised as persistent and mobile in terrestrial and aquatic environments. Extended chlorantraniliprole use is expected to cause accumulation of residues in soil from year to year. Major routes of dissipation are expected to be alkaline-catalysed hydrolysis, photodegradation in water, leaching, and run-off.

Unchanged parent chlorantraniliprole was the major identified residue in primary and rotational crops. See EFSA (2011) for metabolites. Soil studies demonstrated that the degradation rate of chlorantraniliprole is very slow; the maximum DT90 from field studies was higher than 1,000 days (EFSA 2013). Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 1.42 x 10-16 Pa.m3/mole.

The adsorption coefficients (Koc) in various soil types were reported to be between 153 and 509. These values suggest that chlorantraniliprole may have high mobility through some soils. In addition, chlorantraniliprole is persistent (soil half-lifes ranging from 228 to 924 days) and extended use is expected to cause accumulation of residues in soil from year to year, ex New York State (2009).

If released into water, chlorantraniliprole is expected to adsorb to suspended solids and sediment based upon the Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant.

The water solubility of chlorantraniliprole is about 0.9 mg/L. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination

### Removal methods

The strong adsorption in most soils suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of chlorantraniliprole in water. Granular activated carbon, and the newer advanced oxidation process would be probably effective too.

### Recommended analytical techniques

#### Referee method

No MAV. See JMPR.

### Health considerations

Chlorantraniliprole has a very low acute toxicity, acute oral toxicity LD50 of >5,000 mg/kg for the rat. Chlorantraniliprole was determined to be toxic only via the chronic oral exposure duration.

Chlorantraniliprole has been classified as a “not likely human carcinogen”. It is not expected to pose a cancer risk to humans. No reproduction toxicity was observed in a two-generation reproduction study with chlorantraniliprole in rats. In developmental toxicity studies in rats and rabbits, chlorantraniliprole exhibited no effects on any parameter in pregnant females or their offspring at levels up to and including the maximum tested dose of 1,000 mg/kg bw/day. The NOAEL for this study is 1,000 mg/kg/day.

In a chronic feeding/oncogenicity study in mice, the presence of eosinophilic foci accompanied by hepatocellular hypertrophy and increased liver weight were reported in males at a dose of 935 mg/kg/day; the no-observed-effect-level (NOEL) was 158 mg/kg/day. Chlorantraniliprole did not cause any effects in female mice at a dose level of 1,155 mg/kg/day, the highest dose tested. The USEPA Office of Pesticide Programs established a reference dose (RfD) for chlorantraniliprole of 1.58 mg/kg/day based on the NOEL from this study and an uncertainty factor of 100, ex New York State (2009). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 1.58 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for chlorantraniliprole is 11.1 mg/L (no acute one-day value available.)

The risk assessment did not quantify the risks from known degradates because they were commonly of lower toxic potency than the parent.

The Acceptable Daily Intake (ADI) adopted in Australia for chlorantraniliprole is 1.58 mg/kg body weight, with a NOEL of 158 mg/kg bw in an 18-month dietary study in mice. The NOEL is based on the appearance of eosinophilic foci accompanied by hepatocellular hypertrophy and increased liver weight. The ADI incorporates a safety factor of 100.

The JMPR 2008 Meeting established an acceptable daily intake (ADI) for chlorantraniliprole of 0–2 mg/kg bw on the basis of eosinophilic foci accompanied by hepatocellular hypertrophy and increased liver weight in mice in an 18-month feeding study for which the NOAEL was 158 mg/kg bw per day, and using a safety factor of 100. There was no available information on the chemical-specific mechanism of action with which to evaluate the relevance of the liver foci to exposure of humans. The meeting noted, however, that this is a possible species- and sex-specific response that is of questionable toxicological significance and relevance, and thus the NOAEL of 158 mg/kg bw per day (and consequently the ADI) identified on the basis of these end-points is likely to be conservative. The meeting concluded that it was not necessary to establish an acute reference dose (ARfD) for chlorantraniliprole in view of its low acute toxicity, the absence of developmental toxicity, and the absence of any other toxicological effects that would be likely to be elicited by a single dose (FAO/WHO 2008).

JMPR (2013 and 2016) reports an ADI of 0–2 mg/kg bw and that an ARfD was considered to be unnecessary.

EFSA (2013 and 2015) and EC (2013) quote an ADI of 1.56 mg/kg bw/day with an ARfD being not necessary.

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlordane

CAS No. 57-74-9; also allocated 12789-03-6. The IUPAC name for chlordane is 1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methanoindene. The CAS name is 1,2,4,5,6,7,8,8-octachloro-2,3,3a,4,7,7a-hexahydro-4,7-methano-1H-indene. IARC (1991) reviewed chlordane, technical-grade chlordane, cis-chlordane, trans-chlordane and γ-chlordane.

USEPA (1997) states:

CAS No. 57-74-9 refers to a mixture of chlordane isomers, other chlorinated hydrocarbons and numerous other components. For example, the mixture used by the National Cancer Institute in its 1977 bioassay was described as 94.8 percent chlordane (cis [or alpha]-chlordane, 71.7 percent; trans [or gamma]-chlordane, 23.1 percent) with heptachlor, 0.3 percent; trans-nonachlor, 1.1 percent; cis-nonachlor, 0.6 percent; chlordene isomers, 0.25 percent; 3 percent other compounds, and hexachlorocyclopentadiene, 0.25 percent.

CAS No. 12789-03-6 (technical chlordane) refers to a mixture of chlordane and chlordane related compounds having a lower percentage of the cis and trans isomers and a larger percentage of other compounds relative to mixtures with the above CAS number. Dearth and Hites (1991) identified 147 different compounds in a preparation of technical chlordane. The identity and percent of total for the 12 most abundant compounds were: cis-chlordane 15 percent; trans-chlordane 15 percent; trans-nonachlor 9.7 percent; octachlordane 3.9 percent; heptachlor 3.8 percent; cis-nonachlor 2.7 percent; “compound K” 2.6 percent; dihydrochlordene 2.2 percent; nonachlor III 2 percent; and three stereoisomeric dihydroheptachlors totalling 10.2 percent. These 12 compounds comprised 67 percent of the mixture, and the remaining 33 percent of the mixture consisted of 135 other compounds.

### Maximum Acceptable Value

Based on health considerations, the concentration of chlordane in drinking-water should not exceed 0.0002 mg/L (0.2 g/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.002 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.002 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects. Although there are no registered products that contain chlordane in Australia, de-registered compounds may still be detected in water.

Chlordane is one of the “priority pollutants” under the US Clean Water Act.

Chlordane is one of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention. See <http://chm.pops.int/>. Hence, monitoring may occur in addition to that required by drinking-water guidelines. Chlordane appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

### Sources to water

Chlordane, a chlorinated cyclodiene insecticide, may have entered source waters as the result of its application as a versatile broad-spectrum contact insecticide used mainly for non-agricultural purposes, first used in 1947. It has also been used in the timber preservation industry. Chlordane and heptachlor were considered together (IARC 1991) because of their close structural similarity and because technical-grade products each contain approximately 20 percent of the other compound. One description of the approximate composition of technical chlordane is as follows: trans-chlordane 24 percent; cis-chlordane 19 percent; chlordene isomers 21.5 percent; heptachlor 10 percent; nonachlor 7 percent; octachlorocyclopentene 1 percent; hexachlorocyclopentadiene 1 percent; other 16.5 percent (IARC 1991).

Chlordane is no longer registered for use of in New Zealand but it was used extensively in the past. Chlordane was designated as a persistent organic pollutant in 1997 by the Governing Council of the United Nations Environment Programme.

### Forms and fate in the environment

Chlordane is a mixture of isomers, mainly cis and trans chlordane. Technical chlordane contains at least 26 different compounds, including 60–75 percent chlordane isomers, heptachlor and nonachlor. Chlordane is very resistant to chemical and microbial degradation. It is very immobile and dissipation from soils is mainly due to volatilisation. The soil half-life is up to four years.

Chlordanes are unlikely to migrate to groundwater, where they have been found only rarely. Once in water bodies it is not removed by photodegradation, hydrolysis or biodegradation. The water solubility of chlordane is 0.1 mg/L.

NPIC (1994) quotes for chlordane a soil half-life of 350 days, water solubility of 0.06 mg/L and a sorption coefficient (soil Koc) of 20,000. This resulted in a pesticide movement to groundwater rating of extremely low.

USGS (2006) give the following values:

* **cis-chlordane:** log Kow = 6.0; log Koc (where Koc is in mL/g) = 5.5; water solubility = 0.056 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -0.466; half-life in aerobic soil = NA days; half-life in water = >7.2 x 107 days
* **trans-chlordane:** log Kow = 6.0; log Koc (where Koc is in mL/g) = 5.5; water solubility = 0.056 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -0.582; half-life in aerobic soil = NA days; half-life in water = >10,000 days
* **nonachlor:** log Kow = 5.66; log Koc (where Koc is in mL/g) = 4.86; water solubility = 0.06 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -1.69; half‑life in aerobic soil = NA days; half-life in water = NA days
* **oxychlordane:** log Kow = 2.6; log Koc (where Koc is in mL/g) = 2.48; water solubility = 200 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -1.52; half‑life in aerobic soil = NA days; half-life in water = NA days.

### Typical concentrations in drinking-water

Chlordane was not detected (<0.00004 mg/L, ie, <0.04 μg/L) in all of 230 samples from 212 supplies sampled in New Zealand between 1988 and 1992.

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of chlordane (limit of detection = 0.00001 mg/L) (ESR 2001).

In the United States, chlordane has been detected rarely in drinking water, and when found, concentrations were usually below 0.0001 mg/L.

Thirty-nine water utilities in the US reported detecting chlordane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, at 0.0005 mg/L. One water utility in the US reported detecting alpha chlordane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, at 0.00003 mg/L. One water utility in the US reported detecting gamma chlordane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, at 0.00003 mg/L.

### Removal methods

Specific information concerning the removal of chlordane from water is not available. However, its low solubility and attraction to soil particles makes it likely that some removal by chemical coagulation is possible. Isotherm adsorption data also indicate that removal by adsorption on to activated carbon should be possible; 0.1 μg/L should be achievable using GAC.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6630C).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

### Health considerations

Animal studies indicate that a portion of cis-chlordane ingested is absorbed. Chlordane and its metabolites, mainly oxychlordane, are distributed quickly throughout the body and stored at the highest levels in adipose tissue. Oxychlordane has been detected in adipose tissue of the general human population. Chlordane, mainly as oxychlordane, has been detected in human milk.

Chlordane is moderately toxic in acute exposure. In animals, acute exposure to chlordane produces ataxia, convulsions, respiratory failure and cyanosis.

In experimental animals, prolonged exposure in the diet causes liver damage. Chlordane produces liver tumours in mice, but the weight of evidence indicates that it is not genotoxic. Chlordane can interfere with cell communication in vitro, a characteristic of many tumour promoters.

Humans exposed accidentally to chlordane by inhalation or ingestion reported neurological symptoms, including headache, dizziness, vision problems, loss of coordination, irritability, excitability, weakness, muscle twitching and convulsions. Following ingestion of drinking-water contaminated with chlordane at concentrations of up to 1.2 g/L, 13 people showed gastrointestinal and/or neurological symptoms.

The chronic oral reference dose or RfD (USEPA 1997 and 2006/2009/2011) is 0.0005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.02 mg/L.

The Tolerable Daily Intake (TDI) adopted in Australia is 0.0005 mg/kg body weight based on a no-observed-effect level (NOEL) of 0.045 mg/kg bw/day from a 130-week dietary rat study. The NOEL is based on effects in the liver. The TDI incorporates a safety factor of 100, and was established in 2003. Previously, the acceptable daily intake (ADI) had been 0.0005 mg/kg bw/day.

The International Agency for Research on Cancer re-evaluated (in 1991) the evidence for carcinogenicity in humans associated with chlordane and heptachlor. Available studies were inadequate to evaluate an association between human exposure to chlordane/heptachlor and carcinogenicity. Chlordane was classified in Group 2B (possibly carcinogenic to humans) in 1987.

USEPA (1997) states that using the 1996 Proposed Guidelines for Carcinogen Risk Assessment, chlordane would be characterised as a likely carcinogen in humans. The USEPA (2009/2011) quotes a health advisory of 0.01 mg/L for chlordane, representing a 10-4 cancer risk.

Chlordane appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

As at July 2013 and February 2018 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for chlordane of:

* 0.001 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.0006 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0006 mg/kg/day for chronic-duration oral exposure (>364 days).

Chlordane is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

The Joint FAO/WHO Meetings on Pesticide Residues (JMPR) re-reviewed chlordane in 1986 and the results of this review have been used for the derivation of the MAV for chlordane in drinking-water. The no-observable-adverse-effect level used in the derivation is based on a long-term dietary study in rats for increased liver weights, serum bilirubin levels and incidence of hepatocellular swelling.

The MAV for chlordane (total isomers) in drinking-water was derived as follows:

0.05 mg/kg body weight/day x 70 kg x 0.01 = 0.000175 mg/L (rounded to 0.0002 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 0.05 mg/kg body weight per day based on a long-term dietary study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01
* uncertainty factor = 100 (for inter and intra-species variation).

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# Chlordecone

CAS No. 143-50-0. The IUPAC name for chlordecone is perchloropentacyclo[5.3.0.02,6.03,9.04,8]decan-5-one. The CAS name is 1,1a,3,3a,4,5,5,5a,5b,6-decachlorooctahydro-1,3,4-metheno-2H-cyclobuta[cd]pentalen-2-one. It has also been called decachlorotetracyclodecanone and decachloroketone. Also called kepone.

### Maximum Acceptable Value

Chlordecone is not mentioned by WHO, and does not have a MAV in the DWSNZ.

Chlordecone was added to the Persistent Organic Pollutants (POP) Stockholm Convention list in May 2009 (ICS 2009, <http://chm.pops.int/>).

### Sources to water

Chlordecone is a cyclodiene insecticide, with a common trade name of kepone. It was used on leaf-eating insects, ants and cockroaches, and as a larvicide for flies. Chlordecone production in the United States ended in 1975 after intoxication from severe industrial exposure was observed in employees who worked at the only chlordecone manufacturing plant in the country.

Chlordecone does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). Its use is banned in most countries, starting in the 1970s, but still used in some in the early 1990s. Chlordecone is also a contaminant in mirex formulations and is a degradation product of mirex (USEPA 2009). It is related to DDT. Hexachlorocyclopentadiene (qv) has been found at 0.1 percent of the technical product.

The Stockholm Convention meeting stated that: “chlordecone is a synthetic chlorinated organic compound, which was mainly used as an agricultural pesticide. It was first produced in 1951 and introduced commercially in 1958. Current use or production of the chemical is not reported”.

### Forms and fate in the environment

Chlordecone is very stable in the environment and has a high potential for bioaccumulation and biomagnification. Investigators have detected chlordecone in soil at a level of 0.02 μg/g of soil 12 years after an application rate of mirex of 1 μg/g.

No degradation products have been identified, although microbial action has been shown to transform chlordecone into monohydro- and possibly dihydrochlordecone. When released to soil, chlordecone will adsorb to soils. Some leaching to groundwater may occur. Chlordecone has a high potential for bioaccumulation in fish and other aquatic organisms. The half-life of chlordecone in a model river is 2.8 to 46 years. Water solubility is about 2.5–3 mg/L.

### Removal methods

Because it is strongly attracted to particles, coagulation processes should remove chlordecone fairly readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Chlordecone was an insecticide, and is also a ketone analogue and degradation product of mirex. Chlordecone absorption in humans has been demonstrated by the measurement of chlordecone concentrations in blood, subcutaneous fat, and other body fluids and tissues following subchronic occupational exposure, presumably through ingestion, inhalation, and dermal contact.

In its 1987 re-evaluation, IARC considered chlordecone is reasonably anticipated to be a human carcinogen based on sufficient evidence of carcinogenicity in experimental animals (Group 2B). Chlordecone impairs fertility and is foetotoxic. USEPA (2009) states that chlordecone is “likely to be carcinogenic to humans” based on data from an oral cancer bioassay in rats and mice demonstrating an increase in the incidence of hepatocellular carcinomas in both sexes of both species. There are no studies in humans that assess the carcinogenic potential of chlordecone.

The oral RfD for chlordecone was calculated (USEPA 2009) to be 0.0003 mg/kg/d, based on a BMDL10 of 0.08 mg/kg/d and an uncertainty factor of 300.

Chlordecone is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.01 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.0005 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0005 mg/kg/day for chronic-duration oral exposure (>364 days).

Kepone is one of the Substances from the Carcinogenic Potency Database which are of particular concern even if ingested at doses at or below 0.0025 μg/kg body weight per day (EFSA 2016).

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlorethephon

CAS No. 16672-87-0; seems also to have been allocated 82375-49-3. The IUPAC name for chlorethephon is 2-chloroethylphosphonic acid. The CAS name is (2‑chloroethyl)phosphonic acid. In most of the world this product is called ethephon. Also called 2-chloroethanephosphonic acid.

### Maximum Acceptable Value

Neither ethephon nor chlorethephon is mentioned by WHO, and do not have a MAV in the DWSNZ.

### Sources to water

Chlorethephon is an organophosphorus or phosphonate plant growth regulator, and a defoliant. It is a foliar absorbed growth regulator which controls the plant’s development following the release of ethylene into the plant. Often used to stiffen the stems of cereal such as barley. Also sold mixed with mepiquat chloride (qv).

Chlorethephon appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The manufacturing impurities mono 2-chloroethyl ester, 2-chloroethyl phosphonic acid and 1,2-dichloroethane are of toxicological concern and must not exceed respectively 20 g/kg and 0.5 g/kg in the technical material and 2 percent and 0.04 percent of the ethephon declared content in the technical concentrate (EC 2008).

### Forms and fate in the environment

Ethephon was found to have low to moderate mobility in soils ranging in texture from loamy sand to peat and silt loam. Therefore, the potential for contamination of groundwater appears to be low to moderate. In soil, rapid degradation to phosphoric acid, ethylene, and chloride ions was reported. It is highly soluble in water.

Ethephon hydrolyses rapidly at pH 7 and 9 with the half-life of 2.4 and 1.0 day, respectively. At pH 5, it degrades more slowly with a half-life of 73.5 days. Ethylene gas and methylated phosphoric acid were the only degradation products found. The studies on aerobic soil degradation of ethephon in five different soils at 20–25°C indicate that ethephon applied on soil degraded over time with different rates with the formation of ethylene. DT50 values ranged from 2.7–38 days for the five soils tested. Photolysis was insignificant. The log Kow (–1.8 to –0.6 at 20°C) indicates that ethephon is highly water-soluble (JMPR 2015).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The No Observable Effect Level (NOEL) for plasma cholinesterase activity in a rat study was 4.5 mg/kg/day for both sexes and the Lowest Effect Level (LEL) for this effect was 45 mg/kg/day for both sexes (EXTOXNET 1995).

The USEPA (1991) derived an oral RfD of 0.005 mg/kg/d based on a human study where 10 humans/sex were orally dosed with ethephon at 0.5 mg/kg/day for 16 days, followed by a recovery period of 29 days. Dose related effects occurred in plasma cholinesterase activity, but not in red blood cell cholinesterase activity. The effect was reversible within 15 days. A statistically significant decrease in plasma cholinesterase activity also occurred in the control group (approximately 71 to 83 percent of initial control values) at the same periods of analysis reported for the test subjects, but the test subjects demonstrated a larger decrease (approximately 56 to 49 percent of paired initial values) than the control group. When the control group and test groups were compared by the Wilcoxon Rank Sum Test, the results were statistically significant (p<0.05). In addition, no dose related effects occurred in hematology, blood chemistry, or urine analyses.

EXTOXNET (1996) quotes an ADI of 0.05 mg/kg/d and an RfD of 0.005 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.06 mg/kg/d, and an ARfD of 0.06 mg/kg/d for ethephon. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for ethephon is 0.60 mg/L.

The Acceptable Daily Intake (ADI) adopted for ethephon in Australia is 0.02 mg/kg body weight, with a NOEL of 0.17 mg/kg bw.

The EC (2008) quotes an ADI of 0.03 mg/kg bw, and an ARfD of 0.05 mg/kg/d. The oral RfD was calculated at 0.005 mg/kg/d (USEPA 1991).

JMPR (2015) confirmed an earlier ADI of 0–0.05 mg bw for ethephon on the basis of a NOAEL of 0.5 mg/kg bw per day in studies in humans given repeated ethephon doses and application of a 10-fold safety factor. They also confirmed the ARfD of 0.05 mg/kg that had been based on human data. An important metabolite is 2-hydroxyethyl phosphonic acid (or 2-hydroxyethephon, HEPA), however it is not considered to be a toxicologically relevant metabolite.

No dose-related evidence of carcinogenicity/oncogenicity has been reported (EXTOXNET 1996).

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlorfenvinphos

CAS No. 470-90-6 (formerly 2701-86-2). The IUPAC name for chlorfenvinphos is (EZ)‑2‑chloro-1-(2,4-dichlorophenyl)vinyl diethyl phosphate. The CAS name is 2‑chloro-1-(2,4-dichlorophenyl)ethenyl diethyl phosphate. Also called clofenvinfos and the analogous dimethyl ester has the JMAFF common name [dimethylvinphos](http://www.alanwood.net/pesticides/dimethylvinphos.html).

CAS No. 18708-87-7 is the (Z)-isomer; 18708-86-6 is the (E)-isomer. The (E)-isomer is usually no more than 10 percent of the commercial product.

### Maximum Acceptable Value

Chlorfenvinphos is not mentioned by WHO, and does not have a MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.002 mg/L; excursions above this level even for a short period are of concern, as the health-based guideline is based on both short-term and long-term effects.

### Sources to water

Chlorfenvinphos, a non-systemic organophosphorus insecticide and acaricide, was widely used to control household pests such as flies, fleas, and mice, and farm animals against fly strike. It was commonly used in the US until 1991 when all products containing chlorfenvinphos as an active ingredient were cancelled in the United States.

Chlorfenvinphos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Its use in Australia is limited to the control of ectoparasites on cattle, sheep, horses, deer, goats and working dogs. This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

If chlorfenvinphos is released to water, moderate adsorption to particulate matter will transport chlorfenvinphos from the water column and partition it to suspended solids and sediment. The processes that can result in the transformation and degradation of chlorfenvinphos in water are hydrolysis, photosensitised oxidation, and biodegradation. The hydrolysis half-life value for chlorfenvinphos in water is highly dependent on pH and temperature. At a pH of 6 and 8 and a temperature of 20–30°C, the half-life values were 170 and 80 days, respectively (ATSDR 1996). See JMPR for a discussion on metabolites. Water solubility is about 145 mg/L.

### Removal methods

Because it is strongly attracted to particles, coagulation processes should remove chlorfenvinphos fairly readily. Activated carbon will increase the removal rate. Ozone destroys the chlorfenvinphos molecule.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

There is no evidence that long-term exposure to small amounts of chlorfenvinphos causes any harmful health effects in people. It is not known whether chlorfenvinphos causes cancer in people; IARC has not classified chlorfenvinphos. The major effect of chlorfenvinphos is on the nervous system.

The main impurity in the technical material is 2,2-dichloro-1-(2,4-dichlorophenyl) vinyl diethyl phosphate (about 3.8 percent). (INCHEM 1971).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0005 mg/kg body weight, with a NOEL of 0.05 mg/kg bw from a four-week dietary study in rats, a two-year dietary study in rats and a two-generation reproduction study in rats. This NOEL is based on plasma and/or brain cholinesterase inhibition. The ADI incorporates a safety factor of 100. The ARfD is 0.02 mg/kg bw based on a NOEL of 1.9 mg/kg bw/day from a 14-day mouse study for inhibition of red blood cell cholinesterase activity. The ARfD incorporates a safety factor of 100.

It is not known whether chlorfenvinphos can affect reproduction or cause birth defects in people. One animal study reported decreased fertility in rats given chlorfenvinphos in their food, and another study reported that chlorfenvinphos interfered with the development of rats when the pregnant animals were fed chlorfenvinphos.

An exposure route was by using pharmaceutical products that contain lanolin, a natural grease from sheep’s wool (chlorfenvinphos was often used to control flies in animals and their surroundings and can contaminate sheep’s wool).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.002 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.002 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0007 mg/kg/day for chronic-duration oral exposure (>364 days).

### Derivation of Maximum Acceptable Value

No MAV. Young et al (1996) report that chlorfenvinphos has a taste threshold in drinking-water of about 0.004 mg/L.

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Young WF, Horth H, Crane R, et al. 1996. Taste and odour threshold concentrations of potable water contaminants. *Water Research* 30: 331–40.

# Chloridazon

CAS No. 1698-60-8. The IUPAC name for chloridazon is 5-amino-4-chloro-2-phenylpyridazin-3(2H)-one. The CAS name is 5-amino-4-chloro-2-phenyl-3(2H)-pyridazinone. May also be called 1-phenyl-4-amino-5-chloropyridaz-6-one, pyrazone or pyrazon.

### Maximum Acceptable Value

Chloridazon is not mentioned by WHO, and does not have a MAV in the DWSNZ.

### Sources to water

Chloridazon, a pyridazinone herbicide, is commonly used on beets and onions. It acts as systemic soil and leaf herbicide by inhibiting photosynthesis.

Chloridazon appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Chloridazon should not contain more than 60 g/kg (6 percent) of the 4-amino-5-chloro-isomer.

### Forms and fate in the environment

The half-life of chloridazon in aerobic soil is about four months, and about 15 months in anaerobic soil. In water-sediment systems chloridazon dissipated slowly from the water phase.

Chloridazon is stable to sterile aqueous hydrolysis at environmentally relevant pH values. Photolysis of chloridazon was investigated in pH 7 aqueous solution at 25ºC. The photolytical half-life in aqueous solutions decreased from 76 to 22 days from March to June (Northern Hemisphere). Disappearance time for the active substance in the total system (water and sediments) was calculated to be 182 days. Ultimate biodegradation is negligible with moderate transformation to bound residues.

Solubility in water is about 400 mg/L.

NPIC (1994) quotes for pyrazon (chloridazon) a soil half-life of 21 days, water solubility of 400 mg/L and a sorption coefficient (soil Koc) of 120. This resulted in a pesticide movement to groundwater rating of moderate.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The agreed ADI is 0.1 mg/kg bw/day, with the use of a safety factor 100, based on the long-term study in rats (EFSA 2007). An ARfD was considered unnecessary. The degradate chloridazon-desphenyl was considered to be of comparable toxicity to the parent compound (EFSA 2015).

EC (2007) established an ADI of 0.1 mg/kg/d; an ARfD was not considered necessary due to the low acute toxicity of chloridazon.

The Acceptable Daily Intake (ADI) adopted in Australia for chloridazon is 0.04 mg/kg body weight, with a NOEL of 4.1 mg/kg.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.18 mg/kg/d for pyrazon. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyrazon is 1.26 mg/L (no acute one-day value available.)

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2007. *Review Report for the Active Substance* chloridazon. *SANCO*/2822/07 – rev. 2 [9 pp]. <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2007. Conclusion regarding the peer review of the pesticide risk assessment of the active substance chloridazon. *EFSA Scientific Report* 108: 1–82. See: <http://www.efsa.europa.eu>

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FAO. 1997. Chloridazon. *FAO Specifications for Plant Protection Products*, AGP: CP/346 [23 pp]. [www.fao.org/ag/AGP/AGPP/Pesticid/Specs/docs/Pdf/old/Chloridazon\_97.pdf](http://www.fao.org/ag/AGP/AGPP/Pesticid/Specs/docs/Pdf/old/Chloridazon_97.pdf) or via <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/lpe/en/>

NPIC. 1994. *OSU Extension Pesticide Properties Database*. National Pesticide Information Centre. <http://npic.orst.edu/ingred/ppdmove.htm>

# Chlorimuron

CAS No. 99283-00-8. The IUPAC name for chlorimuron is 2-(4-chloro-6-methoxypyrimidin-2-ylcarbamoylsulfamoyl)benzoic acid. The CAS name is 2‑[[[[(4‑chloro-6-methoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]benzoic acid. It is often sold as the ester: [chlorimuron-ethyl](http://www.alanwood.net/pesticides/derivatives/chlorimuron-ethyl.html) (CAS No. 90982-32-4).

### Maximum Acceptable Value

Chlorimuron is not mentioned by WHO, and does not have a MAV in the DWSNZ.

### Sources to water

Chlorimuron, a broad spectrum, pre-emergence pyrimidinylsulfonylurea herbicide. The commonest use overseas is on soybeans and berry fruit.

Chlorimuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Chlorimuron will leach in some soils and has the potential to contaminate groundwater at very low concentrations.

Solubility in water is pH dependant: 9 mg/L at pH 5, 450 mg/L at pH 6.5 and 1,200 mg/L at pH 7.

NPIC (1994) quotes for chlorimuron ethyl a soil half-life of 40 days, water solubility of 1,200 mg/L and a sorption coefficient (soil Koc) of 110. This resulted in a pesticide movement to groundwater rating of high.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Chlorimuron-ethyl has low or minimal acute toxicity via the oral, dermal and inhalation routes of exposure (USEPA 2009). In subchronic toxicity studies with chlorimuron-ethyl, no adverse effects were observed up to the limit dose tested in mice; decreased body weight gain and liver pathology (margination of hepatocyte cytoplasmic content in the centrilobular areas) were observed in rats (males only); and mild hemolytic anemia, atrophy of the thymus and prostate and increased liver weights were seen in dogs. Chronic exposure of dogs to chlorimuron-ethyl also led to mild anemia (decreased erythrocyte count, hematocrit, and haemoglobin concentration), but atrophy of the thymus and prostate were not seen. In rats, treatment-related effects observed were limited to decreased body weight and body weight gain in both sexes after long-term exposure. Prostatitis (males) and fatty replacement in the pancreas (both sexes) were also observed but considered incidental occurrences; and biliary hyperplasia/fibrosis seen in females was attributed to aging. In mice, there were no treatment-related effects observed up to the highest dose tested (216 mg/kg/day).

There were no treatment-related increases in tumours in rat and mouse carcinogenicity studies after exposure to chlorimuron-ethyl. Chlorimuron-ethyl is classified as “not likely to be carcinogenic to humans”.

There are no studies identifying an acute dietary endpoint based on toxic effects observed following a single dose, therefore no acute dietary risk assessment was performed. For chronic dietary exposure, a no observed adverse effect level (NOAEL) of 9 mg/kg/day was identified from a chronic dog study in which mild anemia was observed at the lowest observed adverse effect level (LOAEL) of 51 mg/kg/day (USEPA 2004). The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for chlorimuron-ethyl is 0.63 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) based on the one-year dog feeding study (NOEL of 6.25 mg/kg/day) and using a 100-fold safety factor is calculated to be 0.0625 mg/kg/day. The oral RfD is 0.02 mg/kg/d bw, based on a one-year dog feeding study (USEPA 1989). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.09 mg/kg/d.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

NPIC. 1994. *OSU Extension Pesticide Properties Database*. National Pesticide Information Centre. <http://npic.orst.edu/ingred/ppdmove.htm>

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USEPA. 1989. Chlorimuron-ethyl. *Integrated Risk Information System (IRIS)*. See: <http://www.epa.gov/iris/subst/0406.htm>

USEPA. 2004. *Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Chlorimuron Ethyl*. <http://www.epa.gov/pesticides/reregistration/status.htm>

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# Chlormequat chloride

CAS No. 999-81-5. The IUPAC name for chlormequat chloride is 2-chloroethyl trimethylammonium chloride. CAS name is 2-chloro-N,N,N-trimethylethanaminium chloride. Sometimes called chlorcholine chloride.

### Maximum Acceptable Value

Chlormequat chloride is not mentioned by WHO, and does not have a MAV in the DWSNZ.

### Sources to water

Chlormequat chloride, a derivative of [chlormequat](http://www.alanwood.net/pesticides/chlormequat.html) (CAS No. 7003-89-6), belongs to the quaternary ammonium, or tertiary amine, class of chemicals and is used as a plant growth regulator for all varieties of winter and spring sown wheat and oats. It acts to reduce stem break, straw length and lodging all of which can adversely affect yields.

Chlormequat chloride appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 18.5 tonnes of chlormequat chloride were used in New Zealand in 2004, at an application rate of 3000 grams of active ingredient per hectare. By weight, it is the most heavily used pesticide in the UK as at 2012.

The EC has regulated the 1,2-dichloroethane content to a maximum of 100 mg/kg, and the chloroethene (vinyl chloride) content to a maximum of 0.5 mg/kg.

### Forms and fate in the environment

Chlormequat chloride exhibited moderate persistency in soil, first-order DT50 values were in the range from 27 to 34 days. In dark natural water sediment systems chlormequat chloride degraded exhibiting low persistence without forming major metabolites.

Solubility in water is extremely high (about 7.5 percent).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

EFSA (2008) states that in repeated dose studies, the dog appeared to be the most sensitive species, showing neuropharmacological effects, with an overall NOAEL of 4 mg/kg bw/day in the one-year study. In mutagenicity and long-term tests, chlormequat chloride was not shown to have any genotoxic or carcinogenic properties. During the reproductive toxicity testing, fertility was affected at a maternal toxic dose level, leading to an overall parental NOAEL of 75 mg/kg bw/day and a reproductive NOAEL of 74 mg/kg bw/day. However, based on reduced body weight gain and focal muscular dystrophy, the offspring NOAEL was 41 mg/kg bw/day. No variations, retardations or malformations were observed in the developmental studies with rats and rabbits, and the maternal NOAEL was 75 mg/kg bw/day in rats and 20 mg/kg bw/day in rabbits. In mechanistic studies in vitro for neurotoxicity, chlormequat chloride showed a weak agonistic activity on muscarinic and nicotinic receptors. With regard to the toxicological reference values, the agreed values reported as chlormequat chloride were 0.04 mg/kg bw/day for the Acceptable Daily Intake (ADI), and 0.09 mg/kg bw for the Acute Reference Dose (ARfD).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.90 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for chlormequat chloride is 9 mg/L.

JMPR established an ADI of 0–0.05 mg/kg bw in 1997 on the basis of the NOAEL of 4.7 mg/kg bw per day for diarrhoea, vomiting, and salivation in a one-year study of toxicity in dogs, and using a safety factor of 100. The 2017 meeting reaffirmed the ADI; the ARfD is also 0.05 mg/kg bw.

There is no concern for potential acute and chronic dietary exposure from drinking water associated with the registered non-food uses of chlormequat chloride (USEPA 2007).

The Acceptable Daily Intake (ADI) adopted in Australia for chlormequat is 0.07 mg/kg body weight, with a NOEL of 7.5 mg/kg, and the ARfD is 0.07 mg/kg bw.

EFSA (2016) reports an ADI of 0.04 mg/kg bw per day, and an ARfD of 0.09 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2009. *Review Report for the Active Substance* chlormequat. *SANCO*/175/08 final. European Commission Health and Consumers Directorate-General [7 pp]. See: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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USEPA. 2007. Re‑registration eligibility decision for chlormequat chloride. *Prevention, Pesticides and Toxic Substances*, EPA 738-R-07-014 [73 pp]. See: <http://www.epa.gov/pesticides/reregistration/status.htm>

# Chlorobenzilate

CAS No. 510-15-6. The IUPAC name for chlorobenzilate is ethyl 4,4′-dichlorobenzilate. CAS name is ethyl 4-chloro-α-(4-chlorophenyl)-α-hydroxybenzeneacetate. Also called ethyl di(para-chlorophenyl)glycollate.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because chlorobenzilate is unlikely to occur in drinking-water, a guideline value has not been derived.

### Sources to water

Chlorobenzilate, a chlorinated hydrocarbon, was introduced in 1952. It is used for mite control on citrus crops, deciduous fruit trees and in beehives. It is non-systemic, meaning that it is not absorbed or transported throughout a plant. It has little insecticidal action, killing only ticks and mites.

Chlorobenzilate does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. Chlorobenzilate appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

Following a five-day application of chlorobenzilate to several different citrus groves employing various tillage treatments, chlorobenzilate was not found in subsurface drainage waters, nor in surface run-off waters.

### Forms and fate in the environment

Its half-life in fine sandy soils was 10 to 35 days after application of 0.5 to 1.0 mg/L. The removal is probably due to microbial degradation (EXTOXNET 1996).

Because chlorobenzilate is practically insoluble in water and it adsorbs strongly to soil particles (Koc = 1,065) in the upper soil layers, it is expected to exhibit low mobility in soils, and therefore be unlikely to leach to groundwater.

Solubility in water is approximately 1–10 mg/L.

NPIC (1994) quotes for chlorobenzilate a soil half-life of 20 days, water solubility of 13 mg/L and a sorption coefficient (soil Koc) of 2,000. This resulted in a pesticide movement to groundwater rating of very low.

### Removal methods

Because it is strongly attracted to particles, coagulation processes should remove chlorobenzilate readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Chlorobenzilate is rapidly excreted by humans, usually within three to four days.

IARC (1983) considered that data was insufficient to assess human carcinogenicity (Group 3).

No information is available on the carcinogenic effects of chlorobenzilate in humans. In a National Toxicology Program (NTP) study, chlorobenzilate was found to be carcinogenic in orally exposed mice, with increased incidences of liver tumours observed. The use of chlorobenzilate has been restricted in the US because the compound is tumour-forming (oncogenic) in rats and mice.

The oral RfD was calculated at 0.02 mg/kg/d (USEPA 1989).

It is unlikely that chlorobenzilate will cause reproductive toxicity in humans at expected exposure levels, but is a possible human carcinogen; the ADI and RfD are 0.02 mg/kg/d (EXTOXNET 1996). PMEP (1984) quotes an ADI of 0.125 mg/kg/day.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EXTOXNET. 1996. Chlorobenzilate. Extension Toxicology Network. *Pesticide Information Profiles*. See: <http://extoxnet.orst.edu/pips/ghindex.html>

IARC. 1983. Miscellaneous pesticides. *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* 30. <http://monographs.iarc.fr/ENG/Monographs/allmonos30.php>

NPIC. 1994. *OSU Extension Pesticide Properties Database*. National Pesticide Information Centre. <http://npic.orst.edu/ingred/ppdmove.htm>

PMEP. 1984. Chlorobenzilate Chemical Factsheet 12/84. Accessed 2011 via PMEP. *Pesticide Active Ingredient Information: Insecticides.* <http://pmep.cce.cornell.edu/profiles/index.html>

USEPA. 1989. Chlorobenzilate. *Integrated Risk Information System (IRIS)*. <http://www.epa.gov/iris/subst/0400.htm>

WHO. 2011. *Guidelines for Drinking-water Quality 2011* (4th edition). Geneva: World Health Organization. Available at: [http://www.who.int/water\_sanitation\_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/index.html](http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html)

# 3-chloro-p-toluidine hydrochloride

CAS No. 7745-89-3. Sometimes called 3-chloro-4-toluidine hydrochloride, 2-chloro-4-aminotoluene hydrochloride, 3-chloro-4-methylbenzenamine hydrochloride, CPTH, DRC 1339 and starlicide.

The free base is 3-chloro-p-toluidine, CAS No. [33240-95-8](http://www.commonchemistry.org/ChemicalDetail.aspx?ref=33240-95-8); also called 3-chloro-4-methylaniline.

N-(3-chloro-4-methylphenyl acetamide) – CAS No. [7149-79-3](http://www.commonchemistry.org/ChemicalDetail.aspx?ref=33240-95-8) – is called DRC 2698, and has similar uses overseas. Also called [3-chloro-4-acetotoluidide](http://www.chemindustry.com/chemicals/0508639.html) and 3-chloro-4-methylacetanilide.

[3-Chloro-4-aminotoluene](http://www.chemindustry.com/chemicals/0222076.html) – CAS No. [95-74-9](http://www.commonchemistry.org/ChemicalDetail.aspx?ref=33240-95-8) – is called DRC 1347, and has similar uses overseas. Also called [3-chloro-4-](http://www.chemindustry.com/chemicals/0222076.html)methylaniline and 3-chloro – p-toluidine.

### Maximum Acceptable Value

3-Chloro-p-toluidine hydrochloride does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.00003 mg/L (0.03 µg/L) for 3‑chloro-p-toluidine hydrochloride in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

3-Chloro-p-toluidine hydrochloride is used as an avicide, applied in various baits, often at 0.1 percent active ingredient. Its usage is based on being highly toxic to a limited number of bird species, of low toxicity to humans and other animals. 3-Chloro-p-toluidine hydrochloride appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

3-Chloro-p-toluidine hydrochloride is used to control rooks on New Zealand farmland; it also kills non-target species of birds. It is usually applied as a powder containing about 975 g/kg of ai. It can be used in conjunction with chloralose (Nelson 1994). It is also used industrially overseas to manufacture products such as dyestuffs.

The free base is used in the US to control starlings in urban areas where baits cannot be used effectively. This has the code name DRC 1339.

### Forms and fate in the environment

3-Chloro-p-toluidine hydrochloride does not hydrolyse but does photodegrade in water, with a half-life of approximately 16 hours. It binds to organic matter in soils. 3‑Chloro-p-toluidine hydrochloride is an organochlorine, but does not appear to have the persistence or the tendency to accumulate in the food chain that other organochlorines such as DDT have.

The primary soil degradate is N-acetyl-3-chloro-4-methylaniline; 3-hydroxy-p-toluidine is the major degradate in water.

Solubility of the hydrochloride in water is very high, about 9 percent. The free base is only soluble in hot water.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The ADE was reported to be 0.086 mg/kg/bw/day. A NOAEL of 43 mg/kg bw/day was reported, but no details on toxicity data were provided (ERMA New Zealand 2002, quoted in MoH 2010).

The Tolerable exposure limit (TEL) TELwater = 0.6 mg/L; Environmental exposure limit (EEL) EELfreshwater = 0.03 μg/L (Animal Control Products Ltd, Safety Data Sheet (http://www.pestoff.co.nz/msd/drc.pdf).

3-Chloro-p-toluidine hydrochloride was not mutagenic in three mutagenicity studies and was not carcinogenic (USEPA 1995). The National Cancer Institute conducted a study with rats and mice which indicated that starlicide is not oncogenic, since the administration of the free base (3-chloro-p-toluidine) for 78 weeks to rats and mice produced only body weight depression, at 3,629 ppm, the highest dose treated.

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlorothalonil

CAS No. 1897-45-6. The IUPAC name for chlorothalonil is tetrachloroisophthalonitrile. The CAS name is 2,4,5,6-tetrachloro-1,3-benzenedicarbonitrile. Sometimes called TPN, 1,3-dicyanotetrachlorobenzene or 2,4,5,6-tetrachloro-1,3-dicyanobenzene.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for chlorothalonil in drinking-water.

A guideline value was not derived in WHO 2004 or 2011 because it was considered that chlorothalonil was unlikely to occur in drinking-water.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.05 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.53 µg/L for chlorothalonil in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to drinking-water

#### 1 To source waters

Chlorothalonil is an aromatic halogen compound, a member of the chloronitrile chemical family. Chlorothalonil is a broad spectrum non-systemic fungicide in the same family as hexachlorobenzene (HCB) and pentachlorophenol (PCP). In New Zealand, chlorothalonil is applied to a variety of fruit, vegetables and ornamentals for the control of various diseases including among others powdery mildew, blackspot, botrytis, blight, and leaf spot.

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). There are currently (2009) 25 products containing chlorothalonil that are registered for agricultural use in New Zealand. ERMA notes that 18 tonnes of chlorothalonil were used in New Zealand in 2004, at an application rate of 1,500 grams of active ingredient per hectare. In June 2013 EPA stated that antifouling paints containing chlorothalonil will no longer be able to be manufactured in or imported into New Zealand because the approvals to do so have been declined. All chlorothalonil-containing products will no longer be available for sale to anybody in New Zealand from 11 November 2017. By weight, it is the second most heavily used pesticide in the UK as at 2012.

Chlorothalonil should not contain more than 0.1 g/kg of hexachlorobenzene. Other impurities can include tetrachlorophthalonitrile, tetrachloroterephthalonitrile, pentachlorobenzonitrile, partially chlorinated dicyanobenzenes, and unchlorinated dicyanobenzenes.

Chlorothalonil was the most commonly found agricultural chemical residue in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme). It has been found greater than the MRL in bok choi, celery and spinach.

### Forms and fate in the environment

In aerobic soils, the half-life for chlorothalonil is from one to three months. Increased soil moisture or temperature increases chlorothalonil degradation. It is not degraded by sunlight on the soil surface. Chlorothalonil has high binding and low mobility in silty loam and silty clay loam soils (Koc values are in the range of 900 to 7,000), but has low binding and moderate mobility in sand. Generally it is not expected to leach to groundwater.

In studies conducted in water over ten weeks, chlorothalonil, at low levels, was generally stable and is expected to adsorb to suspended solids and sediment. In very basic water (pH 9.0), about 65 percent of the chlorothalonil was degraded into two major metabolites after ten weeks. An aqueous photolysis half-life of 65 days was measured for chlorothalonil, suggesting photolysis in sunlit surface waters is possible. Degradation may occur in natural water with the production of the 4-hydroxy metabolite, 4-hydroxy-2,5,6-trichloroisophthalonitrile. Half-lifes for dissipation of the 4‑hydroxy metabolite in soils range between 6 and 43 days.

Described as “insoluble” in water, or about 0.8 mg/L, independent of pH.

NPIC (1994) quotes for chlorothalonil a soil half-life of 30 days, water solubility of 0.6 mg/L and a sorption coefficient (soil Koc) of 1380. This resulted in a pesticide movement to groundwater rating of low.

USGS (2006) give the following values: log Kow = 2.64; log Koc (where Koc is in mL/g) = 3.2; water solubility = 0.6 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 1.77; half-life in aerobic soil = NA days; half-life in water = >200 days. Volatilisation from moist soil surfaces is not expected to be important.

### Typical concentrations in drinking-water

Chlorothalonil was not found in any of 560 groundwater samples collected from 556 sites. Chlorothalonil was reported to be found in one surface water location in Michigan at 6.5 mg/L (USEPA 1987).

### Removal methods

Being attracted to heavier soils, treatment processes that remove particulate matter should reduce the concentration of chlorothalonil in water.

### Recommended analytical techniques

#### Referee method

A referee method cannot be selected for chlorothalonil because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for chlorothalonil for the above reason.

### Health considerations

Chlorothalonil is excreted rapidly from the body, primarily unchanged. It is not thought to be stored in animal tissues. Rats and dogs fed very high doses for two years eliminated almost all of the chemical in urine, faeces, and expired air. After two years, the amount of the breakdown product found in the liver tissues was considered insignificant in both dogs and rats (USEPA 1987). At lower concentrations, chlorothalonil leaves the body within 24 hours. Residues have not been found in the tissues or milk of dairy cows (Vettorazzi 1979).

Chlorothalonil is not very water soluble and does not store in fatty tissues. Its bioaccumulation factor is quite low, about 425 times the background water concentration.

#### Acute toxicity

Chlorothalonil and its metabolites are highly toxic to fish, aquatic invertebrates, and marine organisms. Fish, such as rainbow trout (LC50 of 0.25 mg/L) are noticeably affected even when chlorothalonil levels are low (less than 1 mg/L).

Chlorothalonil is slightly toxic to mammals, but it can cause severe eye and skin irritation in certain formulations (Walker and Keith). Very high doses may cause a loss of muscle coordination, rapid breathing, nose bleeding, vomiting, and hyperactivity. Dermatitis, vaginal bleeding, bright yellow and/or bloody urine, and kidney tumours may also occur, followed by death.

The oral LD50 is >10,000 mg/kg for rats, and 6,000 mg/kg for mice. The acute dermal LD50 for both albino rabbits and albino rats is 10,000 mg/kg.

The lowest relevant oral NOAEL/NOEL in short-term toxicity testing (90-day rat study) is 1.5 mg/kg/d (EC 2006).

#### Chronic toxicity

In a number of tests of varying lengths of time, rats which were fed a range of doses of chlorothalonil generally showed no effects on physical appearance, behaviour, or survival. Kidney changes such as enlargement were common. In a two-year dietary rat study, the lowest dose of chlorothalonil that produced no adverse effects in the animals was 60 ppm (3 mg/kg).

Chronic studies of rats and dogs fed high dietary levels show that chlorothalonil is toxic to the kidney. In addition to less urine output, changes in the kidney included enlargement, greenish-brown colour, and development of small grains.

Human eye and skin irritation is linked to chlorothalonil exposure. Fourteen out of 20 workers exposed to 0.5 percent chlorothalonil in a wood preservative developed dermatitis. All workers showed swelling and inflammation of the upper eyelids. Allergic skin responses have also been noted in vegetable and in horticultural workers.

In a long-term rat study, high doses fed to both males and females did not affect reproduction or the litters that were produced. However, body weight gains for males and females of each generation were decreased.

Administration of high doses of chlorothalonil to pregnant rabbits through the stomach during the sensitive period of gestation resulted in four of the nine mothers aborting. These studies suggest that chlorothalonil will not affect human reproduction except at very high doses.

Female rats given high doses of chlorothalonil through the stomach during the sensitive period of gestation had normal fetuses, even though that dose was toxic to the mothers. One study of birth defects in rabbits showed no effects. Thus, chlorothalonil is expected to produce no birth defects in humans.

Mutagenicity studies on various animals, bacteria, and plants indicate that chlorothalonil does not cause any chromosomal changes. The compound is therefore not expected to pose mutagenic risks to humans.

The reference dose or RfD (USEPA 1988/2006/2009/2011) is 0.015 mg/kg/d. USEPA (1999) quoted an RfD of 0.02 mg/kg/day which was determined based on the NOEL of 2 mg/kg/day established in a two-year dietary study in rats and using an uncertainty factor of 100. The LOEL of 4 mg/kg/day was based on increased kidney weights and hyperplasia of the proximal convoluted tubules in the kidneys as well as ulcers and forestomach hyperplasia. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1.5 mg/kg bw from a long-term (two-year) dietary study in mice and dogs. The NOEL is based on lesions in the kidney and the stomach. The ADI incorporates a safety factor of 100.

EC (2006) established an ADI of 0.015 mg/kg/d and an ARfD of 0.06 mg/kg/d.

The toxicological profile of chlorothalonil was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI of 0.015 mg/kg bw per day and an ARfD of 0.06 mg/kg bw. Toxicological reference values were also derived for metabolite 2,5,6‑trichloro-4-hydroxyphtalonitrile (SDS-3701) which was observed in the plant and animal metabolism studies. An ADI of 0.01 mg/kg bw per day and an ARfD of 0.01 mg/kg bw were derived. A cumulative effect of parent chlorothalonil and SDS-3701 is not expected as both compounds act through a different mode of action. (EFSA 2002).

EFSA (2015) states: Data were sufficient to derive an acceptable daily intake (ADI) of 0.015 mg/kg bw per day and an acute reference dose (ARfD) of 0.6 mg/kg bw for chlorothalonil. An ADI of 0.01 mg/kg bw per day and an ARfD of 0.01 mg/kg bw was proposed for its metabolite SDS-3701 (2,5,6-trichloro-4-hydroxyphtalonitrile).

EFSA (2015) states: the ADI of chlorothalonil is 0.015 mg/kg bw per day based on kidney toxicity with a NOAEL of 1.5 mg/kg bw per day from the 90-day study in rat, supported by the rat, two-year study, applying an UF of 100. This confirms the ADI previously established during the first review of chlorothalonil by EC (2006). The ARfD is 0.05 mg/kg bw, based on the NOAEL for acute effects in the rabbit developmental toxicity study of 5 mg/kg bw per day for bw loss observed at the beginning of exposure at 10 mg/kg bw per day; 100 UF applied. The previously established ARfD was 0.6 mg/kg bw based on an ARfD-specific study and applying a standard uncertainty factor of 100 by EC (2006).

The 2009 JMPR meeting established an ADI for chlorothalonil of 0–0.02 mg/kg bw based on a NOAEL of 1.8 mg/kg bw per day identified on the basis of kidney toxicity observed in long-term studies of toxicity in rats and using a safety factor of 100. This ADI provides a margin of 200 for the induction of renal tumours in rats. This ADI is similar to the one derived by JMPR in 1974 and 1990 from a two-year study in dogs in which the NOAEL was 3 mg/kg bw per day. Previously, JMPR has based the ADI on data from dogs, arguing that the rat is particularly sensitive to kidney toxicity induced by chlorothalonil. The meeting concluded that whereas there were some uncertainties, it was possible to establish a plausible mode of action for the renal carcinogenesis of chlorothalonil. This comprises initial conjugation with glutathione followed by sequential biotransformation to thiol derivatives in renal proximal tubule cells by β‑lyase. The thiol metabolites are cytotoxic, resulting in renal proximal tubule cell necrosis followed by regenerative proliferation. The final step is the appearance of tumours. As there are no fundamental qualitative differences between rodents and humans in the processes underlying these key events, it was not possible to dismiss human relevance on qualitative grounds. Although quantitative differences in some of the metabolic steps, such as the cysteine S-conjugate β-lyase pathway, have been demonstrated between rodents and humans for some other compounds sharing this mode of action, specific information on chlorothalonil was not available. Hence, the meeting concluded that while it is plausible that humans are less sensitive to the renal effects of chlorothalonil, it was not possible to dismiss relevance to humans on quantitative grounds, nor was it possible to quantify any difference in sensitivity. Studies of acute toxicity have demonstrated that exposure to chlorothalonil on a single day may induce kidney toxicity in rats. The overall NOAEL for kidney toxicity in studies of acute toxicity was 60 mg/kg bw. Based on this NOAEL, the meeting established an acute reference dose (ARfD) of 0.6 mg/kg bw, using a safety factor of 100. Given the species differences in the β-lyase bioactivation pathway, the ADI and ARfD are likely to be conservative. FAO/WHO (2009). In addition to the parent substance an ADI of  
0–0.008 mg/kg bw and an ARfD of 0.03 mg/kg bw were established for the metabolite SDS-3701 (2,5,6-trichloro-4-hydroxyisophthalonitrile). These values were reaffirmed by JMPR (2012) and FAO/WHO (2013).

The 2010 JMPR meeting (FAO/WHO 2010) noted that the soil metabolite R611965 (3-carbamyl-2,4,5-trichlorobenzoic acid or 3-carboxy-2,5,6-trichloro benzamide, formerly known as SDS-46851) is considerably less toxic than the parent compound chlorothalonil (eg, NOAELs of 200 versus 1.8 mg/kg bw per day in two-year rat studies, respectively). The meeting considered it unnecessary to derive a separate ADI and ARfD for this metabolite for risk management purposes.

Chlorothalonil is a potential human carcinogen, known to affect the kidney, ureter, and bladder in experimental animals. Male and female rats fed chlorothalonil daily over a lifetime developed carcinogenic and benign kidney tumours at the higher doses. In another study, where mice were fed high daily doses of chlorothalonil for two years, females developed tumours in the fore-stomach area (attributed to irritation by the compound) and males developed carcinogenic and benign kidney tumours. However, this latter study was inconclusive as to the relationship between dose of chlorothalonil and the presence of cancer in the test animals. In 1999 the IARC classified chlorothalonil as possibly carcinogenic to humans (Group 2B).

As at September 2008 the USEPA has classified chlorothalonil in Group B: a probable human carcinogen. The USEPA (2009/2011) quotes a health advisory of 0.15 mg/L for chlorothalonil, representing a 10-4 cancer risk.

Chlorothalonil appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

See DWI (2010) for a discussion on some major metabolites of chlorothalonil.

USEPA (2015) found that based on weight of evidence considerations, mammalian or fish EDSP Tier 2 testing is not recommended for chlorothalonil since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals of fish.

### Derivation of Maximum Acceptable Value

There are insufficient data to determine a MAV for chlorothalonil in drinking-water.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for chlorothalonil is 0.03 mg/L.

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# Chlorotoluron

CAS No. 15545-48-9. The IUPAC name for chlorotoluron is 3-(3-chloro-p-tolyl)-1,1-dimethylurea. The CAS name is N′-(3-chloro-4-methylphenyl)-N,N-dimethylurea. Sometimes called chlortoluron.

### Maximum Acceptable Value

Based on health considerations, the concentration of chlorotoluron in drinking-water should not exceed 0.04 mg/L.

### Sources to water

Chlorotoluron may enter source waters as a result of its application as a pre- and early post-emergence phenylurea herbicide, used to control annual grasses and broadleaved weeds in winter cereals.

Chlorotoluron has not been used, and is not registered for use, in New Zealand. By weight, it is the fifth most heavily used pesticide in the UK as at 2012. Its active ingredient was found in UK raw water on a regular basis which triggered its withdrawal and there was a lack of data to support its continued use at lower application rates. However, chlorotoluron has been reapproved for use in cereals for early control of annual meadowgrass and a range of broad-leaved weeds (Farmers Weekly 2014).

The commercial product may contain up to 0.8 percent of 3-(3-chloro-4-tolyl)-1-methylurea and of 3-(4-tolyl)-1,1-dimethylurea (JMPR 1990).

### Forms and fate in the environment

Chlorotoluron is degraded slowly in water and is quite persistent; it is mobile in soil. Half-lifes in water range from 80 to greater than 200 days and half-lifes in soil range from one to several months.

EFSA (2011) includes a list of common metabolites.

The water solubility of chlorotoluron is 70 mg/L.

### Typical concentrations in drinking-water

Chlorotoluron has not been used in New Zealand. It has been detected occasionally in waters in the UK at concentrations ranging from 0.00044 to 0.00058 mg/L (0.44 to 0.58 g/L). Chlorotoluron has been detected frequently in German raw waters (ground and surface waters), and in levels up to 0.0012 mg/L (1.2 g/L) in drainage water, soon after normal application on fields in Germany.

### Removal methods

Specific information concerning the removal of chlorotoluron from water is not available. However, phenylamide (or urea) pesticides, such as chlorotoluron, are reported to be broken down by chlorination. Slow sand filtration does not appear to remove this class of pesticide. GAC should reduce the concentration to below 0.0001 mg/L. Other phenylamide pesticides have been reported to be broken down by ozone.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction Gas Chromatographic/Mass Spectrometric Method (EPA 525.2).

#### Some alternative methods

1. An HPLC method may be suitable (Crathorne et al 1987).

2. Separation with reverse-phase high-performance liquid chromatography followed by ultraviolet and electrochemical detection. Detection limits of 0.0001 mg/L have been reported.

### Health considerations

Chlorotoluron is absorbed readily and rapidly following ingestion. No evidence of accumulation of chlorotoluron in any particular organ or tissue has been reported. It is excreted rapidly in the urine in the form of metabolites.

Chlorotoluron is of low acute, short-term and long-term exposures in animals, but it has been shown to cause adenomas and carcinomas of the kidney in male mice given high doses for two-years.

No cases of human poisonings have been reported following chlorotoluron exposure.

EC (2005) states that in long-term toxicity tests, the lowest relevant NOAEL is 3.7 mg/kg/d, found in a two-year rat study, from which they derived an ADI of 0.04 mg/kg/d. EFSA (2011) reaffirmed this ADI and stated that no ARfD was deemed necessary.

Chlorotoluron and its metabolites have shown no evidence of genotoxicity.

Available evidence from animal studies suggests that chlorotoluron has a carcinogenic potential that is both species and sex specific. No information is available concerning the carcinogenicity of chlorotoluron to humans.

### Derivation of Maximum Acceptable Value

As chlorotoluron and its metabolites show no evidence of genotoxicity, a tolerable daily intake approach was used for the derivation of the MAV for chlorotoluron in drinking-water. The no-observable-adverse-effect level used in the derivation is based on a two-year feeding study of systemic effects in mice.

The MAV for chlorotoluron in drinking-water was derived as follows:

11.3 mg/kg body weight/day x 70 kg x 0.1 = 0.04 mg/L

2 L/day x 1,000

where:

* no-observable-adverse-effect level = 11.3 mg/kg body weight per day based on a two-year feeding study in mice
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for evidence of carcinogenicity).

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# Chlorpropham

CAS No. 101-21-3. The IUPAC name for chlorpropham is isopropyl 3-chlorocarbanilate. The CAS name is 1-methylethyl (3-chlorophenyl)carbamate. Also called chloropropham and (3-chlorophenyl)carbamic acid 1-methylethyl ester, and meta-chlorocarbanilic acid isopropyl ester.

### Maximum Acceptable Value

Chlorpropham does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Chlorpropham is a plant growth regulator absorbed predominately by roots (often to prevent sprouting in potatoes), and a selective systemic carbanilate (phenylcarbamate) herbicide commonly used for the control of pre-emergent and/or post-emergent weed control in vegetables.

Chlorpropham appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and was found above its default MRL in celery in an extensive study of New Zealand foods (NZFSA FRSP).

FAO requires that chlorpropham should not contain more than 0.25 mg/kg of 3‑chloroaniline.

### Forms and fate in the environment

Chlorpropham is moderately persistent in soil. It is subject to degradation by soil microbes. Photodegradation and volatilisation do not readily occur. Soil half-lifes of 65 days at 15°C to 30 days at 29°C have been reported. Chlorpropham has some potential to contaminate groundwater because it is soluble in water and it has only a moderate tendency to adsorb to soil particles. However, chlorpropham adsorbs strongly to organic matter, so it is unlikely to leach through soils with high organic matter content. Chlorpropham breaks down very slowly by reaction with water. At pH 4, 7 and 9 at 40°C, about 90 percent of the chlorpropham remained in a solution maintained in the dark for 32 days.

Chlorpropham produces the metabolite 3-chloroaniline (see chloroanilines datasheet).

Water solubility about 100 mg/L.

NPIC (1994) quotes for chlorpropham a soil half-life of 30 days, water solubility of 89 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of moderate.

EFSA (2017) reports that the DT90 of chlorpropham and the major soil metabolite 3‑chloroaniline exceed the 100 days trigger value. The potential for groundwater exposure from the representative uses by chlorpropham and 3-chloroaniline above the parametric drinking water limit of 0.1 μg/L was concluded to be low.

### Typical concentrations in drinking-water

In 199‑ the USEPA removed their drinking-water advisory from USEPA (1988).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The No Observable Effects Level (NOEL) for chlorpropham was established at 5 mg/kg bw/day, and the Acceptable Daily Intake (ADI) for chlorpropham was established at 0.05 mg/kg bw/day (APVMA 1997).

The Acceptable Daily Intake (ADI) adopted in Australia is also 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw.

In 2000, the JMPR established an acceptable daily intake (ADI) of 0–0.03 mg/kg bw based on a no-observed-adverse-effect level (NOAEL) of 10 mg/kg bw per day in a 90-day study of toxicity in Wistar rats, this NOAEL being identified on the basis of a significant decrease in erythrocyte counts and an increase in methaemoglobin formation at the next higher dose of 47 mg/kg bw per day. A safety factor of 300 was applied, which included an additional safety factor of 3 to account for inadequacies in the assessment of methaemoglobinaemia (lack of measurements of methaemoglobin formation at early time-points, a concern since adaptation to this effect can occur), the critical toxicological effect. This ADI also provided an adequate margin of safety for the effects on the thyroid observed in dogs (NOAEL 5 mg/kg bw per day). An acute reference dose (ARfD) equal to the maximum ADI was also established.

The chlorpropham Reference Dose (RfD) of 0.05 mg/kg bwt/day established by the USEPA (1996) for a chronic dietary exposure risk assessment was based on the no effect level of 5 mg/kg bwt/day from a chronic feeding study with dogs. Dietary exposure to chlorpropham can be through either of its two food uses – spinach or potatoes. The contribution to chronic dietary risk from spinach is negligible. The estimate for chronic dietary risk is driven by the primary use of chlorpropham on stored potatoes. The previous oral RfD had been 0.2 mg/kg/d (USEPA 1988). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 2.5 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for chlorpropham is 82.5 mg/L.

EC (2003) reports the lowest relevant NOAEL in long-term toxicity and carcinogenicity tests to be based on a LOAEL of 24 mg/kg/d from a two-year study on rats. They then derived an ADI of 0.05 mg/kg/d from a 60 week dog study, and an ARfD of 0.5 mg/kg/d. EFSA (2017) retained these values, and reported an ADI of 0.007 mg/kg/d and an ARfD of 0.03 mg/kg/d for 3-chloroaniline.

IARC has classified chlorpropham in Group 3: no evidence of human carcinogenicity. As at September 2008 the USEPA has classified chlorpropham as Group E for carcinogenicity (evidence of non-carcinogenicity for humans). EFSA (2017) reports: Chlorpropham is classified carcinogenic category 2 but not toxic for reproduction category 2, in accordance with the provisions of Regulation (EC) No 1272/2008, and added that 3-chloroaniline is unlikely to be genotoxic.

Although chlorpropham is classified as a group E chemical (evidence of non-carcinogenicity for humans) according to the USEPA’s cancer classification guidelines, one of its metabolites, 3-chloroaniline, is structurally similar to a known carcinogen, 4‑chloroaniline. There are no cancer data available on 3-chloroaniline. However, the Agency believes it is appropriate to use the cancer potency from 4‑chloroaniline to gauge any potential risk from 3-chloroaniline. Based on the structure of the compounds, the Agency believes that 3-chloroaniline is probably, at most, equally as potent and not likely to be more potent than 4-chloroaniline (USEPA 1996). EFSA (2012) says the same about 3-chloro-4-hydroxyaniline.

JMPR (2005) established an ADI of 0–0.05 mg/kg bw based on the NOAEL of 5 mg/kg bw per day in a 60-week study in dogs fed with chlorpropham, on the basis of changes in the thyroid at 50 mg/kg bw per day, and using a safety factor of 100. This ADI provided an adequate margin of safety for the haematotoxic effects seen in the studies of repeated doses in rats. The meeting established an ARfD of 0.5 mg/kg bw, on the basis of a NOAEL of 50 mg/kg bw in the study of acute toxicity in dogs given capsules containing chlorpropham identified on the basis of clinical signs of toxicity at the higher doses of 125 and 625 mg/kg bw, and using a safety factor of 100. Slight increases in methaemoglobin levels in this study were not considered to be toxicologically significant at any dose.

### Derivation of Maximum Acceptable Value

No MAV.

The CDHS has an advisory level in drinking-water for chlorpropham of 0.35 mg/L in 1982, and revised this to 1.2 mg/L in 2000.

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# Chlorpyriphos

CAS No. 2921-88-2. The IUPAC name for chlorpyrifos is O,O-diethyl O-3,5,6-trichloro-2-pyridyl-phosphorothioate. The CAS name is O,O-diethyl O-(3,5,6-trichloro-2-pyridinyl) phosphorothioate. Also called chlorpyrifos.

CAS No. 5598-13-0 refers to chlorpyrifos-methyl, where the ethyl groups are replaced by methyl.

### Maximum Acceptable Value

Based on health considerations, the concentration of chlorpyriphos in drinking-water should not exceed 0.04 mg/L.

The maximum acceptable concentration in Canada for chlorpyrifos is 0.09 mg/L.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.002 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.01 mg/L; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

EC (2005) states that the impurity O,O,O’,O’-tetraethyl dithiopyrophosphate (Sulfotep) shows toxicological or environmental concerns and a maximum level of 3.0 g/kg was established in the technical specifications of chlorpyrifos.

### Sources to water

Chlorpyrifos is a broad-spectrum non-systemic organophosphorus insecticide used for the control of mosquitos, flies, various crop pests in soil and on foliage, household pests and aquatic larvae. Although it is not recommended for addition to water for public health purposes by WHOPES, it may be used in some countries as an aquatic larvicide for the control of mosquito larvae.

In New Zealand, chlorpyrifos is applied to fruit, vegetables, cereals, ornamentals, pasture and turf. It is also used as an ectoparasiticide for the control of fly strike, lice and blowflies. It is also used as a bait for cockroaches and is available as a ready-for-use formulation in the domestic market. It is commonly found in grapes, bok choi and celery, often above the NZFSA MRL. It has also been found in mandarins, tomatoes and spinach.

Formulations containing chlorpyrifos have been registered for use in New Zealand since 1972. There are 15 products containing chlorpyrifos that are currently (as at 2009) registered for agricultural use in New Zealand. The total annual usage of chlorpyriphos in New Zealand in the late 1980s was 116,500 kg. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 17 tonnes of chlorpyrifos were used in New Zealand in 2004, at an application rate of 1500 grams of active ingredient per hectare.

### Forms and fate in the environment

Chlorpyrifos is strongly absorbed by soil and does not readily leach from it, degrading slowly by microbial action. In soil, chlorpyriphos is degraded slowly, with a half-life of approximately 80 to 100 days (up to 280 days on some soil types), and it undergoes further degradation to organochlorine compounds and carbon dioxide. Chlorpyrifos is not expected to volatilise from dry soil surfaces based on its vapour pressure.

It has a low solubility in water and great tendency to partition from aqueous into organic and particulate phases in the environment. Half-lifes ranging from 35 to 78 days have been reported in water with a pH of 7 and a temperature of 25°C. The water solubility is 0.4–2 mg/L. The rate of hydrolysis of chlorpyrifos in water increases with pH and temperature and is enhanced by the presence of copper; between 30 and 60 percent of the total amount of chlorpyrifos in the aqueous phase may disappear within 24 hours through adsorption, degradation and vaporisation (Health Canada 1989).

Chlorpyrifos-methyl water solubility is 2.7 mg/L.

Octanol-Water Partition Coefficient (Kow): 4.7. Henry’s constant: 4.2 to 6.7 x 10-6 atm·m3/mol. Soil Sorption Coefficient (Koc): 360 to 31,000 depending on soil type and environmental conditions.

NPIC (1994) quotes for chlorpyrifos a soil half-life of 30 days, water solubility of 0.4 mg/L and a sorption coefficient (soil Koc) of 6070. This resulted in a pesticide movement to groundwater rating of very low.

USGS (2006) give the following values: log Kow = 4.92; log Koc (where Koc is in mL/g) = 3.78; water solubility = 0.73 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.0374; half-life in aerobic soil = 30.5 days; half-life in water = 29 days.

The processes primarily responsible for the transformation and degradation of chlorpyrifos in water are abiotic hydrolysis and photosensitised oxidation. Neutral hydrolysis is favoured below pH 9. Under field conditions, chlorpyrifos exhibits very short persistence in the water compartment of aquatic ecosystems, and half-lifes as short as several hours have been observed. This is due to its considerable volatility from water (arising from low solubility and moderate vapour pressure) and its high association with sediment.

A major metabolite of chlorpyrifos and chlorpyrifos-methyl is trichloropyridinol (3,5,6‑trichloro-2-pyridinol or TCP); this is also a metabolite of triclopyr (qv). TCP adsorbs weakly to soil particles and is moderately mobile and persistent in soils. See JMPR (2009) and EFSA (2011a) for discussion on metabolites.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 342 zones, did not find any detectable concentrations of chlorpyriphos (limit of detection = 0.0002 mg/L) (ESR 2001).

Chlorpyrifos has been found in groundwater in Poverty Bay at 0.00003 mg/L (MAF 2006).

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Chlorpyrifos was detected in one well at a concentration of 0.056 µg/L, ie, 0.000056 mg/L.

Chlorpyrifos has been detected in surface waters in USA, usually at concentrations below 0.0001 mg/L; also detected in groundwater in less than 1 percent of the wells tested, usually at concentrations below 0.00001 mg/L (WHO 2004/2017). Chlorpyrifos was not detected in a survey of 511 samples from Canadian municipal and private drinking water supplies between 1971 to 1986; detection limits ranged from 0.0002 to 0.00004 mg/L.

### Removal methods

Should be amenable to treatment by coagulation (10–20 percent removal), activated carbon adsorption, and ozonation. Chlorination breaks down chlorpyrifos completely.

### Recommended analytical techniques

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector or Flame Photometric Detector (HMSO 1986).

2. Extraction separately into hexane and dichloromethane, separation by gas chromatography and flame thermionic or flame photometric detection. The detection limit is 0.001 mg/L.

### Health considerations

Organophosphates are absorbed readily through the skin, and through the respiratory and gastrointestinal tracts.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand for chlorpyrifos is 0.003 mg/kg body weight, with a NOEL of 0.03 mg/kg bw based on plasma cholinesterase inhibition in a 28-day human volunteer study. The ADI was established in 1998 and reaffirmed in 2000, and incorporates a safety factor of 10. The ARfD is 0.1 mg/kg bw based on a NOEL of 1 mg/kg bw/day. The NOEL was based on inhibition of red blood cell acetylcholinesterase inhibition from a three-day human volunteer oral study. The ARfD incorporates a safety factor of 10.

The Acceptable Daily Intake (ADI) adopted in Australia for chlorpyrifos-methyl is 0.01 mg/kg body weight, with a NOEL of 0.1 mg/kg bw.

Chlorpyrifos was last evaluated by the JMPR in 2004 when an ADI of 0–0.01 mg/kg bw/day and an ARfD of 0.1 mg/kg bw/day were established, and a number of maximum residue levels were estimated. JMPR (2009) and FAO/WHO (2009) state that an ADI of 0–0.01 mg/kg bw and an ARfD of 0.1 mg/kg bw were established by the meeting for chlorpyrifos-methyl. Reaffirmed in JMPR (2013).

The acceptable daily intake (ADI) of chlorpyrifos is 0.003 mg/kg/day (PMEP 1984). By USEPA (1996) the RfD was 0.003 mg/kg/d. The oral reference dose or RfD (USEPA 2002/2006/2009/2011) was adjusted to 0.0003 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.01 mg/L. The ARfD was revised in 2014 to 0.0047 mg/kg/d Michigan Government (2015).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.001 mg/kg/d, and an ARfD of 0.01 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for chlorpyrifos methyl is 0.10 mg/L.

The long-term toxicity to mammals: rat 2 generations, NOAEL = 1 mg/kg bw/day (EFSA (2011).

In long-term toxicity and carcinogenicity studies, the lowest relevant NOAEL was 1 mg/kg/d (EC 2005). Their ADI and ARfD are reported to be 0.01 mg/kg/d. EFSA (2011a) states that the chlorpyrifos-methyl data were sufficient to derive an ADI of 0.01 mg/kg bw/day and an ARfD of 0.1 mg/kg bw. New available toxicological data led to the decrease of the reference values established in 2005: the Pesticides Peer Review meeting agreed on a new ADI and AOEL of 0.001 mg/kg bw per day, and an ARfD of 0.005 mg/kg bw, based on significant decrease of RBC ChE in rats, using an uncertainty factor of 100. After repeated exposure, the NOAEL is 0.1 mg/kg bw per day for chlorpyrifos and the NOAEL is 0.01 mg/kg bw per day for chlorpyrifos-oxon, both based on RBC ChE inhibition. After acute exposure, the NOAEL is 0.5 mg/kg bw per day for chlorpyrifos. TCP, which is a major metabolite in products of both animal and plant origin, is not of higher toxicity than chlorpyrifos. An ADI of 0.03 mg/kg/d was derived for TCP. The 0.25 mg/kg bw ARfD for TCP, a value of from the teratogenicity study in rabbit (UF of 100), was considered reliable (EFSA 2014/2015).

As at September 2008 the USEPA has classified chlorpyriphos in Group E: evidence of non-carcinogenicity for humans. JMPR concluded that chlorpyrifos is unlikely to pose a carcinogenic risk to humans. Chlorpyrifos was not genotoxic in an adequate range of studies in vitro and in vivo. In long-term studies, inhibition of cholinesterase activity was the main toxicological finding in all species, that is, it can overstimulate the nervous system causing nausea, dizziness, confusion, and at very high exposures (eg, accidents or major spills), respiratory paralysis and death (USEPA 2002).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.003 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.003 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.001 mg/kg/day for chronic-duration oral exposure (>364 days).

USEPA (2015) found that based on weight of evidence considerations, EDSP Tier 2 testing is not recommended for chlorpyriphos since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

The MAV for chlorpyriphos in drinking-water was derived as follows:

0.01 mg/kg x 70 kg x 0.1 = 0.035 mg/L (rounded to 0.04 mg/L)

2 L

where:

* acceptable daily intake = 0.01 mg/kg of body weight on the basis of a NOAEL of 1 mg/kg of body weight per day for inhibition of brain acetylcholinesterase activity in studies in mice, rats and dogs, using a 100-fold uncertainty factor
* acceptable daily intake = 0.01 mg/kg of body weight on the basis of a NOAEL of 0.1 mg/kg of body weight per day for inhibition of erythrocyte acetylcholinesterase activity in a study of human subjects exposed for nine days, using a 10-fold uncertainty factor
* average weight of adult = 70 kg
* proportion of acceptable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult = 2 L/day.

In the 1995 datasheet and 1995 DWSNZ, the MAV had been derived by the MoH as follows:

0.01 mg/kg x 70 kg x 0.2 = 0.07 mg/L

2 L

where:

* acceptable daily intake = 0.01 mg/kg of body weight
* average weight of adult = 70 kg
* proportion of acceptable daily intake allocated to drinking-water = 0.2
* average quantity of water consumed by an adult = 2 L/day.

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# Chlorsulfuron

CAS No: 64902-72-3. The IUPAC name for chlorsulfuron is 1-(2-chlorophenylsulfonyl)-3-(4-methoxy-6-methyl-1,3,5-triazin-2-yl)urea. The CAS name is 2-chloro-N-[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]benzenesulfonamide.

### Maximum Acceptable Value

Chlorsulfuron is not mentioned in the DWSNZ or WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.2 mg/L; excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Chlorsulfuron is a sulfonylurea herbicide that controls selected broadleaf weeds and undesirable grasses; it is used widely with cereal crops and for controlling roadside weeds. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Chlorsulfuron is likely to be persistent and highly mobile in the environment. It may be transported to non-target areas by run-off and/or spray drift. Degradation by hydrolysis appears to be the most significant mechanism for degradation of chlorsulfuron, but is only significant in acidic environments (23 day half-life at pH = 5); it is stable to hydrolysis at neutral to high pH. Degradation half-lifes in soil environments range from 14 to 320 days (USEPA 2005).

Water solubility at 25°C is about 600 mg/L at pH 5, and 3 percent at pH 7.

NPIC (1994) quotes for chlorsulfuron a soil half-life of 40 days, water solubility of 7,000 mg/L and a sorption coefficient (soil Koc) of 40. This resulted in a pesticide movement to groundwater rating of high.

### Removal methods

The high water solubility suggests that coagulation and filtration processes will not be effective at reducing the concentration of chlorsulfuron; activated carbon may be more promising.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Chlorsulfuron causes moderate body weight and food consumption decreases when fed to rats and mice for 18 months to two years. Chlorsulfuron caused no adverse health effects when fed to dogs at high doses for six months. However, it did cause decreases in weight gain and changes in the blood when fed to dogs in high doses for one year.

The oral RfD was calculated at 0.05 mg/kg/d (USEPA 1990). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.02 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for chlorsulfuron is 0.14 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw from a long-term (two-year dietary) study. This NOEL is based on haematological changes observed in rats. The ADI incorporates a safety factor of 100.

EC (2010) reports an ADI of 0.2 mg/kg/d; based on the low toxicity of chlorsulfuron no ARfD has been allocated.

Chlorsulfuron causes a decrease in female fertility when fed to rats in moderate doses over three generations. It caused no birth defects when fed to rats in high doses during pregnancy.

Rats and mice fed moderate to high doses of chlorsulfuron for 18 months to two years showed no increased incidence of tumours. As at September 2008 the USEPA has classified chlorsulfuron as having no evidence of carcinogenicity, based on a lack of evidence in rat and mice studies. Multiple studies show that chlorsulfuron is not a mutagen. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. However, USEPA (2005) stated because chlorsulfuron data show no evidence of carcinogenicity, no cancer risk assessment was conducted.

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlorthal-dimethyl

CAS No: 1861-32-1. The IUPAC name for chlorthal-dimethyl is dimethyl tetrachloroterephthalate. The CAS name is dimethyl 2,3,5,6-tetrachloro-1,4-benzenedicarboxylate; sometimes called DCPA, dacthal (trade name), or dimethyl tetrachloroterephthalate.

The main degradates are monomethyl tetrachloroterephthalate (CAS No. 887-54-7) and tetrachloroterephthalic acid (CAS No. 2136-79-0).

### Maximum Acceptable Value

Chlorthal-dimethyl is not mentioned in the DWSNZ, nor in the WHO Guidelines.

The USEPA (2009/2011) established a lifetime health advisory of 0.07 mg/L for dacthal, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

### Sources to water

Chlorthal-dimethyl is a pre-emergence phthalate herbicide, commonly used to control grasses and some broadleaf weeds growing amongst vegetables. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Chlorthal-dimethyl should not contain more than 0.01 mg/kg of 2,3,7,8-tetrachlorodibenzo-p-dioxin or hexachlorodibenzo-p-dioxin, or 100 mg/kg of hexachlorobenzene.

### Forms and fate in the environment

DCPA is not particularly mobile or persistent in the environment (log Kocrange of 3.77–3.81). Biodegradation and volatilisation are the primary dissipation routes. Soil metabolism converts chlorthal-dimethyl into the minor degradate mono-acid (monomethyl tetrachloroterephthalate or MTP), and the main di-acid degradate tetrachloroterephthalic acid (TPA) which is known to leach through soil where some of it breaks down to the di-acid and enters groundwater where it is very stable. DCPA’s average half-life is up to 100 days in most general soil types. It is toxic to aquatic organisms with long-lasting effects. The half-life of MTP is shorter (2.8 days) and that of TPA is longer (virtually no degradation in 300 days) (USEPA 1998; 2008, 2008a, 2008b).

Water solubility is about 0.5 mg/L. The degradates are more soluble.

NPIC (1994) quotes for DCPA dacthal parent a soil half-life of 100 days, water solubility of 0.5 mg/L and a sorption coefficient (soil Koc) of 5000. This resulted in a pesticide movement to groundwater rating of very low.

USGS (2006) give the following values: log Kow = 4.28; log Koc (where Koc is in mL/g) = 3.75; water solubility = 0.5 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -0.66; half-life in aerobic soil = 16 days; half-life in water = >200 days.

### Typical concentrations in drinking-water

Dacthal has been detected in groundwater samples from wells in Massachusetts, New York, Oregon and Wisconsin at levels ranging from 0.0005–0.25 mg/L.

Forty-nine water utilities in the US reported detecting dacthal in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.039 mg/L.

Twenty-eight water utilities in the US reported detecting DCPA di-acid degradate in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.012 mg/L.

Three water utilities in the US reported detecting DCPA mono acid degradate in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.019 mg/L.

### Removal methods

Potential treatment technologies for removing dacthal and its degradates from water include membrane processes, activated carbon, and advanced oxidation. High pressure technologies that use nanofiltration and reverse osmosis are capable of removing dissolved organic contaminants including dacthal and its degradates. Contaminants with double bonds and low water solubility such as dacthal generally have a high affinity for carbon. MTP and TPA which are more water soluble than dacthal, are expected to be less amenable to activated carbon treatment (USEPA 2008b).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Chlorthal-dimethyl has been classified (by USEPA in 1995, and still listed as at September 2008) as a Group C, possible human carcinogen, based on increased incidence of thyroid tumours in both sexes of the rat (although, only at an excessive dose in the female), and liver tumours in female rats and mice, at doses which were not excessive. Dacthal is not classified as carcinogenic by ERMA New Zealand. Based on approved usage patterns, the USEPA concluded that chlorthal-dimethyl and its metabolites do not currently pose a significant cancer or chronic non-cancer risk from non-turf uses to the overall US population from exposure through contaminated drinking-water.

Hexachlorobenzene, a USEPA B2 (probable human carcinogen) (see datasheet), is an impurity in chlorthal-dimethyl. Newer products have a lower concentration of hexachlorobenzene. The manufacturing process has been improved in an effort to reduce contamination by polyhalogenated dibenzo-p-dioxins/dibenzofurans (see datasheet) as well.

USEPA (1994) derived a RfD of 0.01 mg/kg bw based on a NOAEL of 1 mg/kg-day resulting from a two-year rat feeding study of the effects on the lungs, liver, kidney, thyroid and thyroid hormones in males and females and eyes of females. Since the available data indicate that neither MTP nor TPA is more toxic than their parent compound, DCPA, the USEPA believes that the RfD for the DCPA parent would be protective against exposure from the two DCPA metabolites (USEPA 2008).

USEPA (2008b) reports the 10-day Health Advisory for a 10 kg child for dacthal of 2.15 mg/L (rounded to 2 mg/L), and 125 mg/L (rounded to 100 mg/L) for tetrachloroterephthalic acid. For a 10 kg child, the longer-term HA for dacthal is 1 mg/L and 4 mg/L for a 70 kg adult. For a 10 kg child, the longer-term HA for tetrachloroterephthalic acid is 50 mg/L and 200 mg/L for a 70 kg adult. The lifetime health advisory for dacthal is 0.07 mg/L from which is derived a value of 0.35 mg/L for the Drinking Water Equivalent Level (DWEL).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

The reference dose or RfD (USEPA 1994/2006/2009/2011) is 0.01 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.35 mg/L.

The USEPA believes that no adverse health effects in humans are likely to result from drinking water with 4 mg/L or less of dacthal.

USEPA (2015) found that based on weight of evidence considerations there was no convincing evidence of potential interaction with the estrogen or androgen pathways. DCPA demonstrated a potential for interaction with the thyroid hormone pathway in the absence of overt or systemic toxicity.

### Derivation of Maximum Acceptable Value

No MAV.

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# Chlorthiamid

CAS No: 1918-13-4. The IUPAC name for chlorthiamid is 2,6-dichlorothiobenzamide. The CAS name is 2,6-dichlorobenzenecarbothioamide; sometimes called DCBN.

### Maximum Acceptable Value

Chlorthiamid is not mentioned in the DWSNZ or WHO Guidelines.

### Sources to water

WHO believes (as at 2004) that chlorthiamid, a systemic benzonitrile herbicide, is no longer used as a pesticide. Chlorthiamid does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). IUPAC describes chlorthiamid as an obsolete pre-emergence herbicide once used for total weed control in non-crop and aquatic situations.

Chlorthiamid was approved in the UK (MAFF 1985) for direct application to water to control some submerged weeds and some rooted floating weeds, at a maximum water concentration of 3 mg/L. This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Dichlobenil (see datasheet) is a major degradation product of chlorthiamid. Conversion of chlorthiamid to dichlobenil is rapid in the soil. After four weeks, less than 3 percent remains of chlorthiamid that was applied to clay, medium loam and sandy loam, and less than 17 percent remained in peat. The important metabolite 2,6‑dichlorobenzamide was formed in all four soil types after application of either chlorthiamid, fluopicolide or dichlobenil. At 8–10 weeks after application the benzamide residues in the soil were generally greater than those of the dichlobenil, except in peat. In clay, which was studied in most detail, the benzamide penetrated to greater depths than did the dichlobenil or chlorthiamid (Beynon and Wright 2006).

Another major chlorthiamid metabolite is 2,6-dichlorobenzonitrile.

Solubility in water is about 1,000 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Chlorthiamid fed to rats: 70 percent elimination in urine within 24 hours.

APVMA adopted an ADI of 0.02 mg/kg/d 2,6-dichlorobenzamide (BAM) for Australia (<https://apvma.gov.au/>) based on a two-year dietary rat study; a NOAEL of 2 mg/kg bw/d was based on reduced body weight, increased incidences of eosinophilic and basophilic foci in the livers and fat deposition and cellular degeneration in the liver at the next higher dose. The ARfD is 0.6 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

MAFF (1985) reports that the threshold odour concentration of chlorthiamid is 0.01 mg/L.

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# Cholecalciferol

CAS No: 67-97-0. The IUPAC name for cholecalciferol is (3β,5Z,7E)-9,10-secocholesta-5,7,10(19)-trien-3-ol. Also called vitamin D3, activated 7-dehydrocholesterol, toxiferol and calciol.

The term vitamin D should be used as a general term to describe all steroids that exhibit qualitatively the biological activity of calciol. This term should be used in derived terms such as vitamin D activity, vitamin D deficiency, vitamin D antagonist.

Nomenclature for vitamin D compounds (see IUPAC 1981 for more compounds):

|  |  |  |
| --- | --- | --- |
| **Current trivial name** | **Recommended trivial name** | **Systematic steroid name** |
| cholecalciferol | calciol or cholecalciferol, vitamin D3 | (5Z,7E)-(3S)-9,10-seco-5,7,10(19)-cholestatrien-3-ol |
| 25-hydroxycholecalciferol | calcidiol | (5Z,7E)-(3S)-9,10-seco-5,7,10(19)-cholestatriene-3,25-diol |
| 1a,25-dihydroxycholecalciferol | calcitriol | (5Z,7E)-(1S,3R)-9,10-seco-5,7,10(19)-cholestatriene-1,3,25-triol |
| ergocalciferol, calciferol | ercalciol or ergocalciferol, vitamin D2 | (5Z,7E,22E)-(3S)-9,10-seco-5,7,10(19),22-ergostatetraen-3-ol |

### Maximum Acceptable Value

Cholecalciferol is not mentioned in the DWSNZ, nor the WHO Guidelines.

### Sources to water

Cholecalciferol is a secosteroid that is used as the active ingredient in lethal gel baits for possum and rodent control, commonly at rates up to 8,000 mg/kg (0.8 percent) of bait. Cholecalciferol comprises 0.8 percent w/w of the trade product feracol.

Cholecalciferol is produced industrially for use in vitamin supplements and to fortify foods by the ultraviolet irradiation of 7-dehydrocholesterol extracted from lanolin found in sheep’s wool or also from lichens. From NSW Government (2013).

Cholecalciferol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Booth et al (1999) exposed cereal pellets used for possum control containing cholecalciferol to 400 mm of simulated rainfall and found that the cholecalciferol concentration remained at the same level as unexposed baits even though the pellets had been reduced to a water-saturated paste. They also found that soil under the exposed baits contained very small quantities of cholecalciferol (2 percent of the concentration in the baits), even after the baits had been exposed to 500 mm of simulated rainfall.

Very sensitive to UV radiation and will rapidly break down when exposed. Cholecalciferol in rodent baits is oxidised and inactivated by moist air within a few days. From NSW Government (2013).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Cholecalciferol is synthesised in the human skin from 7-dehydrocholesterol under the action of ultraviolet B light. It reaches an equilibrium after several minutes depending on several factors including conditions of sunlight (latitude, season, cloud cover, altitude), age of skin, and colour of skin.

Cholecalciferol is added to foods and used as a health supplement. One gram of pure vitamin D3 is 40,000,000 (40 x 106) [IU](http://en.wikipedia.org/wiki/International_unit), where one IU is equivalent to 0.025 μg. Recommendations are: 5 micrograms (200 IU or International Units) daily for all individuals (males, female, pregnant and lactating women) under the age of 50 years old. For all individuals from 50–70 years-old, 10 micrograms daily (400 IU) is recommended. For those who are over 70 years old, 15 micrograms daily (600 IU) is suggested. Some have questioned whether the current recommended adequate levels are sufficient to meet physiological needs, particularly for individuals deprived of regular sun exposure. The upper limit for vitamin D has been recommended as 2,000 IU daily due to toxicities that can occur when taken in higher doses. Vitamin D toxicity can result from regular excess intake of this vitamin, and may lead to hypercalcemia and excess bone loss.

### Derivation of Maximum Acceptable Value

No MAV.

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# Clethodim

CAS No: 99129-21-2. Also appears in some publications as CAS No. 110429-62-4. The IUPAC name for clethodim is (5RS)-2-{(E)-1-[(2E)-3-chloroallyloxyimino]propyl}-5-[(2RS)-2-(ethylthio)propyl]-3-hydroxycyclohex-2-en-1-one. The CAS name is 2-[(1E)-1-[[[(2E)-3-chloro-2-propenyl]oxy]imino]propyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one.

Clethodim and sethoxydim (qv) share a common moiety, which accounts for the major part of their structures. Their structures differ in two parts: the oxime oxygen bears an ethyl group in sethoxydim but a 3-chloroallyl group in clethodim, and the imino carbon bears an n-propyl group in sethoxydim but an ethyl group in clethodim (JMPR 2002).

### Maximum Acceptable Value

Clethodim is not mentioned in the DWSNZ, nor the WHO Guidelines.

The USEPA concluded on 22 September 2009 that clethodim is known or anticipated to occur in PWSs and may require regulation. Therefore they added clethodim to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

### Sources to water

Clethodim is a post-emergence cyclohexene oxime herbicide used to control annual and perennial grasses in a wide variety of broad leaf crops.

Clethodim appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Formulations of clethodim may include trimethylbenzene, xylenes, cumene and emulsifier as inert ingredients.

### Forms and fate in the environment

It is not possible to evaluate the individual effects of either the (E,E) or (Z,E) isomers, since isolation of either form would result in a re-established equilibrium when introduced to any test system. References made to clethodim therefore relate to the sum of the determined (E,E) and (Z,E) geometric isomers, expressed as total clethodim (EFSA 2011).

Clethodim is of low persistence in most soils with a reported half-life of approximately three days. Breakdown is mainly by aerobic processes, although photolysis may make some contribution. Volatilisation loss and hydrolysis are probably not important processes in the soil breakdown of clethodim. The main breakdown products in soils under aerobic conditions are sulfoxide, sulfone and oxazole sulfone. Clethodim and these degradates are weakly bound to soils, thus, while it may be somewhat mobile in the soil environment, it is very short-lived. The USEPA has stated “under present use patterns and under most circumstances clethodim does not appear to threaten groundwater”. See JMPR (1999) for comments on metabolites.

Experimental degradation rates in soil and soil adsorption values for the two soil photolysis metabolites 2-[3-chloroallyloxyimino]butanoic acid and trans-3-chloroacrylic acid to address the soil and groundwater exposure assessments of the two photodegradates are not yet available. The soil photolysis metabolites trans-3-chloroacrylic acid and 2-[3-chloroallyloxyimino]butanoic acid still need to be addressed with respect to soil and groundwater compartments (EFSA 2011).

Clethodim may be highly persistent in the aquatic environment. Reported half-lifes for clethodim in the aquatic environment are 128 days in the aqueous phase and 214 days in the sediment. The reported hydrolysis half-life at pH 7 to 9 is approximately 300 days. The main pathway for degradation of clethodim in the aquatic environment is anaerobic metabolism by micro-organisms. However, due to the low persistence and mobility of the compound in soil, it is unlikely to be found in surface waters.

Water solubility is about 5,000 mg/L at pH 7, and 500 mg/L at pH 5.8.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See JMPR (2002).

### Health considerations

In a one-year feeding study of dogs, doses of 75 mg/kg/day resulted in increased relative and absolute liver weights, with anemia-like alterations in blood chemistry such as reduced haemoglobin, erythrocyte and hematocrit counts.

An ADI of 0 to 0.01 mg/kg bw was established on the basis of the NOAEL of 1 mg/kg bw per day from the one-year study in dogs and a safety factor of 100 (IPCS 1994).

JMPR (1999) concluded that an acute RfD for clethodim is unnecessary.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

EFSA (2011) states that the Acceptable Daily Intake (ADI) is 0.16 mg/kg bw/day, based on the two-year rat study and applying a safety factor of 100. Considering the toxicological profile of clethodim, the experts agreed that an Acute Reference Dose (ARfD) is not needed.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.01 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for clethodim is 0.07 mg/L (no acute one-day value available.)

It appears unlikely that reproductive, teratogenic, mutagenic, or carcinogenic effects would occur in humans under normal circumstances. The USEPA classified clethodim as not likely to be a human carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Clodinafop-propargyl

CAS No: 105512-06-9. The IUPAC name for clodinafop-propargyl is prop-2-ynyl (R)-2-[4-(5-chloro-3-fluoro-2-pyridyloxy)phenoxy]propionate. The CAS name is 2-propynyl (2R)-2-[4-[(5-chloro-3-fluoro-2-pyridinyl)oxy]phenoxy]propanoate.

Clodinafop (CAS No: 114420-56-3), refers to the free acid. Clodinafop-propargyl refers to the propargyl ester. The clodinafop molecule has one centre of asymmetry and the ISO common name applies only to the R-enantiomer, not the S-enantiomer. The modified ISO common name, clodinafop-propargyl therefore applies only to the R‑enantiomer.

### Maximum Acceptable Value

Clodinafop-propargyl is not mentioned in the DWSNZ, nor the WHO Guidelines.

### Sources to water

Clodinafop-propargyl is a systemic aryloxyphenoxypropionic (oxyphenoxy acid ester) herbicide, effective on grasses, registered in the US for use on wheat. The oxyphenoxy acid ester chemical class includes the active ingredients fluazifop-butyl, fenoxaprop-ethyl, diclofop methyl (CAS No. 51338-27-3, quizalofop-ethyl and haloxyfop-methyl.

Clodinafop-propargyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is always used together with the safener cloquintocet-mexyl (qv) (EFSA 2005).

### Forms and fate in the environment

The likelihood of drinking-water contamination by the parent compound, clodinafop-propargyl, is low due to high sorption and rapid degradation in the environment. Clodinafop-propargyl may be considered to have low or very low persistence in soil. It hydrolyses only slowly in water under acidic conditions but is rapidly hydrolysed under alkaline conditions. Photolysis occurs rapidly, producing a plethora of products but not including clodinafop (free acid).

In soil laboratory incubations under aerobic conditions in the dark, clodinafop-propargyl exhibited very low persistence, but in anaerobic soil it was stable. In dark aerobic natural sediment conditions, clodinafop-propargyl degraded very rapidly. Clodinafop-propargyl degraded rapidly in aqueous photochemical degradation studies. The potential for groundwater exposure was low. EFSA (2011/2018) includes a list of metabolites. Clodinafop-propargyl and none of its degradation products were considered likely to undergo transformation due to oxidation at the disinfection stage of usual water treatment processes.

Water solubility is about 4 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In accordance with the USEPA Proposed EPA Weight-of-the-Evidence Categories, August 1999, the USEPA’s Cancer Assessment Review Committee (CARC) classified clodinafop-propargyl as “likely to be carcinogenic to humans” by the oral route based on the occurrence of prostate tumours in male rats, ovarian tumours in female rats, and liver tumours in both sexes of mice, as well as blood vessel tumours in female mice. For the quantification of human cancer risk, the CARC recommended a linear low-dose extrapolation approach based on the most potent of these tumour types. This approach is supported by possible genotoxic potential and the lack of confirmation of the mode of action of clodinafop-propargyl. The most potent unit risk, Q1\*(mg/kg/day)-1, of those calculated for clodinafop-propargyl is that for male mouse liver benign hepatoma and/or carcinoma combined tumour rates at 0.129 (mg/kg/day)-1 in human equivalents. As at September 2008 the USEPA considered “there was suggestive evidence of carcinogenic potential”.

USEPA (2000a) quotes a chronic RfD for clodinafop-propargyl of 0.00003 mg/kg/d based on a no-effect level of 0.03 mg/kg/day from a two-year chronic toxicity/carcinogenicity study in rats and a 1,000x uncertainty factor. The acute reference dose (aRfD) of 0.005 mg/kg/day was based on a NOAEL of 5 mg/kg/day from a developmental study in rats and a 1,000x uncertainty factor. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0003 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for clodinafop-propargyl is 1.65 mg/L.

JMPR (2008) considers clodinafop-propargyl is not genotoxic.

The acceptable daily intake (ADI) is set to 0.003 mg/kg bw/day and the acute reference dose (ARfD) to 0.05 mg/kg bw, safety factor of 100 (EFSA 2005). The Acceptable Daily Intake (ADI) adopted in Australia is 0.004 mg/kg body weight, with a NOEL of 0.37 mg/kg bw.

EC (2006) reports an ADI of 0.003 mg/kg/d and an ARfD of 0.05 mg/kg/d. EFSA (2011) reaffirmed these values.

EFSA (2018) reports an acceptable daily intake for clodinafop-propargyl of 0.0003 mg/kg/d based on the NOAEL of 0.03 mg/kg bw/d for prostate carcinomas from the 2-year rat study and an uncertainty factor of 100. The ARfD remains at 0.05 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Clofentezine

CAS No: 74115-24-5. The IUPAC and CAS name for clofentezine is 3,6-bis(2-chlorophenyl)-1,2,4,5-tetrazine.

### Maximum Acceptable Value

Clofentezine is not mentioned in the DWSNZ or the WHO Guidelines.

### Sources to water

Clofentezine is a tetrazine acaricide and mite growth regulator (acting primarily as an ovicide), commonly used on fruit trees. Clofentezine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

All environmental fate data requirements have been satisfied (USEPA 2007). The potential for clofentezine to leach into groundwater was assessed in terrestrial field dissipation studies conducted in several locations and in varying soil types. Half-lifes ranged from 32.4 to 83 days. No evidence of leaching of parent or degradation products was observed. Based upon these and other studies, the USEPA concluded that clofentezine is a relatively short-lived, non-mobile compound which does not pose a risk to groundwater, and will not be expected to accumulate in rotational crops. Thus, the potential for finding significant clofentezine residues in drinking-water is minimal and the contribution of any such residues to the total dietary intake of clofentezine will be negligible. Therefore no Maximum Contaminant Level for clofentezine has been established.

In soil, the degradation of the parent compound proceeded via hydrolytic cleavage of the tetrazine ring, leading to the formation of 2-chlorobenzoic (2‑chlorobenzylidene)hydrazide (maximum 13 percent), and 2-chlorobenzoic acid (maximum 6.2 percent). 2-Chlorobenzonitrile has been noted too (EFSA 2014). Clofentezine was degraded in all three soils under aerobic conditions with a “half-life” of approximately 4, 6 and 8 weeks in the clay, loamy sand and clay loam respectively. See JMPR (2007) for discussion on metabolites. However, EFSA (2014) states that soil degradation studies demonstrate that the degradation rate of clofentezine is slow; the maximum DT90 in field studies was 640.5 days. Volatilisation is not an important process for removal from soil.

At pH 7 and 22°C the half-life in water of clofentezine is approximately 35 hours, whereas at pH 5 and 22°C the half-life is approximately 250 hours. Solubility in water is less than 0.001 mg/L.

NPIC (1994) quotes for clofentezine a soil half-life of 40 days, water solubility of 0.1 mg/L and a sorption coefficient (soil Koc) of 11,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

ICPS (1988) quotes an estimate of acceptable daily intake (ADI) for man of  
0–0.02 mg/kg bw, based on a no-observed-adverse-effect level (NOAEL) of 40 ppm (equivalent to 2 mg/kg bw per day) for hepatotoxicity in rats and a NOAEL of 50 ppm (equal to 1.72 mg/kg bw per day) for hepatotoxicity in dogs.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw.

JMPR (2005) reaffirmed the ADI of 0–0.02 mg/kg bw, but now based on the NOAEL of 1.72 mg/kg bw per day for thyroid changes in a long-term study of toxicity/ carcinogenicity in rats and also for hepatotoxicity in a 12-month study in dogs, and using a safety factor of 100. JMPR concluded that it was not necessary to set an ARfD for clofentezine, since clofentezine has low acute toxicity and does not cause developmental toxicity or any other toxicological effect that would be elicited by a single exposure.

The EC (2010) also adopted the 0.02 mg/kg/d bw ADI; they did not set an ARfD. These values were also adopted by EFSA (2014).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD for clofentezine of 0.013 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for clofentezine is 0.091 mg/L (no acute one-day value available.)

Although clofentezine has been classified by the USEPA in Category C (in the September 2008 list) for oncogenicity (a possible human carcinogen), quantitative oncogenic risk assessment was considered inappropriate for the following reasons:

i. Evidence of tumours was limited to a single site in one sex of one species and occurred only at the high-dose level.

ii. The increased incidence of thyroid follicular tumours was only marginally increased above both concurrent and historical control levels.

### Derivation of Maximum Acceptable Value

No MAV.

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# Clomazone

CAS No: 81777-89-1. The IUPAC name for clomazone is 2-(2-chlorobenzyl)-4,4-dimethyl-1,2-oxazolidin-3-one or 2-(2-chlorobenzyl)-4,4-dimethylisoxazolidin-3-one. The CAS name is 2-[(2-chlorophenyl)methyl]-4,4-dimethyl-3-isoxazolidinone. Also called dimethazone.

### Maximum Acceptable Value

Clomazone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Clomazone is an unclassified (although sometimes classified as an isoxazolidinone) broad spectrum [herbicide](http://en.wikipedia.org/wiki/Herbicide) used for control of broadleaf weeds in a range of crops (including brassicas and carrots); clomazone is an inhibitor of plant pigments. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

In field studies, the half-life of clomazone was 28 to 84 days, depending on soil type and the organic matter content.

Clomazone is highly soluble in water (about 1,100 mg/L), but it has a moderate tendency to adsorb to soil particles. It therefore has a low to moderate potential to contaminate groundwater.

NPIC (1994) quotes for clomazone (dimethazone) a soil half-life of 24 days, water solubility of 1100 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of moderate.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Clomazone does not appear to be mutagenic or teratogenic, and does not cause tumour formation.

The ADI is estimated to be 0.043 mg/kg/day based on a NOEL of 4.3 mg/kg/day in a two-year rat feeding study and a 100-fold safety margin (PMEP 1993). The Australian Acceptable Daily Intake (ADI) for clomazone for a human is 0.1 mg/kg/day, set for the public for daily, lifetime exposure, based on the NOEL of 14 mg/kg/day. The NZFSA uses an ADI of 0.03 mg/kg. PMEP (1999) quotes an RfD of 0.043 mg/kg/d bw.

EC (2007, confirmed 2018) established an ADI of 0.133 mg/kg/d; an ARfD allocation was not considered necessary due to the low acute toxicity of clomazone; these values were reaffirmed by EFSA. 2011. With particular regard to residues, the EC review established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health; however, they request the submission of further data and information on the most abundant plant metabolite, 2-chlorobenzyl alcohol, in order to render possible a generally applicable plant residue definition.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.84 mg/kg/d for clomazone, and an ARfD of 1.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for clomazone is 33 mg/L.

Meanwhile 2-chlorobenzyl alcohol, also named OCB alcohol and (2-chlorophenyl) methanol, is considered to be as toxic as the parent.

### Derivation of Maximum Acceptable Value

No MAV.

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# Clopyralid

CAS No: 1702-17-6. The IUPAC name for clopyralid is 3,6-dichloropyridine-2-carboxylic acid or 3,6-dichloropicolinic acid. The CAS name is 3,6-dichloro-2-pyridinecarboxylic acid. Also used as an ester or a salt: in New Zealand it is used as the amine and the monoethanolamine.

### Maximum Acceptable Value

Clopyralid is not mentioned in the DWSNZ or in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 2 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Clopyralid is a selective pyridine [herbicide](http://en.wikipedia.org/wiki/Herbicide) used for control of broadleaf weeds, especially [thistles](http://en.wikipedia.org/wiki/Thistle) and [clovers](http://en.wikipedia.org/wiki/Clover). This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Clopyralid is notorious for its ability to persist in dead plants and [compost](http://en.wikipedia.org/wiki/Compost), and has accumulated to phytotoxic levels in finished compost in a few cases; it is not to be used on turf in New Zealand and contaminated greenwaste cannot be used for making compost.

The half-life in soil for clopyralid is typically 8–80 days. The major means of clopyralid degradation in the soil is by microbes. Carbon dioxide is the major product of degradation. Solubility in water is about 1,000 mg/L.

Clopyralid is a chemical which can travel (seep or leach) through soil and under certain conditions contaminate groundwater which may be used for irrigation or drinking purposes. Users are advised not to apply clopyralid where soils have a rapid to very rapid permeability throughout the profile (such as loamy sand to sand) and the water table of an underlying aquifer is shallow, or to soils containing sinkholes over limestone bedrock, severely fractured surfaces, and substrates which would allow direct introduction into an aquifer.

EFSA (2018) states that clopyralid was essentially stable in anaerobic soil incubations. Clopyralid exhibited very high mobility in soil. It was concluded that the adsorption of clopyralid was not pH dependent. In field dissipation studies clopyralid exhibited low to moderate persistence.

NPIC (1994) quotes for clopyralid amine salt a soil half-life of 40 days, water solubility of 30 percent and a sorption coefficient (soil Koc) of 6. This resulted in a pesticide movement to groundwater rating of very high.

### Typical concentrations in drinking-water

There is no entry for clopyralid in the “Pesticides in Groundwater Data Base”  
(EPA 734–12–92–001, September 1992).

The potential for groundwater exposure by the active substance clopyralid above the parametric drinking water limit of 0.1 µg/L consequent to the uses assessed, was indicated to be high in up to six out of nine FOCUS groundwater scenarios for the representative use on winter cereals and up to three out of nine of these scenarios for the representative use on grassland (EFSA 2018).

### Removal methods

Poorly removed by most water treatment processes. GAC is not likely to be effective either.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2018).

### Health considerations

USEPA (2002) quotes an acute RfD of 0.75 mg/kg/d and a chronic RfD of 0.15 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.15 mg/kg/d, and an ARfD of 0.75 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for clopyralid is 7.5 mg/L.

The Australian Acceptable Daily Intake (ADI) for clopyralid for a human is 0.5 mg/kg/day, set for the public for daily, lifetime exposure. This is based on the NOEL of 50 mg/kg/day from a long-term (two-year dietary) study. The NOEL is based on decreased bodyweight gain and adverse effects in the stomach epithelium observed in rats. The ADI incorporates a safety factor of 100.

The EC has set an ADI of 0.15 mg/kg/day; an ARfD was considered unnecessary. EFSA (2011) reaffirmed these values. The EC review established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is 6 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems.

EFSA (2018) confirmed the above ADI, and established an ARfD of 0.17 mg/kg bw per day based on the developmental toxicity study in rabbits with a maternal LOAEL at 50 mg/kg bw per day based on early reduction of maternal body weight and an additional UF of 3 (total 300) applied due to the basis of a LOAEL.

Clopyralid does not appear to be teratogenic, mutagenic or oncogenic at typical exposure concentrations. As at September 2008, the USEPA has classified clopyralid as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

No MAV.

In the US there is no established Maximum Concentration Level (MCL) for residues of clopyralid in drinking water, and no drinking water health advisory levels have been established.

### Bibliography

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# Cloquintocet mexyl

CAS No: 99607-70-2. The IUPAC name for cloquintocet mexyl is (RS)-1-methylhexyl (5‑chloroquinolin-8-yloxy)acetate. The CAS name is 1-methylhexyl 2-[(5-chloro-8-quinolinyl)oxy]acetate. Cloquintocet mexyl is a derivative of cloquintocet (CAS No. 88349-88-6).

### Maximum Acceptable Value

Cloquintocet mexyl is not mentioned in the DWSNZ, nor in the WHO Guidelines.

### Sources to water

Cloquintocet mexyl is a herbicide safener.

Although a component of clodinafop-propargyl, pinoxaden and pyroxsulam (qv), cloquintocet mexyl does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2016 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm).

USEPA (2005) states that cloquintocet mexyl is used in a 1:4 ratio, safener to active ingredient.

### Forms and fate in the environment

Cloquintocet mexyl is not persistent in soil (typical half-life five days), and has low leachability. It is persistent in water in the dark (half-life about 140 days) reducing to about three days in daylight.

The main metabolite is 5-chloro-8-quinolinoxyacetic acid.

Water solubility is about 0.60 mg/L. Octanol-water partition coefficient at pH 7 and 20oC is logP = 5.03. Henry’s Law constant at 20oC is 4.3 x 10-7, ie, moderately volatile.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

USEPA (2000) established a chronic RfD for cloquintocet mexyl of 0.04 mg/kg/d, and an acute RfD of 1.0 mg/kg/d, and classified it as “not likely to be a human carcinogen”.

The Acceptable Daily Intake (ADI) adopted in Australia for cloquintocet acid is 0.04 mg/kg body weight; there is no ARfD (<https://apvma.gov.au/>).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Clothianidin

CAS No: 210880-92-5 (E-isomer), or 205510-53-8 (unspecified stereochemistry). The IUPAC name for clothianidin is (E)-1-(2-chloro-1,3-thiazol-5-ylmethyl)-3-methyl-2-nitroguanidine. The CAS name is [C(E)]-N-[(2-chloro-5-thiazolyl)methyl]-N′-methyl-N″-nitroguanidine.

### Maximum Acceptable Value

Clothianidin is not mentioned in the DWSNZ, nor in the WHO Guidelines.

### Sources to water

Clothianidin is a systemic nitroguanidine (or thiazole or neonicotinoid or chloronicotinyl) insecticide, commonly used for treatment of cereal seeds. It operates as an acetylcholine receptor (nAChR) agonist. The product is registered for use on apples, pears, peaches and nectarines in Australia, and olives and some vegetables in Europe. It is also sprayed on to surfaces in animal housing from where it may enter the environment via manures (ECHA 2014). Clothianidin is a major metabolite of thiamethoxam (qv).

Clothianidin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). See generic note on pp. 5/6.

EFSA (2015) reports that the uses as seed treatment and soil treatment of plant protection products containing clothianidin, thiamethoxam or imidacloprid have been prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing these active substances have been prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering.

### Forms and fate in the environment

The fate and disposition of clothianidin in the environment suggest that it is persistent and mobile, stable to hydrolysis, and has potential to leach to groundwater, as well as run-off to surface waters. Soil half-lifes have been recorded at >1 year, with [N-methyl-N-nitroguanidine](http://sitem.herts.ac.uk/aeru/iupac/Reports/1418.htm) being a significant metabolite. Significant abiotic degradation products in water include N-(2-chlorothiazol-5-ylmethyl)-N’-methylurea, methylguanidine, 4-hydroxy-2-methylamino-2-imidazolin-5-one, formamide and methyl urea. It undergoes rapid photolysis with a half-life of 3.3 hours at pH 7 at 25°C.

EFSA (2015) reports that the soil DT50 of clothianidin ranges from 143 to 1,001 days under laboratory conditions and 13.3 to 305.4 days under field conditions.

The use of clothianidin is banned in some countries (eg, Germany) until the product is proved safe for bees.

Water solubility is about 320 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Clothianidin is classified as a “not likely” human carcinogen. There are no to low concerns and no residual uncertainties with regard to pre- and/or postnatal toxicity from clothianidin. However, due to evidence of effects on the rat immune system and that juvenile rats appear to be more susceptible to these effects, and due to the lack of a developmental immunotoxicity study, a 10X database uncertainty factor is applied to all dietary exposure endpoints (USEPA 2003).

The Acceptable Daily Intake (ADI) adopted in Australia for clothianidin is 0.05 mg/kg body weight, with a LOEL of 9.7 mg/kg bw, and the ARfD is 0.2 mg/kg bw.

IUPAC (2009) quotes an acceptable daily intake (ADI) and an acute reference dose (ARfD) of 0.1 mg/kg bw/d. EC (2004) and EFSA (2012/2014) quoted an ADI of 0.097 mg/kg bw and an ARfD of 0.1 mg/kg bw/d.

FAO/WHO (2010) established an acceptable daily intake (ADI) of 0–0.1 mg/kg bw on the basis of the NOAEL in the chronic study in the rat of 9.7 mg/kg bw per day for decreased body weight and feed consumption. A safety factor of 100 was applied. An acute reference dose (ARfD) of 0.6 mg/kg bw was established on the basis of the NOAEL of 60 mg/kg bw in the acute neurotoxicity study in the rat, based on reduced locomotor activity at 100 mg/kg bw. A safety factor of 100 was applied. The JMPR meeting considered that the effects seen in mice at 50 mg/kg bw per day in pharmacological studies were marginal and transient (less than 0.5–1 hour) at this dose level, whereas at the next dose level, 100 mg/kg bw per day, several effects were evident simultaneously in the same animals for longer times (three hours). These values were reaffirmed in JMPR (2014).

The acute population adjusted dose (PAD) of 0.025 mg/kg bwt/day based on an acute NOAEL of 25 with an uncertainty factor (UF) of 1,000 was used to assess acute dietary exposure. A chronic RfD has been developed by the USEPA (2003)= 0.0098 mg/kg/d. This was based on an offspring NOAEL of 9.8 mg/kg bw and an uncertainty factor of 1,000, from a two-generation reproduction study offspring LOAEL = 31.2 mg/kg/day based on decreased mean body weight gain and delayed sexual maturation, decreased absolute thymus weights in F1 pups and an increase in stillbirths in both generations. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.098 mg/kg/d, and an ARfD of 0.25 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for clothianidin is 2.5 mg/L.

All guideline studies conducted to characterise toxicological profile showed no endocrine related toxicity or tumourgenicity (USEPA 2004).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Coumaphos

CAS No: 56-72-4. The IUPAC name for coumaphos is O-3-chloro-4-methyl-2-oxo-2H-chromen-7-yl O,O-diethyl phosphorothioate or 3-chloro-7-diethoxyphosphinothioyloxy-4-methylcoumarin. The CAS name is O-(3-chloro-4-methyl-2-oxo-2H-1-benzopyran-7-yl) O,O-diethyl phosphorothioate.

### Maximum Acceptable Value

Coumaphos is not mentioned in the DWSNZ or in the WHO Guidelines.

### Sources to water

Coumaphos is an insecticide used for control of a wide variety of livestock insects and ectoparasites. Coumaphos has a residual period of two to three weeks on livestock. Coumaphos is also used in impregnated plastic strips in beehives to control varroa mites and small hive beetles.

Coumaphos is an [organothiophosphate acaricide](http://www.alanwood.net/pesticides/class_acaricides.html#organothiophosphate_acaricides) or heterocyclic organothiophosphate insecticide. Coumaphos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Coumaphos should not contain more than 0.06 percent of sulfotep.

### Forms and fate in the environment

Coumaphos is relatively immobile in a sandy loam soil and is unlikely to contaminate groundwater. A general characteristic of organophosphates such as coumaphos is that they bind fairly well to soil particles; therefore, they do not readily move (leach) with water percolating through the soil.

Coumaphos is relatively resistant to breakdown in water (hydrolysis). It is nearly insoluble in water (1.5 mg/L), and is stable over a wide pH range in water.

Coumaphos oxon is a metabolite of coumaphos (CAS No. 321-54-0).

### Typical concentrations in drinking-water

The USEPA considers that acute and chronic exposures to coumaphos in drinking water, based on surface and groundwater screening modelling, are not of concern.

### Removal methods

A general characteristic of organophosphates such as coumaphos is that they adsorb, or bind, fairly well to soil particles so treatment systems that remove particulate matter should reduce the concentration of coumaphos.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Rats that were given daily doses of 1.25 or 5 mg/kg in a two-year chronic feeding study had shortened life spans by 10 percent and 25 percent, respectively. A dose-related inhibition of cholinesterase was observed at 0.5 mg/kg or higher.

Once in the bloodstream, coumaphos may cross the placenta. No reproductive effects were observed in three generations of mice fed a dietary doses of 1.25 mg/kg/day.

Coumaphos was not found to be cancer-causing, or carcinogenic, in tests done on mice and rats. There was no increase in the number of tumours reported in rats given doses of 1.25 or 5 mg/kg/day of coumaphos in a two-year chronic feeding study. Coumaphos is classified by USEPA as a Group E chemical, indicating that it is “Not Likely” to be carcinogenic in humans via relevant routes of exposure.

An ADI of 0.0005 mg/kg was derived temporarily (EXTOXNET 1994). A Provisional Acceptable Daily Intake (PADI) for coumaphos is 0.0007 mg/kg/day and is based on the two-year rat feeding/oncogenicity study NOEL of 0007 mg/kg/day (based on plasma cholinesterase inhibition in females) and uncertainty factor of 100 (PMEP 1989).

The USEPA (1996) derived a NOAEL of 0.025 mg/kg/d based on plasma and RBC ChE inhibition in both male and female dogs seen at the LOAEL of 0.77 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0003 mg/kg/d, and an ARfD of 0.0025 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for coumaphos is 0.025 mg/L.

Coumaphos was first evaluated by the JMPR in 1968 when a temporary ADI was recommended. The temporary ADI was withdrawn by the 1980 JMPR and the temporary MRLs were converted to Guideline Levels. Countries were requested to provide data on current GAP to the JMPR.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0005 mg/kg body weight, with a NOEL of 0.05 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Coumatetralyl

CAS No: 5836-29-3. The IUPAC name for coumatetralyl is 4-hydroxy-3-[(1RS)-1,2,3,4-tetrahydro-1-naphthyl]coumarin. The CAS name is 4-hydroxy-3-(1,2,3,4-tetrahydro-1-naphthalenyl)-2H-1-benzopyran-2-one. Coumatetralyl technical grade is a racemic mixture of R and S enantiomers.

### Maximum Acceptable Value

Coumatetralyl is not mentioned in the DWSNZ or in the WHO Guidelines.

### Sources to water

Coumatetralyl is a coumarin rodenticide (used especially on rats) which operates as an [anticoagulant](http://en.wikipedia.org/wiki/Anticoagulant) of the [warfarin](http://en.wikipedia.org/wiki/Warfarin) type.

Coumatetralyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Coumatetralyl is stable to hydrolysis but in aqueous solutions is degraded rapidly by light to a number of degradation products, of which salicylic acid (ie, 2-hydroxybenzoic acid – qv) was identified as a major product.

Coumatetralyl can be classified as a moderately leachable compound in sandy soil. In loamy sand and sandy loam no leaching of coumatetralyl was observed. Its half-life in soils is about 3 months.

Water solubility is about 4.5 mg/L at pH 5; 46 mg/L at pH 7; 4650 mg/L at pH 9.

### Recommended analytical techniques

#### Referee method

See EC (2009).

### Health considerations

The NOAEL is set at 0.0068 mg coumatetralyl/kg bw/day in males and 0.0083 mg coumatetralyl/kg bw/day in females based on a subchronic toxicity study of coumatetralyl conducted in rat by oral dosing.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.000003 mg/kg body weight, with a NOEL of 0.0068 mg/kg bw.

Justification for a waiver for long-term/carcinogenicity studies is based on the lack of mutagenic/genotoxic effects, the absence of any other effects that may lead to non-genotoxic carcinogenesis, the absence of any carcinogenic effects following long-term administration of warfarin (also a coumarin compound) in humans, and the absence of potential for long-term exposure of the public population.

Vitamin K1 can be used as an antidote.

### Derivation of Maximum Acceptable Value

No MAV.

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# Cyanazine

CAS No: 21725-46-2. The IUPAC name for cyanazine is 2-(4-chloro-6-ethylamino-1,3,5-triazin-2-ylamino)-2-methyl propionitrile. The CAS name is 2-[[4-chloro-6-(ethylamino)-1,3,5-triazin-2-yl]amino]-2-methylpropanenitrile.

### Maximum Acceptable Value

Based on health considerations, the concentration of cyanazine in drinking-water should not exceed 0.0007 mg/L (0.7 μg/L). Cyanazine is included in the plan of work of the rolling revision of the WHO *Guidelines for Drinking-water Quality*.

USEPA (1999) refers to cyanazine being phased out in the US. Despite that, the USEPA (2009/2011) established a lifetime health advisory of 0.001 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The maximum acceptable concentration in Canada is 0.01 mg/L.

### Sources to water

Cyanazine is a member of the triazine family of herbicides. It is used as a pre- and post-emergence selective herbicide for the control of annual grasses and broadleaf weeds. Cyanazine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Cyanazine should not contain more than 20 g/kg of 2-(4-amino-6-chloro-1,3,5-triazin-2-ylamino)-2-methyl propionitrile, 3 g/kg of 2-(4,6-dichloro-1,3,5-triazin-2-ylamino)-2-methyl propionitrile, or 10 g/kg of simazine.

No information is available on the annual usage of specific active ingredients in New Zealand, although cyanazine is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Cyanazine is quite soluble in water: 171 mg/L (Merck & Co 1996).

Cyanazine has a half-life in soil of 14 days (Hort Research 2000). It can be degraded in soil and water by micro-organisms and by hydrolysis. Four degradation products can be identified for cyanazine – the amide, two acids, and the amine. Aerobically and anaerobically aged cyanazine residues, primarily the amine degradation product, are intermediately mobile to mobile in sandy clay loam soil. The degradation products have all been identified in soil leachate, as has unaltered cyanazine (WHO 1998).

If released to soil, cyanazine is expected to have moderate mobility based upon a range of measured Koc’s of 182–372. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 2.57 x 10-10 atm-cu m/mole. Cyanazine is not expected to volatilise from dry soil surfaces based upon its vapour pressure. The half-life of cyanazine determined in field studies ranged from 6–30 days. The half-life of cyanazine measured under laboratory conditions ranged from 3–19 days at 30° and 5°C, respectively (34 percent moisture content) to greater than 200 days at 20°C and 8 percent moisture content. If released into water, cyanazine is expected to adsorb to suspended solids and sediment based upon the range of Koc’s. The half-life of cyanazine ranged from 30–40 days in constructed wetlands. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. An estimated BCF of 5 suggests the potential for bioconcentration in aquatic organisms is low. The un-catalysed aqueous chemical hydrolysis half-life of cyanazine is at least 200 days; however, laboratory studies have suggested that natural water constituents, such as humic and fulvic acid, may catalyse the chemical hydrolysis of cyanazine. Photodegradation of cyanazine is not expected to be an important fate process (EAWAG accessed February 2015).

NPIC (1994) quotes for cyanazine a soil half-life of 14 days, water solubility of 170 mg/L and a sorption coefficient (soil Koc) of 190. This resulted in a pesticide movement to groundwater rating of low.

USGS (2006) give the following values: log Kow = 2.22; log Koc (where Koc is in mL/g) = 2.3; water solubility = 171 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -6.52; half-life in aerobic soil = 17 days; half-life in water = >200 days.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included cyanazine.

In the New Zealand national pesticides surveys conducted for groundwater every four years since 1990, cyanazine has been detected once, at a concentration of 0.001 mg/L. Monitoring conducted by Environment Canterbury has also detected cyanazine in groundwater at two locations in the Level Plain area in South Canterbury. At one location it has been detected in four monitoring rounds at concentrations ranging from 0.00007 to 0.00475 mg/L, whilst at the other location it has been detected once, at a concentration of 0.00004 mg/L (Close et al 2001). Cyanazine has been found in a Canterbury groundwater at 0.0007 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Cyanazine occurred at 1.0 µg/L.

Cyanazine was detected in nine of 1,128 samples of municipal and private water supplies in Quebec (1986), Ontario (1979 to 1986) and Alberta (1978 to 1986) (detection limits ranged from 0.000025 to 0.001 mg/L). Concentrations ranged from less than 0.0001 mg/L in Quebec water supplies to 0.004 mg/L in Ontario water supplies (Health Canada 1989). Cyanazine has also been detected at trace levels in surface and groundwater in some US states (WHO 1998).

Cyanazine has been found in groundwater in the Netherlands at concentrations above 0.0001 mg/L. It was not detected in surface water used as a source for drinking-water (Council of Europe 1993, cited in WHO 1998).

Has been detected in surface water and groundwater, usually at concentrations of a few micrograms per litre, although levels as high as 1.3 and 3.5 mg/L have been measured in surface water and groundwater, respectively (WHO 2004/2017).

Four water utilities in the US reported detecting cyanazine (bladex) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest concentration being 0.00058 mg/L.

### Removal methods

Oxidation of triazines by ozone is reported to be effective (Chiron et al 2000). The water chemistry, in particular the alkalinity and pH, will affect the oxidation rate. Use of activated carbon following ozonisation should be considered to adsorb oxidation products; 0.1 μg/L should be achievable using GAC (WHO 2017).

Nanofiltration (membrane technology) in water with a low natural organic matter concentration is reported to remove approximately 50 percent of atrazine and simazine (Agbekodo et al 1996). The percentage is increased to 90–100 percent when 3.6 mg/L of natural organic matter is present. Similar results may be expected for cyanazine as it is from the same chemical family and of comparable molecular size.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of cyanazine, although a guide to the efficiency of the process cannot be provided.

### Recommended analytical techniques

#### Referee method

Liquid/extraction/gas chromatography (EPA).

#### Some alternative methods

HPLC (Method #4; USEPA). Methylene chloride extract is dried and concentrated to 10 mL or less. HPLC is used to separate compounds, and measurement is conducted with an ultraviolet detector. Detection limit is 0.0003 mg/L. See WHO (2003) for further information.

### Health considerations

There is no information available regarding the greatest source of exposure to cyanazine for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

Cyanazine is rapidly absorbed from the gastrointestinal tract of experimental animals. Between 80 and 88 percent of doses of radioactively labelled cyanazine are eliminated from rats and dogs within four days, and within 21 days in cows. In rats, elimination in urine was almost equal to elimination in faeces. In dogs and cows, approximately one-half of the dose was eliminated in the urine, and about one-third was eliminated in the faeces. In cows, the amount of residues excreted daily was constant throughout the study period. Cyanazine was also detected in cow’s milk (WHO 1998).

#### Acute poisoning

The acute oral LD50 for rats is 182–334 mg/kg, mice 380 mg/kg, rabbits 141 mg/kg (RSocC 1987). These values suggest a relatively high acute oral toxicity compared with other pesticides. WHO (1996) has classified cyanazine as “moderately hazardous”.

Poisoned animals have laboured breathing and blood in their saliva (Occupational Health Services. Material Safety Data Sheet on Cyanazine. 3/17/87 OHS: NY). The pesticide also causes inactivity and depression in laboratory animals.

#### Chronic exposure

The reference dose or RfD (USEPA 2006/2009/2011) is 0.002 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.07 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw.

On the basis of the available mutagenicity data on cyanazine, evidence for genotoxicity is equivocal.

Cyanazine causes mammary gland tumours in Sprague-Dawley rats but not in mice. The mechanism of mammary gland tumour development in Sprague-Dawley rats is currently under investigation and may prove to be hormonal (WHO 1998). Cyanazine is also teratogenic (causes birth defects) in Fischer 344 rats at dose levels of 25 mg/kg of body weight per day and higher.

The International Agency for Research on Cancer has not classified cyanazine for its ability to cause cancer. Atrazine, which has a chemical structure similar to that of cyanazine, has been found to increase the incidence of mammary tumours in rats and has been classified by IARC (1991) in Group 2B (agent is possibly carcinogenic to humans). As at September 2008 the USEPA has classified cyanazine in Group C: a possible human carcinogen. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV for cyanazine in drinking-water. The NOAEL was established on the basis of hyperactivity in male rats in a two-year toxicity/carcinogenicity study. The MAV was derived as follows:

0.198 mg/kg body weight per day x 70 kg x 0.1 = 0.00069 mg/L (rounded to 0.0007 mg/L)

2 L x 1,000

where:

* no-observable-adverse-effect level = 0.198 mg/kg body weight per day identified on the basis of hyperactivity in male rats in a two-year toxicity/carcinogenicity study
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 1,000 (100 for interspecies and interspecies variation and 10 for limited evidence of carcinogenicity).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for cyanazine is 0.001 mg/L; the acute limit (one-day exposure) is 0.002 mg/L.

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# Cyantraniliprole

CAS No. [736994-63-1](http://www.commonchemistry.org/ChemicalDetail.aspx?ref=736994-63-1). The IUPAC name for cyantraniliprole is 3-bromo-1-(3-chloro-2-pyridyl)-4′-cyano-2′-methyl-6′-(methylcarbamoyl)pyrazole-5-carboxanilide. The CAS name is 3-bromo-1-(3-chloro-2-pyridinyl)-N-[4-cyano-2-methyl-6-[(methylamino)carbonyl]phenyl]-1H-pyrazole-5-carboxamide. DuPont markets it as Exirel and Benevia in New Zealand.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for cyantraniliprole; it is not mentioned in the WHO Guidelines.

### Sources to water

Cyantraniliprole is described a diamide or [pyrazole insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#pyrazole_insecticides) with a ryanodine receptor activation mode of action similar to chlorantraniliprole and flubendiamide. Despite its structural similarity to some of the phenylpyrazole insecticides, this substance has a different mode of action, which it shares with other [diamide insecticides](http://www.alanwood.net/pesticides/class_insecticides.html#diamide_insecticides) (or anthranilic diamides), similar to chlorantraniliprole (qv). It is also described as belonging to the ryanoid insecticides. Because of its uncommon [mechanism of action](http://en.wikipedia.org/wiki/Mechanism_of_action) as a ryanoid, it has activity against pests such as [Diaphorina citri](http://en.wikipedia.org/wiki/Diaphorina_citri) that have developed resistance to other classes insecticides.

In New Zealand Benevia is intended for application on potatoes, tomatoes and onions. Exirel is intended for application on brassicas (turnips, swede, forage rape and kale).

Cyantraniliprole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

DT50 values for cyantraniliprole in aerobic soil degradation studies (incubated in the dark) with five soils ranged from 8.7 to 92 days (geomean = 30.7 days); slightly faster in anaerobic soils. Cyantraniliprole is classified as having medium to high mobility in soil, and mobility of the metabolites ranged from highly to very highly mobile. The potential for groundwater exposure from the representative uses by cyantraniliprole was concluded to be low.

The rate of hydrolysis of cyantraniliprole in water is pH and temperature dependent, with DT50 values at 20°C calculated from aqueous photolysis studies being 260, 61 and 1.8 days, respectively, at pH 4, 7 and 9. Photochemical degradation of cyantraniliprole in water was very rapid, with a DT50 of <1 days. In laboratory incubations in dark aerobic natural sediment water systems, cyantraniliprole exhibited moderate persistence at pH 6.1 and low persistence at pH 7.6, forming the major metabolite IN‑J9Z38 (maximum 48 percent AR in water after nine days and maximum 77 percent AR in sediment after 56 days, which exhibited high persistence). Figure 9 in JMPR (2013) shows the degradation of cyantraniliprole in outdoor water-sediment.

Soil degradation studies demonstrated that cyantraniliprole is of moderate to high persistence, with a maximum DT90 of 376 days, whilst several metabolites demonstrated a moderate to very high persistence with DT90 values estimated to be in the range of four to nine years (EFSA 2014).

Under anaerobic conditions, cyantraniliprole degraded in the water phase and also partitioned to the sediment where it was further degraded to other metabolites that eventually were incorporated into the sediment organic fraction.

Cyantraniliprole is highly toxic to bees.

JMPR (2013) tabulates several metabolites.

The water solubility of cyantraniliprole is about 12–17 mg/L at 20°C; it hydrolyses at pH 9. Henry’s Law constant = 1.7 x 10-13 Pa/m3/mol. Octanol/water partition coefficient = log Kow = 1.94.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The toxicokinetics of cyantraniliprole showed an oral absorption value of 70 percent, an extensive distribution in the body, no significant bioaccumulation, and an excretion occurring mainly within 48h after administration. Cyantraniliprole did not show evidence of acute toxicity in the available studies (EFSA 2014). EFSA (2015) quotes an ADI of 0.01 mg/kg/d, and that an ARfD is not necessary.

JMPR (2013) established an ADI 0–0.03 mg/kg bw on the basis of the overall NOAEL of 3.08 mg/kg bw per day in dog studies, based on liver effects at 5.67 mg/kg bw per day; a safety factor of 100 was applied. It was not necessary to establish an acute reference dose (ARfD) for cyantraniliprole in view of its low acute toxicity and the absence of developmental toxicity and any other toxicological effects that would be likely to be elicited by a single dose. The JMPR meeting concluded that cyantraniliprole is unlikely to be genotoxic and is unlikely to pose a carcinogenic risk to humans.

APVMA (2013) established an ADI of 0.01 mg/kg bw/day, based on a NOAEL of 1 mg/kg bw/d in a one-year oral study in beagle dogs, using a default 100-fold safety factor. An acute reference dose (ARfD) was not established for cyantraniliprole, as cyantraniliprole is of low acute toxicity, and did not demonstrate evidence of a genotoxic, neurotoxic, or reproductive/developmental toxicity potential after a single dose (<https://apvma.gov.au/>).

The following Acceptable Daily Exposure (ADE) and Potential Daily Exposure (PDE) values have been set for cyantraniliprole in New Zealand (EPA 2013):

* ADE = 0.01 mg/kg bw/day
* PDEFood = 0.007 mg/kg bw/day
* PDEWater = 0.002 mg/kg bw/day
* PDEOther = 0.001 mg/kg bw/day.

The acceptable daily intake (ADI) for cyantraniliprole is 0.01 mg/kg bw per day, based on the one-year dog study and applying an uncertainty factor (UF) of 100. On the basis of the available data, an acute reference dose (ARfD) is not required for cyantraniliprole (EFSA 2014).

USEPA (2014) classified cyantraniliprole as “not likely to be carcinogenic to humans” based on the absence of increased tumour incidence in acceptable/guideline carcinogenicity studies in rats and mice. In addition, there are no genotoxicity, mutagenicity, neurotoxicity, or immunotoxicity concerns. There are also no developmental or reproductive toxicity concerns. There is no evidence of an adverse effect attributable to a single dose. The chronic RfD = 0.01 mg/kg/day based on a one-year oral study in dogs; LOAEL = 6 mg/kg/day based on effects indicative of liver toxicity (increased liver weights and alkaline phosphatase activity), and significant decreases in albumin level.

### Derivation of Maximum Acceptable Value

No MAV.

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# Cyazofamid

CAS No. 120116-88-3. The IUPAC name for cyazofamid 4-chloro-2-cyano-N,N-dimethyl-5-p-tolylimidazole-1-sulfonamide. The CAS name is 4-chloro-2-cyano-N,N-dimethyl-5-(4-methylphenyl)-1H-imidazole-1-sulfonamide. A trade name is Ranman.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for cyazofamid; it is not mentioned in the WHO Guidelines.

### Sources to water

Cyazofamid is an [imidazole](http://www.alanwood.net/pesticides/class_fungicides.html#imidazole_fungicides) or sulfonamide or cyanoimidazole fungicide.

Cyazofamid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2016 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). It is used to control foliar fungal diseases of various horticultural crops, including late blight in potatoes and downy mildew in grapes, brassicas, onions and cucurbits, blights in tomatoes and peppers.

### Forms and fate in the environment

If released to soil, cyazofamid is expected to have low to slight mobility based upon Koc values of 736 to 2172. Volatilisation from moist soil surfaces is not expected to be an important fate process based on its Henry’s Law constant of 3.9 x 10-7 atm-cu m/mole. Biodegradation half-lifes in aerobic soil are reported as 3.7 to 6.4 days, indicating that biodegradation is an important environmental fate process. Cyazofamid’s fate in soil as well as its limited mobility in soil environments appears to be controlled by biotic degradation as well as its strong affinity for adsorption to soil. If released into water, cyazofamid is expected to adsorb to suspended solids and sediment based upon the Koc values. Biodegradation half-lifes of cyazofamid in aerobic aquatic environments were 14.7 to 18.0 days, aqueous anaerobic half-lifes were 5.6 to 6.2 days. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 60 suggests the potential for bioconcentration in aquatic organisms is moderate. Photodegradation of cyazofamid in aqueous systems has a reported half-life of 30 minutes. Hydrolysis half-lifes of cyazofamid in aqueous environments averaged 11.9 days over a pH range of 4 to 9.

USEPA (2004) quotes half-lifes of 5.5 days (aerobic soil), 16.4 days (aerobic aquatic) and 0.02 days (aquatic photolysis). Cyazofamid is not persistent or mobile in the environment. The combined data on cyazofamid and its degradates indicate that the terminal major degradation products are CCIM and CTCA. CTCA is expected to be the terminal persistent/mobile degradate in soils and therefore may contaminate groundwater by leaching or surface water by run-off. In contrast, CCIM is expected to be the major terminal degradate in water bodies with low biological activity because it expected to form in the system mainly as a result of abiotic hydrolysis of the parent and is stable to hydrolysis.

According to the soil degradation studies evaluated in the framework of the peer review, laboratory DT90 values of cyazofamid, metabolite CCIM, and metabolite CCIM-AM range between 17–50 days, 12–71 days, and 123–187 days, respectively (EFSA 2015).

The water solubility of cyazofamid is about 0.1 mg/L at 20°C from pH 5 to 9. The octanol/water partition coefficient, LogP (log Kow) = 3.2.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of cyazofamid.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

USEPA (2004) an acute RfD (and aPAD) of 1.0 mg/kg/d, and a chronic RfD (and cPAD) of 0.95 mg/kg/d.

EFSA (2015) adopted an ADI of 0.17 mg/kg body weight (bw) per day; no acute reference dose (ARfD) was deemed necessary.

The Acceptable Daily Intake (ADI) adopted in Australia is 1.24 mg/kg body weight, with a NOEL of 124 mg/kg bw from the 18–month carcinogenicity study in mice. An ARfD was considered unnecessary (APVMA 2015).

Cyazofamid is classified as not likely to be carcinogenic to humans based on the lack of evidence of carcinogenicity in both the rat and the mouse (USEPA 2004).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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USEPA. 2004. *Cyazofamid: Pesticide factsheet* [25 pp]. <https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-085651_01-Sep-04.pdf>

# Cyflufenamid

CAS No. 180409-60-3. The IUPAC name for cyflufenamid is (Z)-N-[α-(cyclopropylmethoxyimino)-2,3-difluoro-6-(trifluoromethyl)benzyl]-2-phenylacetamide. The CAS name is [N(Z)]-N-[[(cyclopropylmethoxy)amino][2,3-difluoro-6-(trifluoromethyl)phenyl]methylene]benzeneacetamide.

The product includes an E-isomer too; apple and cucumber metabolism studies showed that no significant isomeric conversion from the Z-isomer to the E-isomer occurred (EFSA 2014).

### Maximum Acceptable Value

The DWSNZ do not have a MAV for cyflufenamid; it is not mentioned in the WHO Guidelines.

### Sources to water

Cyflufenamid is an amide or phenylacetamide or amidoxime fungicide. Although its mode of action is still unknown, the compound has shown to be effective against powdery/downy mildew in plants.

Cyflufenamid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at October 2015 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Under aerobic soil conditions cyflufenamid exhibits low to high persistence (DT90 301 day) and forms its relevant soil metabolites: 149–F10, 149–F1111, 149–F112 and 149–F613. The DT90 values for cyflufenamid and its metabolites 149–F1 (DT90 = 1093 days) and 149–F6 (DT90 = 2,138 days).

Cyflufenamid is hydrolytically stable at pH 4, 5, and 7. The environmental phototransformation half-life of cyflufenamid in water is ca. 220 days with no major degradation products (PMEP 2013).

In a field leaching study using a sandy soil where it was concluded there was a very low potential for cyflufenamid or its degradation products to leach to groundwater. In field dissipation studies, there was limited movement of cyflufenamid or its main metabolites through the soil profile (APVMA 2012).

Partition coefficient (octanol/water) at pH 4 : log Pow = 4.68; pH 6.75: log Pow = 4.70; pH 9.95: log Pow = 24.55. Henry’s Law constant = 2.81 x 10-2 Pa.m3/mol (APVMA 2012).

The water solubility of cyflufenamid is about 0.52 mg/L at 20°C.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of cyflufenamid.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Cyflufenamid has low acute toxicity via the oral route. In the mammalian toxicology database, the liver was the primary target organ for cyflufenamid toxicity. Cyflufenamid is classified as “likely to be carcinogenic to humans”. This was based on the presence of two tumour types in two species: thyroid follicular cell tumours in male rats, and liver tumours in male mice. There is no concern for mutagenicity or clastogenicity. A chronic RfD of 0.044 mg/kg/d was derived (USEPA 2012).

APVMA (2012) developed an ADI for cyflufenamid at 0.04 mg/kg bw/d (rounding down), based on a NOEL of 4.14 mg/kg bw/d in male dogs for elevated ALP levels in a 52-week oral study and applying a default safety factor of 100 for potential interspecies and intraspecies variability. The ARfD was established at 0.1 mg/kg bw based on a NOEL of 10 mg/kg bw/d from an oral rabbit developmental study for both maternal (decreased body weight gain and food consumption) and developmental toxicity (increased minor skeletal variations/abnormalities) and applying a default safety factor of 100 for potential interspecies and intraspecies variability. In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The acceptable daily intake (ADI) for cyflufenamid is 0.04 mg/kg bw per day based on two-year rat and one-year dog studies, and an acute reference dose (ARfD) of 0.05 mg/kg bw based on a rabbit developmental toxicity study (maternal toxicity) (EFSA 2014).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2012. *Public Release Summary on the Evaluation of the New Active Cyflufenamid in the Product Cyflamid 50EW Fungicide* [55 pp]. <http://apvma.gov.au/sites/default/files/publication/13656-prs-cyflufenamid.pdf>

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# Cyfluthrin

CAS Nos. are:

* 68359-37-5 (unstated stereochemistry)
* 86560-92-1 (diastereoisomer I)
* 86560-93-2 (diastereoisomer II)
* 86560-94-3 (diastereoisomer III)
* 86560-95-4 (diastereoisomer IV).

The IUPAC name for cyfluthrin is (RS)-α-cyano-4-fluoro-3-phenoxybenzyl (1RS,3RS;1RS,3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, or (RS)-α-cyano-4-fluoro-3-phenoxybenzyl (1RS)-cis-trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate. The CAS name is cyano(4-fluoro-3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.

Cyfluthrin contains the four diastereoisomers in the following proportions:

* 23–27 percent diastereoisomer I
* 17–21 percent diastereoisomer II
* 32–36 percent diastereoisomer III
* 21–25 percent diastereoisomer IV.

Cyfluthrin has a trade name of baythroid.

Beta-cyfluthrin is an enriched isomeric form of the two biologically active diastereoisomeric pairs (II and IV) of isomers of cyfluthrin, with small amounts of diastereoisomers I and III (<5 percent). JMPR considers it a new compound and is evaluated together with cyfluthrin as data generated with cyfluthrin are used in support of beta-cyfluthrin and vice versa.

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.05 mg/L for cyfluthrin (beta-cyfluthrin); minor excursions above this level even for a short period are of concern, as the health-based guideline is based on short- to medium-term effects.

### Sources to water

Cyfluthrin is a Type II (alpha-cyano) synthetic pyrethroid, a non-systemic chemical used to control a wide range of insect pests. It is sometimes mixed with other pesticides, and/or with piperonyl butoxide (qv). Cyfluthrin is authorised for use in veterinary medicinal products for bovine and caprine (EFSA 2016).

Cyfluthrin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

NPIC (1994) quotes for cyfluthrin a soil half-life of 30 days, water solubility of 0.002 mg/L and a sorption coefficient (soil Koc) of 100,000. The half-life in water is less than a day. This resulted in a pesticide movement to groundwater rating of extremely low. Cyfluthrin is sensitive to breakdown by sunlight; on the surface of soils, its half-life is 48–72 hours.

The water solubility of cyfluthrin is 1.9 to 4.3 µg/L at pH 3 to 7, for all four isomers.

Beta-cyfluthrin exhibited low to moderate persistence on bare soil plots. In laboratory incubations in dark aerobic natural sediment water systems, where cyfluthrin was dosed, the relative amounts of diastereoisomers II and IV were summed up and combined with the measured concentration (% AR) of cyfluthrin to account for beta-cyfluthrin. Beta-cyfluthrin exhibited moderate persistence, forming the major metabolites DCVA (maximum 36.0 percent AR in water and 23.7 percent AR in sediment, exhibiting high persistence based on the available data), FPB aldehyde (maximum 1.1 percent AR in water and 15.7 percent AR in sediment, exhibiting low persistence) and FPB acid (maximum 29.1 percent AR in water and 24.3 percent AR in sediment, exhibiting low persistence). The potential for groundwater exposure from the representative uses of beta-cyfluthrin above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios for beta-cyfluthrin and its metabolites DCVA and FPB acid (EFSA 2018).

EC (2002) and JMPR (2007) discuss metabolites of cyfluthrin.

### Removal methods

Because most pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2018).

### Health considerations

USEPA (2005) established an acute RfD of 0.02 mg/kg/d and a chronic RfD of 0.024 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.024 mg/kg/d, and an ARfD of 0.02 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cyfluthrin is 0.20 mg/L.

The acceptable daily intake (ADI) for cyfluthrin in Australia is 0.02 mg/kg body weight, with a NOEL of 2.5 mg/kg bw. The acceptable daily intake (ADI) for beta-cyfluthrin in Australia is 0.01 mg/kg body weight, with a NOEL of 1.5 mg/kg bw.

The ADIs and ARfDs quoted in EC (2002) are 0.003 mg/kg/d and 0.02 mg/kg/d respectively, for both cyfluthrin and beta-cyfluthrin. EFSA (2013) confirmed these values for cyfluthrin. EFSA (2016) confirmed these values for beta-cyfluthrin. But EFSA (2018) derived an value of 0.01 mg/kg bw (per day) for the ADI and ARfD for beta-cyfluthrin on the basis of the 4-week rat study with the application of an uncertainty factor (UF) of 100.

JMPR established a common ADI of 0.04 mg/kg/d and ARfD of 0.04 mg/kg/d for cyfluthrin and beta-cyfluthrin (ie, cyfluthrin: sum of isomers) (JMPR 2012; FAO/WHO 2013).

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for cyfluthrin since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

EFSA (2018) found that based on the overall weight of evidence from the available studies, beta-cyfluthrin is considered unlikely to be genotoxic in vivo or carcinogenic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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EFSA. 2013. Reasoned opinion on the modification of the existing MRL for cyfluthrin in artichokes. *EFSA Journal* 11(10): 3448 [26 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm>

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WHO. Cyfluthrin. *WHO Specifications and Evaluations for Public Health Pesticides* [29 pp]. http://www.who.int/whopes/quality/en/Cyfluthrin\_spec\_eval\_WHO\_Nov\_2004.pdf

# Cyhalothrin

CAS No. for cyhalothrin is 68085-85-8. The IUPAC name for cyhalothrin is (RS)-α-cyano-3-phenoxybenzyl (1RS,3RS)-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate, or (RS)-α-cyano-3-phenoxybenzyl (1RS)-cis-3-[(Z)-2-chloro-3,3,3-trifluoropropenyl]-2,2-dimethylcyclopropanecarboxylate. The CAS name is cyano(3-phenoxyphenyl)methyl (1R,3R)-rel-3-[(1Z)-2-chloro-3,3,3-trifluoro-1-propenyl]-2,2-dimethylcyclopropanecarboxylate.

Cyhalothrin is a chlorotrifluoro derivative of chrysanthemic acid. Although theoretically it could be a mixture of 16 enantiomers, this number has been reduced to four in actual practice. Some subsets of isomers of this substance have their own ISO common name, eg, [gamma-cyhalothrin](http://www.alanwood.net/pesticides/gamma-cyhalothrin.html) and [lambda-cyhalothrin](http://www.alanwood.net/pesticides/lambda-cyhalothrin.html). See JMPR (2008) for more details.

Lambda-cyhalothrin (CAS No. 91465-08-6) is a synthetic pyrethroid insecticide; it is manufactured as enantiomer pairs cis A and cis B. Lambda-cyhalothrin is the optimised product containing largely pair cis B, which in turn is a racemic mixture of two enantiomers: 1R,cis,Z-S‟and 1S,cis,Z-R‟.

Gamma-cyhalothrin (CAS No. 76703-62-3) is a single, resolved isomer of the pyrethroid insecticide cyhalothrin, and as such shares physical, chemical, and biological properties with both cyhalothrin and lambda-cyhalothrin, which are mixtures of four and two isomers respectively. Gamma-cyhalothrin is the most insecticidally active isomer of cyhalothrin/lambda-cyhalothrin, and thus the technical gamma-cyhalothrin product may be considered a refined form of cyhalothrin/lambda-cyhalothrin in that it has been purified by removal of less active and inactive isomers. Thus, similar levels of insecticidal efficacy for gamma-cyhalothrin can be obtained with significantly reduced application rates as compared with either cyhalothrin or lambda-cyhalothrin (USEPA 2004).

Commercial cyhalothrin comprises approximately 50 percent lambda-cyhalothrin (cis 1RαS and cis 1SαR enantiomers, enantiomeric pair B) and 50 percent R157836 (cis 1RαR and cis 1SαS enantiomers, enantiomeric pair A).

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

### Sources to water

Lambda-cyhalothrin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Cyhalothrin was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in spinach.

### Forms and fate in the environment

On soil surfaces and in aqueous solutions at pH 5, lambda-cyhalothrin is degraded in sunlight with a half-life of approximately 30 days. The main degradation products are 3-(2-chloro-3,3,3-trifluoroprop1-enyl)-2-dimethylcyclopropane carboxylic acid, the amide derivative of cyhalothrin, and phenoxybenzoic acid (IPCS HSG 1990).

In laboratory studies, lambda-cyhalothrin hydrolysed in water (pH 9) with a half-life of approximately seven days. No hydrolysis occurred in water at lower pH values (pHs 5 and 7). The low water solubility and high binding affinity of lambda-cyhalothrin indicates a low potential to contaminate ground water (NPIC). NPIC (1994) quotes for lambda-cyhalothrin a soil half-life of 30 days, water solubility of 0.005 mg/L and a sorption coefficient (soil Koc) of 180,000. This resulted in a pesticide movement to groundwater rating of extremely low. JMPR (2008) discusses metabolites of lambda-cyhalothrin. According to the soil degradation studies the DT90 value of lambda-cyhalothrin is 112 days (EFSA 2015).

In soil laboratory incubations under aerobic conditions in the dark, gamma-cyhalothrin exhibited moderate persistence. Gamma-cyhalothrin can be considered immobile in soil. In laboratory incubations in dark aerobic natural sediment water systems, dissipation of gamma-cyhalothrin from the water phase primarily through partitioning to sediment was relatively rapid. Water solubility is about 0.002 mg/L. The half-life in water is 46 days, 27 days in soil, and 1,000 days in sediment (EFSA 2014).

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (20017).

### Health considerations

USEPA (2004) developed an acute RfD of 0.0025 mg/kg/d and a chronic RfD of 0.001 mg/kg/d for gamma-cyhalothrin. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.001 mg/kg/d, and an ARfD of 0.0025 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for gamma cyhalothrin is 0.025 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.001 mg/kg/d, and an ARfD of 0.005 mg/kg/d for both cyhalothrin and lambda-cyhalothrin. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cyhalothrin and lambda-cyhalothrin is 0.05 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for gamma-cyhalothrin is 0.0005 mg/kg bw, NOEL of 0.5 mg/kg bw (ARfD = 0.005 mg/kg bw); and for lambda-cyhalothrin: 0.001 mg/kg body weight, with a NOEL of 0.1 mg/kg bw.

A group ADI for cyhalothrin and lambda-cyhalothrin was established by JMPR in 2008 at 0–0.02 mg/kg bw and a group ARfD, 0.02 mg/kg bw (JMPR 2015).

The Acceptable Daily Intake (ADI) adopted by EFSA (2014/17) for gamma-cyhalothrin is 0.0012 mg/kg bw, based on the NOAEL of 0.5 mg cyhalothrin/kg bw per day from the multigeneration study in rat, applying an uncertainty factor (UF) of 400, ie, a standard UF of 100 and an additional factor of four to convert from cyhalothrin to gamma-cyhalothrin. The ARfD is 0.0025 mg/kg.

The acceptable daily intake (ADI) adopted by EFSA (2014a, 2015/17) for lambda-cyhalothrin is 0.0025 mg/kg bw per day, based on the NOAEL of 0.5 mg cyhalothrin/kg bw per day from the multigeneration study in rat, applying an uncertainty factor (UF) of 200, ie, a standard UF of 100 and an additional factor of two to convert from cyhalothrin to lambda-cyhalothrin. The acute reference dose (ARfD) is 0.005 mg/kg bw, based on the NOAEL of 0.5 mg lambda-cyhalothrin/kg bw per day from the one-year study in dogs, applying the standard UF of 100.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for cyhalothrin of:

* 0.01 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.01 mg/kg/day for intermediate-duration oral exposure (15–364 days).

The EC quotes an ADI and ARfD of 0.005 and 0.0075 mg/kg/d respectively for lambda-cyhalothrin (reaffirmed by EFSA 2013), whereas JMPR (2008) and FAO/WHO (2007) quote 0.02 mg/kg/d for both ADI and ARfD, for both cyhalothrin and lambda-cyhalothrin.

### Derivation of Maximum Acceptable Value

No MAV.

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# Cymoxanil

CAS No. 57966-95-7. The IUPAC name for cymoxanil is 1-[(EZ)-2-cyano-2-methoxyiminoacetyl]-3-ethylurea. The CAS name is 2-cyano-N-[(ethylamino)carbonyl]-2-(methoxyimino)acetamide.

### Maximum Acceptable Value

There is no MAV for cymoxanil in the DWSNZ, and it is not mentioned in the WHO Guidelines.

### Sources to water

Cymoxanil is a systemic aliphatic nitrogen (cyanoacetamide or oxime) fungicide, which may be used on crops including potatoes (seed or foliar), tomatoes, and grapes. It is usually used in conjunction with other pesticides, eg, in New Zealand: fluidoxonil and metalaxyl-m (qv).

Cymoxanil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

In principle, N-nitrosamines might be formed in the manufacture of cymoxanil and the manufacturer therefore determined total N-nitrosamines in batches (96/829). The content of total N-nitrosamines was <1 mg/kg in all cases and the JMPR meeting agreed that it was unnecessary to designate them as relevant impurities.

### Forms and fate in the environment

In sterile, aqueous environments cymoxanil degrades rapidly at pH 7 or above; at lower pHs it is stable. Photolysis is a significant degradation pathway. Soil metabolism studies indicate cymoxanil degrades very rapidly under both aerobic and anaerobic conditions with half-lifes of two days or less. Both aerobic and anaerobic metabolism occur via a similar degradation pathway. Aerobic metabolism was studied in a wide variety of soil types and cymoxanil degraded rapidly in all soil types. Soil degradates also declined rapidly in soil with half-lifes less than seven days. Carbon dioxide is the terminal degradation product. While cymoxanil and its degradates are weakly absorbed to soil, they degrade so rapidly that movement into groundwater is unlikely. The half-life of cymoxanil under field conditions was one to nine days (EXTOXNET 1997). In addition, cymoxanil degrades rapidly in an aqueous environment by hydrolytic process at pH >4. Cymoxanil is sensitive to photodegradation.

EFSA (2017) quotes a soil DT90 of 0.5 to 33 days.

Conjugated glycine was identified as a main metabolite. Other metabolites are [1-ethyl 5,6-di-2,4(1H,3H)pyridenedione,](http://sitem.herts.ac.uk/aeru/iupac/Reports/1072.htm) and 2-cyano-2-methoxyiminoacetic acid.

Solubility in water is about 800 mg/L at 20°C.

### Typical concentrations in drinking-water

Cymoxanil is not likely to be found in groundwater.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Technical cymoxanil has low acute toxicity; the acute oral LD50 is 960 mg/kg in rats (EXTOXNET 1997). The RfD was reported in EXTOXNET (1997) to be 0.02 mg/kg bw, and 0.013 in USEPA (1998), based on the NOEL of 4.08 mg/kg/day from a chronic feeding study in rats. The uncertainty factor of 300 was used to account for interspecies extrapolation, intraspecies variation and the enhanced sensitivity of infants and children.

The acute reference dose (ARfD) is reported in IUPAC to be 0.05 mg/kg/d bw.

EC (2010) quote an ADI of 0.013 mg/kg bw and an ARfD of 0.08 mg/kg/d. These values were reaffirmed in EFSA (2011, 2015, 2017).

In a subchronic oral study in mice, the NOEL was 8.25 mg/kg/day for males and 11.3 mg/kg/day for females. In a combined chronic/carcinogenicity study, the NOEL was 4.08 mg/kg/day for males and 5.36 mg/kg/day of females. In a chronic toxicity study in dogs, the NOEL was 5.7 mg/kg/day for males and 3.1 mg/kg/day for females (USEPA 1998).

USEPA (2003)quotes a chronic RfD of 0.041 mg/kg/day is based on a NOEL of 4.08 mg/kg/day from the one-year rat feeding study and an uncertainty factor of 100. The acute NOEL of 4.0 mg/kg/day is based upon maternal clinical signs and weight effects at higher levels in a rat developmental study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0008 mg/kg/d, and an ARfD of 0.04 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cymoxanil is 1.32 mg/L.

Cymoxanil is not considered a reproductive or developmental toxin, and cymoxanil is not considered genotoxic or oncogenic, and adverse endocrine effects are not expected to occur in humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Cypermethrin

CAS No. 52315-07-8 (formerly 69865-47-0). The IUPAC name for cypermethrin is (RS)‑α-cyano-3-phenoxybenzyl (1RS,3RS;1RS,3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, or alternatively (R,S)-alpha-cyano-3-phenoxybenzyl(1RS)-cis,trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane-carboxylate. CAS: cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate.

Cypermethrin is the racemic mixture of all eight isomers, the cis-group being the more powerful insecticide. The ratio of cis- to trans-isomers varies from 50:50 to 40:60.

Alpha-cypermethrin (CAS No. 67375-30-8) contains more than 90 percent of the insecticidally most active pair of the four cis isomers of cypermethrin as a racemic mixture (UKPIS 1998 update). EFSA (2018) called these the 1R-cis-alpha-S isomer and its enantiomer 1S-cis-alpha-R.

Beta-cypermethrin consists of four (2 cis-isomers and 2 trans-isomers) of the eight stereo-isomers that comprise cypermethrin. The CAS name is cyano(3-phenoxyphenyl)methyl 3-(2,2-dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate, has a CAS No. 65731-84-2. Beta-cypermethrin is a mixture of [alpha-cypermethrin](http://www.alanwood.net/pesticides/alpha-cypermethrin.html)  
(360–430 g/kg) and 550–630 g/kg of [theta-cypermethrin](http://www.alanwood.net/pesticides/theta-cypermethrin.html) (CAS No. 71697-59-1).

JMPR (2011) classifies the cypermethrins as follows:

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Isomer** | **Activity ratio** | **Cypermethrin percent** | **Alpha-cypermethrin percent** | **Zeta-cypermethrin percent** |
| 1. 1R-cis-R  2. 1S-cis-S | 0.60  0.03 | 14  14 | –  – | 3  22 |
| 3. 1R-cis-S  4. 1S-cis-R | 13.5  0.04 | 11  11 | 50  50 | 22  3 |
| 5. 1R-trans-R  6. 1S-trans-S | 0.40  0.03 | 14  14 | –  – | 3  22 |
| 7. 1R-trans-S  8. 1S-trans-R | 3.20  0.01 | 11  11 | –  – | 22  3 |

### Maximum Acceptable Value

WHO (2004 and 2011) states that because cypermethrin is unlikely to occur in drinking-water, a guideline value has not been derived.

Cypermethrin is the ISO name for the pure unresolved racemic compound. The technical products commonly available contain more than 90 percent cypermethrin and the ratio of cis- to trans-isomers varies from 50:50 to 40:60. There are eight stereoisomers.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.2 mg/L for cypermethrin isomers; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on medium- to long-term effects.

### Sources to water

Cypermethrin, a non-systemic Type II synthetic [pyrethroid](http://en.wikipedia.org/wiki/Pyrethroid), acts as a fast-acting [neurotoxin](http://en.wikipedia.org/wiki/Neurotoxin) in insects. Cypermethrin is found in many household [ant](http://en.wikipedia.org/wiki/Ant) and [cockroach](http://en.wikipedia.org/wiki/Cockroach) killers. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Alpha-cypermethrin is an insecticide intended to be used indoor by professionals for hard surfaces, crack and crevice treatments and areas behind furnishings applied by low-pressure spraying. Alpha-cypermethin is intended to control a broad range of insects such as cockroaches, fleas and bed bugs. The main emission route of alpha-cypermethrin is via wastewater to sewage water treatment plants and subsequent release via effluents to surface water and sediment after the cleaning of the treated areas or the spraying materials or washing of applicator cloths. There are no direct emissions to surface water or sediment, and aquatic or sediment organisms are not directly exposed to the active substance. Direct exposures of the environment via the pathways air, soil or groundwater are considered to be negligible. The maximum allowable concentration environmental quality standard (MAC-EQS) of 6 x 10-7 mg/L for cypermethrin may not be exceeded by any measured concentration at any point of the water body or at any point in time (ECHA 2014).

Cypermethrin is also used as a veterinary drug.

### Forms and fate in the environment

In pond waters and in laboratory degradation studies, pyrethroid concentrations decrease rapidly due to sorption to sediment, suspended particles, organic matter and plants. Microbial degradation and photodegradation also occur, to less toxic breakdown products.

EC (2005) reports that in some soil studies the metabolite 3-phenoxybenzoic acid has been found even after six months, in both aerobic and anaerobic conditions.

The typical half-life of cypermethrin in soil is 30 days, although it can range from 2–8 months in acidic conditions. It is unlikely to be found in groundwater because it binds tightly to soil particles.

If released to soil, cypermethrin is expected to have no mobility based upon Koc values of 20,800 to 503,000. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 2.4 x 10-7 atm-cu m/mole. Cypermethrin degrades rapidly in soil under aerobic conditions with half-lifes of 4.1 to 17.6 days for trans-cypermethrin and 12.5 to 56.4 days for cis‑cypermethrin. If released into water, cypermethrin is expected to adsorb to suspended solids and sediment based upon the Koc values. Cypermethrin is expected to biodegrade in water with half-lifes of 11.6 to 30.4 days at 15° to 19°C, pH 7.7, and biological oxygen demand of 2.2 mg/L. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. BCFs of 420 in golden ide fish, 430 in rainbow trout and 468 in bluegill suggest bioconcentration in aquatic organisms is high. The abiotic hydrolysis half-life of cypermethrin was 63 weeks at pH 7. The photodegradation half-lifes of the cis- and trans-isomers of cypermethrin in distilled water solution ranged from 2.6 to 3.6 days in sunlight and >10 days in dark controls; the half-lifes in river and seawater ranged from 0.6 to 1.0 days (EAWAG accessed February 2015).

Solubility in water is only 0.01 to 0.2 mg/L at 20°C. WHO (2013) gives 0.013 to 0.016 mg/L for alpha-cypermethrin at 20°C.

NPIC (1994) quotes for cypermethrin a soil half-life of 30 days, water solubility of 0.004 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low. WHO (2013) quotes an octanol/water partition coefficient of log POW = 6.25–6.27 at 23°C and pH 4–7 for alpha-cypermethrin.

EFSA (2014) says beta-cypermethrin exhibits medium to high persistence in soil. Metabolite PBA exhibits low persistence in soil and metabolite CPA exhibits low to moderate persistence in soil. Beta-cypermethrin can be considered immobile in soil; metabolite PBA exhibited high soil mobility and metabolite CPA exhibited very high soil mobility. There was no evidence of a correlation of adsorption with pH for either beta-cypermethrin or metabolites PBA and CPA. A kinetic analysis of the whole system data indicated that beta-cypermethrin is low persistent in the aquatic compartment. Beta-cypermethrin was investigated in two water/sediment systems. Beta-cypermethrin rapidly partitioned from the water to the sediment phase (maximum 50.7 percent AR after 0.25 days). The stereoisomeric test substance 14C-beta-cypermethrin consisted of approximately 40 percent cis-isomers and 60 percent trans-isomers. The trans-isomers degraded in the whole system more quickly than the cis-isomers and at the end of the study there was a greater proportion of cis-isomers in the whole system than trans-isomers. Two major metabolites of C-beta-cypermethrin were formed: PBA and CPA. Water solubility is <0.9 mg/L.

### Typical concentrations in drinking-water

Cypermethrin is expected to bind strongly to organic carbon and have little mobility in soil and therefore it is not likely to leach into groundwater.

### Removal methods

Because it is strongly attracted to particles and its low solubility, coagulation and many filtration processes should remove cypermethrin readily.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

The most widely adopted procedures for the determination of cypermethrin residues in crops, soil, animal tissues and products, and environmental samples are based on extraction of the residue with organic solvent, clean-up of the extract, as necessary, by means of solvent-solvent partition and adsorption column chromatography, followed by determination of the residue using gas chromatography with electron capture detector (GC/ECD). The identity of residues can be confirmed by GC with mass selective detection (GC-MSD) or by thin-layer chromatography (TLC) followed by GC/ECD. (ICPS).

EFSA (2014) states: residues of beta-cypermethrin (as sum of isomers) in drinking water can be monitored by GC-MS with a LOQ of 0.1 μg/L, and in surface water by GC-HRMS with a LOQ of 0.001 μg/L.

### Health considerations

Humans and rats excrete over half of ingested cypermethrin via urine within 24 hours. Pyrethroids in general, like cypermethrin, have relatively low toxicity to humans.

The USEPA human health effects and environmental fate risk assessment for cypermethrin included the assessment for zeta-cypermethrin as well, since zeta-cypermethrin is an S-enantiomer enriched formulation of cypermethrin, which is not distinguished from cypermethrin by the analytical enforcement method, and the toxicological endpoints are the same for both cypermethrin and zeta-cypermethrin. USEPA (2008) quotes an acute RfD of 0.1 mg/kg/d, and a chronic RfD of 0.06 mg/kg/d. The chronic reference dose (RfD) of 0.06 mg/kg/day for zeta-cypermethrin is based on a NOAEL of 6.0 mg/kg/day from a cypermethrin chronic feeding study in dogs and an uncertainty factor (UF) of 100. The endpoint effect of concern was based on clinical signs. The oral RfD had previously been 0.01 mg/kg/d (USEPA 1990). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.06 mg/kg/d, and an ARfD of 0.10 mg/kg/d for cypermethrin, and for zeta-cypermethrin. The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cypermethrin and zeta-cypermethrin are 1.0 mg/L.

The USEPA has classified (in their September 2008 list) cypermethrin (and zeta-cypermethrin) as a possible human carcinogen (Group C), because there is limited evidence that it causes cancer in animals. Mice fed high doses (up to 1,600 mg/kg body weight) over a lifetime did not did not develop cancer (malignant tumours). In humans, urinary excretion of cypermethrin metabolites was complete 48 hours after the last of five doses of 1.5 mg/kg/day.

The 2006 JMPR meeting estimated the acceptable daily intake (ADI) for humans as  
0–0.02 mg/kg bw and estimated the acute reference dose (ARfD) as 0.04 mg/kg bw. The 2008 Meeting defined the residue (for compliance with the MRL and for estimation of dietary intake) for plant and animal commodities as cypermethrin (sum of isomers); reaffirmed in JMPR (2011).

The Acceptable Daily Intake (ADI) adopted in Australia for cypermethrin is 0.05 mg/kg body weight, based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day from a two-year rat study. This NOEL is based on increased liver weights, and haematological and biochemical effects and a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for alpha-cypermethrin is 0.05 mg/kg body weight, based on a NOEL of 4.7 mg/kg bw/day from a 13-week dog study. This NOEL is based on neurological effects and a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for beta-cypermethrin is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw, and the ARfD is 0.05 mg/kg bw based on a NOEL of 4.7 mg/kg bw/day from a three-month dog study. The NOEL was based on neurological effects. The ARfD incorporates a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for zeta-cypermethrin is 0.07 mg/kg body weight, based on a NOEL of 7 mg/kg bw/day from a multigeneration reproduction study in rats. The NOEL is based on clinical signs of toxicity and evidence of neurotoxicity and a safety factor of 100.

EC (2005) established an ADI of 0.05 mg/kg/d and an ARfD of 0.2 mg/kg/d. EFSA (2011) reaffirmed these values, adding that cypermethrin is a mixture of isomers and one of its isomer pairs, the cis-2-isomer, is used also as an active substance alpha-cypermethrin, and has higher toxicity than cypermethrin (ADI of 0.015 mg/kg bw/d; ARfD of 0.04 mg/kg bw).

EFSA (2014) states that beta-cypermethrin is of high acute oral toxicity. Both the acceptable daily intake (ADI) and the acute reference dose (ARfD) for beta-cypermethrin are 0.0016 mg/kg bw (per day), based on the developmental neurotoxicity study and applying an uncertainty factor (UF) of 300 to cover the use of a LOAEL and the uncertainties regarding the relevance of the effects observed in pups after gavage for the human risk assessment.

The acceptable daily intake (ADI) and acute reference dose (ARfD) for alpha-cypermethrin are both 0.00125 mg/kg bw per day based on the lowest observable adverse effect level (LOAEL) for pups in the DNT study and applying an increased uncertainty factor (UF) of 200 (EFSA 2018).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of 0.02 mg/kg/day for acute-duration oral exposure  
(1–14 days) to cypermethrin.

Alpha-cypermethrin is not genotoxic, mutagenic, reproductive or a developmental toxiciticant (ECHA 2014).

USEPA (2015) found that based on weight of evidence considerations, there was no convincing evidence for potential interaction with the estrogen or thyroid pathways. There was convincing evidence for potential interaction with the androgen pathway. Consequently, for mammals, a special study focused on evaluating the potential adverse effect of cypermethrin in the male reproductive system is recommended.

### Derivation of Maximum Acceptable Value

No MAV.

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# Cyproconazole

CAS No. 94361-06-5. The IUPAC name for cyproconazole is (2RS,3RS;2RS,3SR)-2-(4-chlorophenyl)-3-cyclopropyl-1-(1H-1,2,4-triazol-1-yl)butan-2-ol. The CAS name is: α-(4-chlorophenyl)-α-(1-cyclopropylethyl)-1H-1,2,4-triazole-1-ethanol. This structure exists in four stereoisomeric forms: two enantiomeric pairs of diastereoisomers. Cyproconazole is an approximately 1:1 mixture of the two diastereomers, each of which is exactly a 1:1 mixture of the enantiomers. All four stereoisomers are present in similar amounts, see JMPR (2010).

### Maximum Acceptable Value

Cyproconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for cyproconazole in water (set by an approval under Part 5 of the HSNO Act) of 0.77 µg/L (0.00077 mg/L).

### Sources to water

Cyproconazole is a water-based conazole fungicide, commonly used for control of rust and powdery mildew in cereal crops. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Cyproconazole formula 360 SL is approved in the US as a water-based wood preservative that prevents decay from fungi in above-ground applications. Cyproconazole 360 SL contains two decay preventing fungicides, cyproconazole (6 percent) and didecyldimethylammonium chloride (DDAC) or the bromide (qv) (31.6 percent); see <http://www.epa.gov/oppad001/reregistration/cca/cyproconazole.htm>

### Forms and fate in the environment

Cyproconazole is a triazole-derived pesticide. Cyproconazole shares common metabolites with other triazole-derivative chemicals, including free triazole (1,2,4‑triazole) and triazole-conjugated plant metabolites (such as triazole alanine and triazole acetic acid). See JMPR (2010).

The typical half-life of cyproconazole in soil is about three months. Note however that EFSA (eg 2013) states that the degradation rate of cyproconazole in soil is slow with a maximum DT90f exceeding 1,000 days.

Water solubility is about 100–140 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Chronic toxicity: the USEPA (1995/2006) established the reference dose (RfD) for cyproconazole at 0.01 mg/kg/day, based on the chronic feeding study in dogs with a NOAEL of 1.0 mg/kg/day and an uncertainty factor of 100. The LOAEL was 3.2 mg/kg/day, based on hepatotoxicity and organ weight changes. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.01 mg/kg/d, and an ARfD of 0.02 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cyproconazole is 0.66 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

The JMPR 2010 meeting established an acceptable daily intake (ADI) of 0–0.02 mg/kg bw on the basis of the overall NOAEL of 2.2 mg/kg bw per day from the two-year study of toxicity and carcinogenicity and the multigeneration reproduction study in rats based on reduced body weight gain and liver toxicity seen at higher doses. A safety factor of 100 was applied. This ADI was supported by the NOAEL of 2.2 mg/kg bw per day observed in a 90-day toxicity study in mice on the basis of reduced body weight gain observed at 43.8 mg/kg bw per day. The meeting established an acute reference dose (ARfD) of 0.06 mg/kg bw on the basis of a maternal toxicity NOAEL of 6 mg/kg bw per day in studies of developmental toxicity in rats, based on body weight loss during the early treatment period (gestation days 6–11) and reduced feed consumption seen at 12 mg/kg bw per day. The ARfD is protective of developmental toxicity seen at a slightly higher dose in rabbits (FAO/WHO 2010). These ADI and ARfD values were reaffirmed in JMPR (2013).

EFSA (2012 and 2013) quotes an ADI of 0.02 mg/kg bw per day and an ARfD of 0.02 mg/kg bw for cyproconazole and its isomers. EFSA (2012) also lists the ADI and ARfD for the common metabolites. See datasheet for triazole metabolites for latest ADI and ARfD.

Until recently, the USEPA (2006) considered cyproconazole to be a Class B2 carcinogen (a probable human carcinogen, based on male mouse liver adenoma and/or carcinoma combined tumour rates), but USEPA (2008) now states: Cyproconazole has been classified by the Agency as “not likely to be carcinogenic to humans at doses that do not cause a mitogenic response in the liver”. The decision was based on the weight of evidence that supports a non-genotoxic mitogenic mode of action for cyproconazole.

### Derivation of Maximum Acceptable Value

No MAV.

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# Cyprodinil

CAS No. 121552-61-2. The IUPAC name for cyprodinil is 4-cyclopropyl-6-methyl-N-phenylpyrimidin-2-amine. The CAS name is 4-cyclopropyl-6-methyl-N-phenyl-2-pyrimidinamine. Also called N-(4-cyclopropyl-6-methyl-pyrimidin-2-yl)-aniline.

### Maximum Acceptable Value

Cyprodinil does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.09 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Cyprodinil is a systemic anilinopyrimidine (or pyrimidinamine) fungicide that acts by inhibiting the biosynthesis of methionine, commonly used as a folial spray for control of disease on fruit trees and grapes.

Cyprodinil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Cyprodinil residues have been found often in strawberries, sometimes at greater than the maximum residue limit (MRL) during the Food Residue Surveillance Programme: refer NZFSA: <http://www.nzfsa.govt.nz/>

Cyprodinil was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in strawberries.

The maximum estimated concentrations of cyprodinil in surface water and in groundwater are less than the USEPA’s levels of concern.

### Forms and fate in the environment

Cyprodinil does not volatilise readily from moist soil or water surfaces. Cyprodinil does not hydrolyse readily. Photolysis will not account for significant transformation of cyprodinil in soil or in water. Cyprodinil shows strong sorption to soil and low mobility.

The JMPR meeting (ICPS 2003, FAO 2009) received information on the fate of cyprodinil during aerobic degradation in a number of soils. At 20°C and moisture levels above 60 percent field capacity the initial half-life of parent cyprodinil ranged from 11 to 46 days. The rates of loss decreased substantially as the residues aged. Temperature and moisture levels strongly influenced the rate of disappearance with longer half-lifes at lower temperatures and moisture levels. In soil 4-cyclopropyl-6-methyl-pyrimidin-2-ylamine was an important degradation product, demonstrating that amino bridge cleavage occurred readily in soil. This compound and cyprodinil were sufficiently persistent in soil for residues still to be present in the soil at harvest of a root crop.

EFSA (2013) states that soil studies demonstrated that the degradation rate of cyprodinil is slow; the maximum DT90 was 814 days.

Water solubility is about 15 mg/L.

### Typical concentrations in drinking-water

Cyprodinil appears to pose a relatively low risk to groundwater.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of cyprodinil in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See FAO (2009).

### Health considerations

Cyprodinil was shown to be negative in studies for point mutation, for chromosome aberration, and for DNA repair. These results indicate that cyprodinil is unlikely to initiate cancer or cause inheritable genetic defects. Cyprodinil is not teratogenic. Cyprodinil is classified as a “Not Likely” (Class E) carcinogen based on the lack of oncogenic effects in all tested species.

The Reference Dose (RfD) for cyprodinil is 0.0375 mg/kg/day (USEPA 1998). This value is based on the systemic NOEL of 3.75 mg/kg/day in the rat chronic feeding study with a 100-fold safety factor to account for interspecies extrapolation and intraspecies variability. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.027 mg/kg/d, and an ARfD of 1.5 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cyprodinil is 49.5 mg/L.

JMPR (FAO 2009 and JMPR 2003) established an ADI of 0–0.03 mg/kg bw based on a NOAEL of 2.7 mg/kg bw per day in a 24-month study in rats fed with cyprodinil, on the basis of liver effects (spongiosis hepatitis) seen in males at higher doses, and a 100-fold safety factor. The meeting concluded that the establishment of an acute RfD for cyprodinil was not necessary, on the basis of its low acute toxicity, the absence of development toxicity in rats and rabbits, the lack of neurotoxicity following single exposures, and absence of any other toxicological end-point that would be elicited by a single dose. These ADI and ARfD values were reaffirmed in JMPR (2013). These values were reaffirmed in 2017.

The Acceptable Daily Intake (ADI) adopted in Australia for cyprodinil is 0.02 mg/kg body weight, with a NOEL of 2.7 mg/kg bw from a long-term (two-year) dietary study in rats. The NOEL is based on an increased incidence of liver lesions in males at the next highest dose of 36 mg/kg bw/day. The ADI incorporates a safety factor of 100.

NZFSA (2008) adopted an ADI of 0.027 mg/kg bw.

EC (2010) established an ADI of 0.03 mg/kg/d; an ARfD was not considered necessary. Reaffirmed by EFSA (2013).

### Derivation of Maximum Acceptable Value

No MAV.

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# Cyromazine

CAS No. 66215-27-8. The IUPAC and CAS name for cyromazine is N-cyclopropyl-1,3,5-triazine-2,4,6-triamine. Has also been called 2,4-diamino-6-(cyclopropylamino)-s-triazine.

### Maximum Acceptable Value

Cyromazine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Cyromazine is a triazine mite growth regulator (acaricide) and a chitin synthesis inhibitor (systemic insecticide). It is a [cyclopropyl](http://en.wikipedia.org/wiki/Cyclopropyl) derivative of [melamine](http://en.wikipedia.org/wiki/Melamine). As a selective insecticide, it is commonly used on vegetables. Cyromazine is an insect growth regulator for the control of fly larvae in manure and other breeding sites in animal housing. On animals it is used to control fly larvae by interfering with the moulting process.

Cyromazine can also be fed to poultry – caged layers only. The active ingredient is passed through the chicken, leaving a residue in the manure that controls the growth of the fly larvae developing there (PMEP 1986).

Cyromazine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)) as an ectoparasiticide and insecticide.

### Forms and fate in the environment

Supervised trials of cyromazine on peppers were carried out in The Netherlands, Spain and the USA. Residues of cyromazine and melamine were determined in all the trials. In The Netherlands the application rate was 0.4 kg ai/ha with 5 to 10 applications. Residues three days after treatment were 0.85 to 2.7 mg/kg for cyromazine and 0.09 to 0.37 mg/kg for melamine. In one experiment in Spain with the registered use rate residues two days after application were 0.72 mg/kg of cyromazine and 0.05 mg/kg of melamine. In experiments in the USA carried out in California and Texas application rates were 0.14 to 0.28 kg ai/ha with 11 to 12 applications. At day 0 residues of cyromazine were <0.05 to 0.57 mg/kg, while residues of melamine were 0.15 to 1.7 mg/kg. After two to three weeks residues of cyromazine were at about the same level, while residues of melamine were normally increased (FAO 1992).

If released to soil, cyromazine is expected to have low mobility based upon a recommended Koc of 765, determined from a measured Koc range of 81 to 1,800. Cyromazine has also been reported to have moderate mobility in soil, which would correspond to the lower Koc values measured in some soils. An agricultural run-off study found that cyromazine (applied to soil via chicken manure) was present in run-off waters with concentrations increasing as rainfall rates increased. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 5.65 x 10-14 atm-cu m/mole. Studies conducted in the laboratory and field have demonstrated the cyromazine is degraded by biological mechanisms. Field dissipation half-lifes have been reported to range from 75–284 days with a median of 189 days. The aerobic half-life in sand and a sandy loam soil were observed to be 107 and 142 days, respectively. Cyromazine is reported to be stable in anaerobic soil. If released into water, cyromazine may adsorb to suspended solids and sediment based upon the Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. An estimated BCF of 3 suggests bioconcentration in aquatic organisms is low. Cyromazine is reported to be stable to aqueous hydrolysis and stable in aqueous solution exposed to sunlight (EAWAG accessed February 2015).

No unacceptable risk to the aquatic compartment (including surface water and sediment) from the parent compound cyromazine is expected following treated manure application to land (grassland and arable land) according to the proposed use pattern. No aquatic risk (including surface water and sediment) via spreading of manure/slurry on grassland or arable land and via STP exposure was identified for cyromazine’s metabolite melamine (ECHA 2015).

NPIC (1994) quotes for cyromazine a soil half-life of 150 days, water solubility of 13.6 percent and a sorption coefficient (soil Koc) of 200. The solubility was probably a misprint. This resulted in a pesticide movement to groundwater rating of high.

The half-life of cyromazine in soil is about two to three months. Melamine (CAS No. 108-78-1) is a metabolite of cyromazine; see melamine datasheet in Organic Chemicals section. Other metabolites include hydroxy-cyromazine and 1-methyl cyromazine (EFSA 2011).

JMPR (2010) states that cyromazine is resistant to hydrolysis and photolysis.

Water solubility is about 13,000 mg/L (1.3 percent) (FAO 2010).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The 1990 JMPR meeting decided not to include melamine in its assessment of cyromazine mainly because it is considered to be less toxic than cyromazine, despite that in mushrooms, cyromazine residues are often undetectable, whereas melamine may be present at levels up to 7 mg/kg.

The oral Reference Dose (RfD) for cyromazine is 0.0075 mg/kg/day. This value is based on the NOEL of 0.75 mg/kg/day from haematological effects in a six-month dog diet study (USEPA 1987/1991). USEPA (2002) quotes a chronic RfD of 0.075 mg/kg/d, and adds that an acute RfD is not applicable because an appropriate end point attributable to a single dose (exposure) was not observed in oral toxicity studies. The USEPA concluded that pesticidal uses of cyromazine are not likely to pose a carcinogenic risk to humans. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.015 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for cyromazine is 0.105 mg/L (no acute one-day value available.)

EC (2009) quote an acceptable daily intake (ADI) of 0.06 mg/kg bw, and an acute reference dose (ARfD) of 0.1 mg/kg/d, being the values adopted by JMPR in 2006, and confirmed in JMPR (2012) and FAO/WHO (2013).

These JMPR values were reaffirmed in EFSA (2011 and 2015 – see <http://www.efsa.europa.eu/en/efsajournal/doc/4004.pdf>). EFSA added that the toxicological profile of melamine was evaluated in the scientific opinion on melamine in food and feed, which resulted in a TDI of 0.2 mg/kg bw/d. EFSA agreed, as a worst case assumption, that the ADI of the parent (cyromazine) should be considered relevant for melamine risk assessment.

The Acceptable Daily Intake (ADI) adopted in Australia for cyromazine is 0.02 mg/kg body weight, with a NOEL of 1.8 mg/kg bw.

Cyromazine, and its degradate melamine, are considered non-genotoxic and non-teratogenic, and non-carcinogenic in rats and mice. An ADI of 0.02 mg/kg was established based on a NOEL of 1.8 mg/kg/d bw in the long-term toxicity/carcinogenicity study in rats with a safety factor of 100 (EMEA 2001).

### Derivation of Maximum Acceptable Value

No MAV.

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# 2,4-D

CAS No. 94-75-7. Also called 2,4-dichlorophenoxyacetic acid (CAS name), 2‑(2,4‑dichlorophenoxy)acetic acid (IUPAC name). Also called 2,4‑dichlorophenoxyethanoic acid. Sometimes referred to as DCPA (but so is chlorthal dimethyl).

IARC (2017) lists the relevant commercial forms:

* 2,4-D salt (CAS No. 2702-72-9)
* 2,4-D diethanolamine salt (CAS No. 5742-19-8)
* 2,4-D dimethylamine salt (CAS No. 2008-39-1)
* 2,4-D isopropylamine salt (CAS No. 5742-17-6)
* 2,4-D isopropanolamine salt (CAS No. 32341-80-3)
* 2,4-D butoxyethyl ester (CAS No. 1929-73-3)
* 2,4-D butyl ester (CAS No. 94-80-4)
* 2,4-D 2-ethylhexyl ester (CAS No. 1928-43-4)
* 2,4-D isopropyl ester (CAS No. 94-11-1)
* 2,4-D isooctyl ester (CAS No. 25168-26-7)
* 2,4-D choline salt (CAS No. 1048373-72-3)

### Maximum Acceptable Value

Based on health considerations, the concentration of 2,4-D in drinking-water should not exceed 0.04 mg/L.

The guideline value applies to 2,4-D (the acid), because the salts and esters of 2,4-D are rapidly hydrolysed to the free acid in water.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.07 mg/L. The maximum acceptable concentration in Canada is 0.1 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.03 mg/L. Minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

2,4-D may enter source waters as a result of its use as a systemic chlorophenoxy herbicide used widely in the selective post-emergence control of broadleaf weeds (dicotyledons) while sparing monocotyledons. It has also used to control aquatic weeds.

2,4-D is the world’s most widely used herbicide and has been in use for over 50 years. It is also used as a plant growth regulator. Pesticides containing 2,4-D were first registered for agricultural use in New Zealand in 1968. There are 15 products containing 2,4-D that are currently (2009) registered for agricultural use in New Zealand. 2,4-D is a plant growth regulator (a synthetic hormone in the auxin family).

The purity of technical 2,4-D may range from less than 90 percent to 99 percent. 2,4-D should not contain more than 0.01 mg/kg of 2,3,7,8-tetrachlorodioxin. Other impurities may include 2,6-dichlorophenoxyacetic acid, bis (2,4-dichlorophenoxy)acetic acid, phenoxyacetic acid, 2-chlorophenoxyacetic acid, 4-chlorophenoxyacetic acid, dichlorophenols, 2,4,6-trichlorophenol, and other chlorophenols. Trace levels of N‑nitrosamines can occur in amine formulations, especially when nitrate is added as a corrosion inhibitor for containers (IPCS HSG 1987).

The total annual usage in New Zealand of all forms of 2,4-D, including 2,4-DB, was 409,000 kg in the late 1980s, with nearly all the use being in the North Island. The highest usage in a county was 155,000 kg in Rangitikei. ERMA notes that 282 tonnes of 2,4-D and its salts and esters were used in New Zealand in 2004, at an application rate of 4,160 grams of active ingredient per hectare. 2,4-D can be used alone and is also commonly formulated with other herbicides.

### Forms and fate in the environment

2,4-D esters are rapidly hydrolysed to the free acid. 2,4-D is microbially degraded in the environment with hydroxylation, decarboxylation, cleavage of the acid side chain and ring opening occurring. The half-life in soils ranges from 2 to 14 days with a recommended average half-life of 10 days, but longer in acidic soils. The half-life in water ranges from one to several weeks. 2,4-D has a low binding affinity in mineral soils and sediment, and in those conditions is considered intermediately to highly mobile, but rapid mineralisation rates may reduce the potential of 2,4-D to affect groundwater.

Water solubility for 2,4-D acid ranges from about 20,000 mg/L (pH 5) to about 30,000 mg/L at pH 7, to about 40,000 mg/L at pH 9; the sorption coefficient is 20 mL/g. Water solubilities are much greater for the amine salts (18,000 to 4,000,000 mg/L) and much less for the esters (insoluble to 100 mg/L). Reported solubilities can be unreliable because the 2,4-D product is not always stated, and pH not defined. IARC (2017) reports the water solubility of 2,4-D to be 31 mg/L.

If released to soil, 2,4-D is expected to have high to very high mobility based upon Koc values ranging from 20 to 136. The pKa of 2.73 for 2,4-D indicates that this compound will primarily exist in anion form in the environment and anions generally do not adsorb to organic carbon and clay more strongly than the non-ionised form. Volatilisation from moist soil surfaces is not expected to be an important fate process because anions will not volatilise. Biodegradation is by far the most important loss process for 2,4-D in most soils, leading to various hydroxylic aromatic products. The rate of degradation is affected by the concentration of 2,4-D, temperature, organic matter content of soil, and whether there has been pre-exposure of the soil to 2,4-D, its salts, or esters. Typical half-lifes are short, ranging from <1 day to several weeks. If released into water, 2,4-D is not expected to adsorb to suspended solids and sediment based upon the range of Koc values. In water, 2,4-D will biodegrade with the rate dependent upon level of nutrients present, temperature, availability of oxygen, and whether there has been pre-exposure of the water to 2,4-D contamination. Typical half-lifes of 10 to >50 days have been reported with longer half-lifes expected in oligotrophic waters and where a high concentration of 2,4-D is present. Volatilisation from water surfaces is not expected to be an important fate process based on its pKa which indicates 2,4-D will exist almost entirely in the ionised form at pH values of 5 to 9. A BCF of 1 for bluegill sunfish suggests bioconcentration in aquatic organisms is low. Hydrolysis is not expected to occur due to the lack of hydrolysable functional groups. Half-lifes of 2–4 days were reported for 2,4-D photolysis in water solution irradiated at 356 nm (EAWAG accessed February 2015).

The half-life of 2,4-D in aerobic aquatic environments was estimated to be 15 days and in anaerobic aquatic laboratory studies, 41–333 days. A granular formulation of the BEE form degraded rapidly in the water column in alkaline conditions but was present in sediments for 186 days. The ethyl hexyl form is rapidly hydrolysed in water to 2,4-D acid, with a degradation half-life (DT50) of less than one day Ester forms of 2,4-D hydrolyse at rates that are pH dependent; the hydrolysis half-life of the butoxy ester increased from nine hours at pH 8 to more than one year in more acidic conditions with a pH of 5.3. The acid form of 2,4-D is very resistant to abiotic hydrolysis. NPIC.

The fate and behaviour of 2,4-D in dark water sediment was investigated under aerobic conditions. Most of the applied 2,4-D remained in the aqueous phase. 2,4-D exhibited low to moderate persistence (DT50 whole system 20°C = 6–52 days). No major metabolites were found in the water phase. Metabolite 2,4-dichlorophenol exceeded 10 percent AR in the sediment (EFSA 2014).

One of 2,4-D’s main degradation product (and by-product of chlorination) is 2,4‑dichlorophenol, which has a taste threshold of 0.0003 mg/L; as a result, public water supplies containing traces of 2,4-D are often shut down because of objectionable odours or tastes. 2,4-Dichloroanisole (2,4-dichloro-1-methoxybenzene or 2,4-DCA – a major metabolite) and 1,2,4-benzenetriol are other predominant (aesthetically noticeable) degradates; EFSA (2011/2014) also refers to 4-chlorophenoxyacetic acid, 2,4-dichlorophenol and 4-hydroxy-2,5-dichlorophenoxyacetic acid. Under anaerobic conditions 2,4-D exhibited moderate persistence (DT50 = 22–38 days) and two major metabolites were formed: 2,4-dichlorophenol (maximum 38 percent AR) and 4-chlorophenol (maximum 33 percent AR).

NPIC (1994) quotes for 2,4-D acid a soil half-life of 10 days, water solubility of 890 mg/L and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of moderate.

USGS (2006) give the following values: log Kow = 2.81; log Koc (where Koc is in mL/g) = 1.68; water solubility = 890 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -3.61; half-life in aerobic soil = 2.3 days; half-life in water = 732 days.

Henry’s constant for the acid form = 8.6 x 10-6 atm·m3/mol. Log Kow = pH 5: 2.14; pH 7: 0.177; pH 9: 0.102. Koc = 20–136.

### Typical concentrations in drinking-water

Of 230 source water samples obtained from 212 supplies in New Zealand between 1988 and 1992, two samples contained detectable levels of 2,4-D. The concentrations were 0.0003 mg/L and 0.0022 mg/L (2.2 µg/L). In addition, 2,4-D was detected in two wells in the Te Puke area at concentrations between 0.00005–0.0001 mg/L  
(0.05–0.1 µg/L), and has also been found in surface waters.

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, did not find any detectable concentrations of 2,4-D (limit of detection = 0.0001 mg/L) (ESR 2001).

2,4-D has been found four times in groundwaters, in Canterbury, Waikato and the Bay of Plenty, ranging from 0.00005 to 0.0009 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). 2,4-D occurred at 0.9 µg/L, ie, 0.0009 mg/L.

2,4-D was detected in 52 of 805 samples of raw and treated drinking water from municipal and private supplies in surveys conducted in six Canadian provinces from 1971 to 1986. The maximum concentration found was 0.03 mg/L.

Levels in water overseas are usually below 0.0005 mg/L, although concentrations as high as 0.03 mg/L have been measured (WHO 2017).

128 water utilities in the US reported detecting 2,4-D in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.0046 mg/L.

### Removal methods

Conventional treatment will not remove 2,4-D. Isotherm adsorption data indicate that removal by adsorption on to granular activated carbon or powdered activated carbon should be possible; 0.001 mg/L should be achievable using GAC. Some newer advanced oxidation processes show promise.

### Recommended analytical techniques

#### Referee method

Liquid/Extraction and Gas Chromatography with an Electron Capture Detector (EPA 515).

#### Some alternative methods

High Performance Liquid Chromatography with a Photoiodide Array Ultraviolet Detector (EPA 555). See also IARC (2016).

### Health considerations

The 2,4-D degradates detected in the various laboratory environmental fate studies were 1,2,4-benzenetriol (1,2,4-trihydroxy-benzene), 2,4-dichlorophenol (2,4-DCP)\*, 2,4‑dichloroanisole (2,4-DCA)\*, 4-chlorophenol\*, chlorohydroquinone (CHQ), volatile organics, bound residues, and carbon dioxide. The OPP Metabolism Assessment Review Committee (MARC) determined that all residues other than 2,4-D are not of risk concern due to low occurrence under environmental conditions, comparatively low toxicity, or a combination thereof (USEPA 2005). \*There are datasheets for these three.

2,4-D administered orally as the free acid or salt is absorbed rapidly and almost completely by humans. Animal studies have shown that after absorption it is distributed throughout the body, with highest concentrations in blood, kidney, liver, spleen and lung. Humans excrete most of the 2,4-D in urine. The highest acute risk is for females 13–49 years old because these risks are based upon the lower no-observed adverse effect level (NOAEL) of 25 mg/kg/day from a developmental study in rats.

Symptoms of acute exposure to high doses of 2,4-D include effects on the gastrointestinal tract such as nausea, vomiting and diarrhoea, direct myotoxic effects such as muscular weakness, stiffness, muscular spasms, and partial paralysis, effects on the kidney, pulmonary oedema, and effects on the central and peripheral nervous systems, including central nervous system depression, lethargy, slowed respiration, coma and death.

EC (2001) reports an ADI of 0.05 mg/kg/d; an ARfD is not required because there is no risk to consumers via acute residue exposure. EFSA (2011) reaffirmed these values. EFSA (2014) reaffirmed the ADI, but agreed on an acute reference dose (ARfD) of 0.75 mg/kg bw, based on the NOAEL of 75 mg/kg bw from the acute neurotoxicity study in rats, applying the standard UF of 100. These values are likely to be changed to align with 2,4-DB which are 0.02 mg/kg/d ADI and 0.3 mg/kg ARfD (EFSA 2017).

The 2001 JMPR concluded that it was unnecessary to establish an acute RfD for 2,4-D.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw from a long-term (two-year) rat study. The NOEL is based on effects on the kidney. The ADI incorporates a safety factor of 100. The ARfD is 0.8 mg/kg bw based on a NOEL of 75 mg/kg bw/day derived from an acute exposure study in rats which reported effects on the nervous system. The ARfD incorporates a safety factor of 100.

The reference dose or RfD (USEPA 2006/2009/2011) for 2,4-D is 0.005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.2 mg/L. The oral RfD had previously been 0.01 mg/kg/d (USEPA 1988).

ATSDR established Minimal Risk Levels (MRL) in April 2017 for 2,4-D:

* 0.009 mg/kg/d acute oral (duration 1–14 days)
* 0.009 mg/kg/d intermediate oral (duration 15–365 days)

Epidemiological results give limited evidence that occupational exposure to chlorophenoxy herbicides may cause cancer, and long-term studies in animals continue to show equivocal evidence of carcinogenicity, in one sex and species only.

No significant elevations were observed in sister chromatid exchanges or the frequency of chromosomal aberrations in forestry workers exposed to 2,4-D.

As at September 2008 the USEPA has classified 2,4-D (plus salts and esters) in Group D: not classifiable as to human carcinogenicity.

EFSA (2014) states that 2,4-D, as currently manufactured, is unlikely to have a genotoxic potential or pose a carcinogenic risk to humans.

USEPA (2015) presented their weight of evidence analysis of potential interaction with estrogen, androgen and thyroid pathways; conclusions on the Tier 1 Screening Assays for the List 1 Chemicals. There was no convincing evidence of potential interaction of 2,4-D with the estrogen, androgen or thyroid pathways.

The International Agency for Research on Cancer has classified chlorophenoxy herbicides in Group 2B (possibly carcinogenic to humans) – reaffirmed by IARC (2016). However, based on the information available, it is not possible to ascertain the status of 2,4-D with respect to carcinogenicity, as almost all populations studied were exposed to a mixture of chlorophenoxy herbicides. In the only study in which exposure was clearly to 2,4-D only, the association was weak. JMPR (2001) has also concluded that 2,4-D and its salts and esters are not genotoxic.

### Derivation of Maximum Acceptable Value

Because the data on the carcinogenic potential of 2,4-D are inadequate, and because 2,4-D has not been found to be genotoxic, the MAV was derived using a tolerable daily intake approach. The no-observable-adverse-effect level used in the derivation is based on the effects of toxicity in dogs (for a variety of effects, including histopathological lesions in kidneys and liver), and a two-year study of toxicity and carcinogenicity in rats (for renal lesions).

The MAV for the sum of 2,4-D and its salts and esters, expressed as 2,4-D, in drinking-water was derived as follows:

1 mg/kg body weight/day x 70 kg x 0.1 = 0.035 mg/L (rounded to 0.04 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 1 mg/kg body weight per day for effects on the kidney in chronic studies in rats and mice
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter and intra-species variation).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for 2,4-D is 0.07 mg/L.

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# Dalapon

CAS No. 75-99-0. The sodium salt is CAS No. 127-20-8. The IUPAC and CAS name is 2,2-dichloropropionic acid. Also called 2,2-dichloropropanoic acid or 2,2-DPA.

### Maximum Acceptable Value

Dalapon is not mentioned in the DWSNZ or in the WHO Guidelines.

A maximum contaminant level or MCL has been set at 0.2 mg/L because the USEPA (2006/2009/2011) believes, given present technology and resources, this is the lowest level to which water systems can reasonably be required to remove this contaminant should it occur in drinking-water.

The USEPA (2006/2009/2011) also established a lifetime health advisory of 0.2 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.5 mg/L; excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Dalapon is an organochlorine herbicide and plant growth regulator used to control specific annual and perennial grasses in a wide variety of crops, including fruit trees, beans, coffee, corn, cotton and peas. It is also registered for use in a number of non-crop applications such as lawns, drainage ditches, along railroad tracks, and in industrial areas. It is also used for home gardening, and in or near water to control reed and sedge growth. Dalapon is applied both before the target plant comes up and after the plant emerges. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. It is usually sold as the sodium or magnesium salt.

### Forms and fate in the environment

Dalapon has a low to moderate persistence in soil, remaining in the soil for two to eight weeks. Dalapon has residual activity in soil for 3 to 4 months when it is applied at high rates (eg, 22 kg/hectare). Dalapon does not readily bind to soil particles. In clay and clay loam soils, there may be no adsorption. Since it does not adsorb to soil particles, dalapon has a high degree of mobility in all soil types and leaching does occur. However, dalapon movement in soil is usually limited by rapid and complete breakdown of the herbicide into naturally-occurring compounds by soil micro-organisms. Dalapon is rarely found below the first 6-inch soil layer. Higher temperatures and increased soil moisture speed up degradation.

In ponds and streams, dalapon disappears via microbial degradation, hydrolysis, and photolysis. Microbial degradation tends to be the most active form of its breakdown in water. In the absence of microbial degradation, the half-life of dalapon, by chemical hydrolysis, is several months at temperatures less than 25°C. It is very soluble in water.

NPIC (1994) quotes for dalapon sodium a soil half-life of 30 days, water solubility of 90 percent and a sorption coefficient (soil Koc) of 1. This resulted in a pesticide movement to groundwater rating of very high.

### Typical concentrations in drinking-water

4.2 million Americans in 250 communities were served tap water contaminated with dalapon between 1998 and 2003, with four supplies averaging >0.01 mg/L, with the occasional sample exceeding 0.05 mg/L.

756 water utilities in the US reported detecting dalapon in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.036 mg/L.

### Removal methods

Dalapon can be removed from water by passing it through granular carbon filters.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

Dalapon has the potential to cause increased kidney-to-body weight from a lifetime exposure at levels above the MCL.

Dalapon is in USEPA toxicity class II – moderately toxic.

The Acceptable Daily Intake (ADI) adopted in Australia for 2,2-DPA is 0.2 mg/kg body weight, with a NOEL of 15 mg/kg bw from a long-term (two-year dietary) study. The NOEL is based on increased kidney weight in rats. The ADI incorporates a safety factor of 100.

The reference dose or RfD (USEPA 1989/2006/2009/2011) is 0.03 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.9 mg/L.

In California there is a Public Health Goal for dalapon in drinking-water of 0.79 mg/L, despite dalapon not being registered for use in California. The PHG was based on a NOAEL of 8.45 mg/kg-day for increased kidney-to-body weight ratio in male rats, an uncertainty factor of 300 and a relative source contribution of 80 percent.

### Derivation of Maximum Acceptable Value

No MAV.

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# Daminozide

CAS No. 1596-84.5. The IUPAC name for daminozide is N-(dimethylamino)succinamic acid. The CAS name is butanedioic acid mono(2,2-dimethylhydrazide). Also called succinic acid mono-2,2-dimethylhydrazide.

### Maximum Acceptable Value

Daminozide is not mentioned in the DWSNZ, nor in the WHO Guidelines.

### Sources to water

Daminozide is a plant growth regulator, once commonly used on apples. Concerns in the US about the carcinogenicity of daminozide (common trade name in the US is alar) led to a reduction of its use on food. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Daminozide should not contain more than 30 mg/kg of 1,1-dimethylhydrazine or 2 mg/kg of N-nitrosodimethylamine (EC 2005).

### Forms and fate in the environment

Unsymmetrical dimethyl hydrazine (UDMH) is a contaminant of commercial daminozide and a metabolite of daminozide which is formed in the body, during food processing, or when spray mixes containing daminozide are left standing in the mixing tank. Commercial daminozide contains 0.005 percent (50 ppm) UDMH. A metabolism study in swine has indicated that 1 percent of ingested daminozide is converted to UDMH. The USEPA estimates that 0.012 percent of a daminozide solution converts to UDMH when allowed to stand in a tank for 24 hours. See below. Formaldehyde is the major metabolite in aerobic conditions by weight (EC 2005).

Daminozide resists photodegradation, but it is subject to degradation by soil micro-organisms. Daminozide is very soluble in water (about 10–15 percent) and very mobile in soils where it has a half-life of about 21 days. It appears to leach, but because it does not persist in soil, it is unlikely to contaminate groundwater.

NPIC (1994) quotes for daminozide a soil half-life of 30 days, water solubility of 10 percent and a sorption coefficient (soil Koc) of 30. This resulted in a pesticide movement to groundwater rating of high.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

The principal health concern related to use of daminozide is the carcinogenic potential of UDMH, a contaminant and metabolite of daminozide. The USEPA proposed to cancel all food uses of daminozide in May 1989 based on evidence that UDMH causes tumours in laboratory animals and that lifetime dietary exposure to this product may result in an unacceptable risk to public health. The Agency’s proposed cancellation action on daminozide was based in part on a 12-month interim report of a two-year feeding study on mice using UDMH which showed that this chemical causes tumours. UDMH was classified as a B2 probable human carcinogen.

The 1989 JMPR meeting allocated an ADI of 0–0.5 mg/kg bw for daminozide containing less than 30 mg/kg UDMH. This value was confirmed at the 1991 meeting.

EXTOXNET (1996) quoted an ADI of 0.5 mg/kg/d for daminozide and a RfD of 0.15 mg/kg/d.

EC (2005) reports that an ADI is unnecessary for UDMH; they report a short-term NOAEL of <2 mg/kg/d and a long-term NOAEL of 0.2 mg/kg/d. EC (2005) reports an ADI of 0.45 mg/kg/d for daminozide; an ARfD was considered unnecessary (EFSA 2012).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.7 mg/kg body weight, with a NOEL of 75 mg/kg bw.

Daminozide is classified as a probable human carcinogen by the [IARC](http://en.wikipedia.org/wiki/IARC) and the USEPA (Group B) and a carcinogen by the US State of California.

Otherwise, daminozide has a very low acute and sub-acute human toxicity.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Dazomet

CAS No. 533-74-4. The IUPAC name for dazomet is 3,5-dimethyl-1,3,5-thiadiazinane-2-thione or tetrahydro-3,5-dimethyl-1,3,5-thiadiazine-2-thione. The CAS name is tetrahydro-3,5-dimethyl-2H-1,3,5-thiadiazine-2-thione.

### Maximum Acceptable Value

Dazomet is not mentioned in the DWSNZ, nor in the WHO Guidelines.

### Sources to water

Dazomet is a dithiocarbamate fungicide, herbicide and nematicide. Dazomet appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007).

It is usually applied before the planting of crops by soil incorporation, thereby causing it to act as a soil fumigant and disinfectant by decomposing to methyl isothiocyanate. In the US it may also be used as a treatment during the production of pulp and paper, as a material preservative treatment paper coatings, non-food adhesives, epoxy flooring compounds, slurries, and high viscous suspensions, as a biocide treatment to recirculating cooling water systems, as a remedial wood treatment to utility poles.

### Forms and fate in the environment

The average half-life in aerobic soil is about one day; anaerobic soil about 14 days. It decomposes in water and moist air to methyl isothiocyanate (MITC) thereby acting as a soil fumigant and disinfectant; formaldehyde, methylamine, hydrogen sulfide and (in acid soils) carbon disulfide, are also formed.

USEPA (2009) states “While dazomet and its major degradate MITC have certain properties and characteristics in common with chemicals that have been detected in groundwater (MITC is highly soluble in water and has low adsorption to soil), volatilisation is this chemical’s most important route of dissipation.”

EFSA (2015) states that the soil degradation studies demonstrated that the degradation rate of dazomet and its metabolite MITC is rapid; the maximum DT90lab was 4.6 days and 25.5 days, respectively.

Water solubility is about 3,500 mg/L, at pH 5 to 9.

NPIC (1994) quotes for dazomet a soil half-life of seven days, water solubility of 3,000 mg/L and a sorption coefficient (soil Koc) of 10. This resulted in a pesticide movement to groundwater rating of moderate.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

Because dazomet breaks down to gaseous or volatile compounds, the principal health concern related to its use is related to inhalation by users and those nearby. It is highly unlikely to be associated with drinking-water.

The Acceptable Daily Intake (ADI) adopted in Australia for dazomet is 0.0005 mg/kg body weight, with a NOEL of 0.5 mg/kg.

For dazomet EFSA (2015) reports and ADI of 0.01 mg/kg/day, and an ARfD of 0.03 mg/kg. For MITC (methyl isocyanate) EFSA (2015) reports and ADI of 0.004 mg/kg/day, and an ARfD of 0.03 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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WHO. 2002. <http://www.who.int/ipcs/publications/cicad/cicads_alphabetical/en/index.html> and select carbon disulfide, CICAD 46, or go to <http://www.inchem.org/documents/cicads/cicads/cicad46.htm>

# 2,4-DB

CAS No. 94-82-6. IUPAC name is 4-(2,4-dichlorophenoxy)butyric acid. The CAS name is 4-(2,4-dichlorophenoxy)butanoic acid. The commercial product is produced as salts (commonly sodium) and esters, but the acid is considered to be the active agent.

### Maximum Acceptable Value

Based on health considerations, the concentration of 2,4-DB in drinking-water should not exceed 0.1 mg/L.

Because the manufacture of phenoxy acids presents a risk of formation of polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs), a maximum content of 4 ppt (4 x 10-6 mg/kg) of the sum of these impurities was set, expressed as sum of 2,3,7,8-tetrachlorodibenzo[b,e][1,4]dioxine (TCDD) toxic equivalents (EFSA 2016).

### Sources to water

2,4-DB appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). See 2,4-D as well. 2,4-DB is a selective, systemic plant growth regulator (a synthetic hormone in the auxin family).

EC (2002) requires the manufacturer to keep the dioxin and furan levels below detection.

### Forms and fate in the environment

2,4-DB is degraded microbially in the environment with hydroxylation, decarboxylation, cleavage of the acid side chain and ring opening occurring. The half-life in soils ranges from 2 to 14 days with a recommended average half-life of 10 days; the mobility of 2,4-DB in mineral soils was classified as very mobile to moderately mobile, hence groundwater contamination is a possibility. The half-life in water ranges from one to several weeks. The major degradate of 2,4-DB is 2,4-D; 2,4-D was found at a maximum of 5.0–15 percent of applied 2,4-DB in soil dissipation studies (USEPA 2005). Minor metabolites may include 2,4-dichlorophenol, 4-chlorophenoxyacetic acid and 2,5‑dichloro-4-hydroxyphenoxybutyric acid; see EFSA (2011/16) for a list of metabolites.

Hydrolysis of 2,4-DB in water was investigated in buffered solutions (pH 5, 7 and 9) at 25°C; 2,4-DB may be considered stable in this range of pH, and direct photolysis is not expected to contribute significantly to the degradation of 2,4-DB in aquatic environment under natural conditions. The DT50 was measured at 79.9–115.1 days), so 2,4-DB can be considered persistent. The major metabolite found is 2,4-D. Groundwater contamination is unlikely (EFSA 2016).

Water solubility of the sodium salt is 62 mg/L at pH 5; 4385 mg/L at pH 7; 45 percent at pH 9 (EC 2002).

NPIC (1994) quotes for 2,4-DB acid a soil half-life of five days, water solubility of 46 mg/L and a sorption coefficient (soil Koc) of 440. This resulted in a pesticide movement to groundwater rating of very low.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, did not find any detectable concentrations of 2,4-DB (limit of detection = 0.0001 mg/L) (ESR 2001).

Chlorophenoxy herbicides are not frequently found in drinking-water; when detected, concentrations are usually no greater than a few micrograms per litre (WHO 2004/2017).

### Removal methods

No information is available on methods of removing 2,4-DB from water, but chlorophenoxy acids have been reported to be oxidised by ozone. A concentration of 0.0001 mg/L should be achievable using GAC.

### Recommended analytical techniques

#### Referee method

Liquid/Extraction and Gas Chromatography with an Electron Capture Detector (EPA 515.).

#### Some alternative methods

High Performance Liquid Chromatography with a Photoiodide Array Ultraviolet Detector (EPA 555). Also see EFSA (2016).

### Health considerations

In general, chlorophenoxy herbicides are absorbed rapidly from the gastrointestinal tract and evenly distributed throughout the body. Accumulation in human tissues is not expected, and a steady-state level in the human body will be achieved within  
3–5 days of exposure. Elimination occurs primarily in the urine, mostly in the unchanged form. Biological half-lifes of chlorophenoxy herbicides in mammals range from 10 to 33 hours. Metabolic conversions occur only at high doses. The salt and ester forms are hydrolysed rapidly and follow the same pharmacokinetic pathways as the free acid forms.

Short-term exposure studies on beagle dogs fed diets containing high doses of 2,4-DB reported effects including diarrhoea, inactivity, depression, weakness, cysts, increased mortality, reduced body weight and food consumption, haematological effects, abnormal blood chemistry and urinalysis, jaundice, increased relative thyroid, liver, spleen, and kidney weights and decreased relative testes weight. Long-term exposure studies on rats reported similar symptoms.

Chlorophenoxy herbicides as a group, including 2,4-D and MCPA, have been classified by the International Agency for Research on Cancer in Group 2B (possibly carcinogenic to humans). However, based on the available data from studies on exposed populations and on animals, it is not possible to assess the carcinogenic potential of any specific chlorophenoxy herbicide. Therefore drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects. As at September 2008, the USEPA has classified 2,4-DB as “not likely to be carcinogenic to humans”. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

The oral RfD was calculated at 0.008 mg/kg/d (USEPA 1992). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.03 mg/kg/d, and an ARfD of 0.60 mg/kg/d.

The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for 2,4-DB is 19.8 mg/L.

EC (2002) reported an ADI of 0.02 mg/kg/d; adding that an ARfD is considered unnecessary. EFSA (2011) reaffirmed these values. EFSA (2016) added an ARfD of 0.3 mg/kg bw based on developmental toxicity in rats with a NOAEL of 31.25 mg/kg bw per day for skeletal variations and malformations and maternal toxicity in rats and rabbits including deaths; an UF of 100 was applied. They added that 2,4-DB is overall considered devoid of genotoxic potential.

### Derivation of Maximum Acceptable Value

As it is not possible to assess the carcinogenic potential to humans of any specific chlorophenoxy herbicide, a tolerable daily intake approach been used for the derivation of the MAV for 2,4-DB in drinking-water. The no-observable-adverse-effect level used in the derivation is for effects on the body and organ weights, blood chemistry and haematological parameters in a two-year study in rats.

The MAV for 2,4-DB in drinking-water was derived as follows:

3 mg/kg body weight/day x 70 kg x 0.1 = 0.1 mg/L

2 L/day x 100

where:

* no-observable-adverse-effect level = 3 mg/kg body weight per day for effects on the body and organ weights, blood chemistry and haematological parameters in a two-year study in rats. The NOAEL used in the guideline value derivation is similar to the NOAEL of 2.5 mg/kg of body weight per day obtained in a short-term study in beagle dogs and the NOAEL for hepatocyte hypertrophy of 5 mg/kg of body weight per day obtained in a three-month study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter- and intra-species variation).

The NOAEL used in the WHO guideline value derivation is similar to the NOAEL of 2.5 mg/kg body weight per day obtained in a short-term study in dogs and the NOAEL for hepatocyte hypertrophy of 5 mg/kg body weight per day obtained in a three-month study in rats.

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# DDT and its derivatives

CAS No. 107917-42-0. This relates to the commercial insecticide product, along with its isomers. The CAS numbers for the ‘pure’ chemicals are:

* **DDD:** 72-54-8. The IUPAC name for p,p’-DDD or 4,4’-DDD is: 1,1-dichloro-2,2-bis(4-chlorophenyl)ethane. The CAS name is 1,1′-(2,2-dichloroethylidene)bis[4-chlorobenzene]. Also called p,p’-TDE, etc.
* **DDD:** 53-19-0. The IUPAC name for o,p’-DDD or 2,4’-DDD is: 2,4’‑dichlorodiphenyldichloroethane. Also called o,p’-TDE, etc.
* **DDE:** 72-55-9. The IUPAC name for p,p’-DDE or 4,4’-DDE is: 1-chloro-4-[2,2-dichloro-1-(4-chlorophenyl)ethenyl]benzene.
* **DDT:** 50-29-3. The IUPAC name for p,p’-DDT or 4,4’-DDT is 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane. The CAS name is 1,1′-(2,2,2-trichloroethylidene)bis[4-chlorobenzene].
* **DDT:** 789-02-6. The IUPAC name for o,p’-DDT or 2,4’-DDT is 1,1,1-trichloro-2-(2-chlorophenyl)-2-( 4-chlorophenyl)ethane.

Generally the term DDT refers to the technical product, of variable composition, containing 11 or more compounds. The pure compound has the ISO common name p,p’-DDT, or p,p’-dichlorodiphenyltrichloroethane. The acronym is derived from an old and imprecise name, DichloroDiphenylTrichloroethane. Also once called chlorophenothane and clofenotane.

IARC (2017) describes further related compounds, sourced from WHO (1989):

* DDMU 1,1’-(2-chloroethenylidene)-bis[4-chlorobenzene]
* DDMS 1,1’-(2-chloroethylidene)-bis[4-chlorobenzene]
* DDNU 1,1’-bis(4-chlorophenyl)ethylene
* DDOH 2,2-bis(4-chlorophenyl)ethanol
* DDA 2,2-bis(4-chlorophenyl)-acetic acid.

### Maximum Acceptable Value

Based on health considerations, the concentration of DDT and its derivatives (ie, the sum of) in drinking-water should not exceed 0.001 mg/L (1 g/L).

The WHO GV for DDT and its metabolites is 0.001 mg/L.

The compound’s structure permits several different isomeric forms, such as o,p’-DDT. The term DDT is also applied to commercial products consisting predominantly of p,p’-DDT, but also containing smaller amounts of other compounds, including p,p’- and o,p’-DDD (dichlorodiphenyldichloroethane) and p,p’- and o,p’-DDE (dichlorodiphenyldichloroethene). Technical DDT was typically composed of about 80 percent p,p’-DDT (the active ingredient) and 20 percent o,p’-DDT (USGS 2006).

DDD, DDE and DDT are “priority pollutants” under the US Clean Water Act.

DDT is one of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention; see <http://chm.pops.int/>. DDT appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.009 mg/L for DDT; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects. Although there are no registered products that contain DDT in Australia, de-registered compounds may still be detected in water. Earlier versions had said: “If present in drinking water, DDT would not be a health concern unless the concentration exceeded 0.02 mg/L. If it is detected, remedial action should be taken to stop contamination.”

DDT is listed as a “priority contaminant” in the Ministry for the Environment’s *Toxicological Intake Values for Priority Contaminants in Soil* (MfE 2011).

### Sources to water

DDT may enter source waters as a result of its use as a non-systemic contact organochlorine insecticide with a broad spectrum of activity.

DDT was initially used by the military in World War II to control malaria, typhus, body lice, and bubonic plague. DDT is not currently used in New Zealand, but was used extensively in the past, particularly on pasture to control grass grub and porina; it had also been used in sheep dips. There are still significant residues in soils in many areas. The registration of DDT was cancelled in New Zealand in 1989. 4,4’-DDE residues have been found in spinach during the Food Residue Surveillance Programme. DDE is still found in New Zealand breast milk, although the concentration has fallen significantly over the past 20 years (Massey University 2010).

DDT is one of the 12 insecticides, and the only organochlorine compound, currently recommended by WHO for use in indoor residual spraying for disease vector control (WHO 2011a). Currently, DDT represents some 71 percent of the global annual amount of insecticides used for vector control; in 2005 an estimated 5,000 tonnes was used (IARC 2017).

A typical sample of technical DDT had the following general analysis (ex IARC 1991):

63–77 percent p,p’-DDT; 8–21 percent o,p’-DDT; 0.3–4.0 percent p,p’-TDE; 0.04 percent o,p’-TDE; 0.1–1.9 percent l-(ortho-chlorophenyl) ethyl-2-trichloro-p-chlorobenzene sulfonate; 0.2 percent 2-trichloro-1-(p-chlorophenyl) ethanol; 0.03–0.6 percent bis(p-chlorophenyl)sulfone; 0.01 percent α-chloro-α-(p-chlorophenyl) acetamide; 0.01 percent α-chloro-α-(chlorophenyl) acetamide; 0.3 percent chlorobenzene; 0.1 percent p-dichlorobenzene; trace of 1,1,1,2‑tetrachloro-2-(p-chlorophenyl)-ethane; 0.02 percent sodium p‑chlorobenzenesulfonate; 0.01 percent ammonium p-chlorobenzene sulfonate; 0.01–0.1 percent inorganics; and unidentified components and losses:  
5.1–10.6 percent.

MfE (2012) developed a national set of soil contaminant standards for 12 priority contaminants and five common land uses; DDT levels range from 45 to 1,000 mg/kg depending on land use.

### Forms and fate in the environment

DDT and its metabolites are persistent in the environment and resistant to microbial degradation, although photochemical degradation does occur. The persistence of DDT in temperate climates is in the order of years; maybe less than a year in the tropics, but in temperate areas the half-life of total DDT products in soil may exceed five years; even 15 years has been reported (NPIC). DDT is adsorbed readily to soils and sediments and most DDT that enters water bodies is firmly attached to soil particles, so it is not expected to transfer to groundwater. DDT is taken up readily by other organisms and bioconcentration is significant.

DDT, DDE, and DDD last in the soil for a very long time, potentially for hundreds of years. Most DDT breaks down slowly into DDE and DDD, generally by the action of micro‑organisms. They stick strongly to soil, and therefore generally remain in the surface layers of soil. Some soil particles with attached DDT, DDE, or DDD may get into rivers and lakes in run-off. Only a very small amount, if any, will seep into the ground and get into groundwater. The length of time that DDT will last in soil depends on many factors including temperature, type of soil, and whether the soil is wet. DDT lasts for a much shorter time in the tropics where the chemical evaporates faster and where micro‑organisms degrade it faster. DDT disappears faster when the soil is flooded or wet than when it is dry. ATSDR (2002) report a study where total DDT isomers were present in water mainly as DDT during the first 30 days, as DDE and DDD during the next 30 days, and as DDD in the last 30 days. When deposited on soil, DDT, DDE, and DDD are strongly adsorbed. DDT biodegrades primarily to DDE under unflooded conditions (eg, aerobic) and to DDD under flooded (eg, anaerobic) conditions. As a result of their strong binding to soil, DDT, DDE, and DDD mostly remain on the surface layers of soil; there is little leaching into the lower soil layers and groundwater. DDT breaks down into DDE and DDD in soil, and the parent-to-metabolite ratio (DDT to DDE or DDD) decreases with time. However, this ratio may vary considerably with soil type. In a 1995–1996 study of agricultural soils in the corn belt of the central United States, the ratio of p,p’-DDT/p,p’-DDE varied from 0.5 to 6.6 with three-quarters of the soils having ratios above 1. In a study of forest soils in Maine, the half-life for the disappearance of DDT residues was noted to be 20–30 years. DDT was much more persistent in muck soils than in dry forest soils. A study of DDT in agricultural soils in British Colombia, Canada reported that over a 19-year period, there was a 70 percent reduction of DDT in muck soils and a virtual disappearance of DDT from loamy sand soils.

Water solubilities (ATSDR):

* p,p`-DDT 0.025 mg/L
* o,p`-DDT 0.085 mg/L
* p,p`-DDD 0.09 mg/L
* o,p`-DDD 0.1 mg/L
* p,p`-DDE 0.12 mg/L
* o,p`-DDE 0.14 mg/L

In surface water, DDT will bind to particles in the water, settle, and be deposited in the sediment.

Neither DDE or DDT dissolve easily in water. While they are frequently found in the sediments at the bottom of contaminated rivers and lakes, the levels in drinking water have seldom been a concern. When detected in water supplies, levels have usually been very low. One of the surveys that has detected DDE in well water was conducted in the Midwest by the US Geological Survey. About 6 percent of the wells tested had positive detections of DDE. A statewide survey of DDE levels in surface water of New York State also found 6 percent of the samples with detectable levels of DDE.

NPIC (1994) quotes for DDD (TDE) a soil half-life of 1,000 days, water solubility of 0.02 mg/L and a sorption coefficient (soil Koc) of 100,000. For DDE a soil half-life of 1,000 days, water solubility of 0.1 mg/L and a sorption coefficient (soil Koc) of 50,000. For DDT a soil half-life of 2,000 days, water solubility of 0.0055 mg/L and a sorption coefficient (soil Koc) of 2,000,000. This resulted in a pesticide movement to groundwater rating of extremely low for DDT, DDD and DDE.

USGS (2006) give the following values:

* **p.p`-DDE:** log Kow = 5.7; log Koc (where Koc is in mL/g) = 5.0; water solubility = 0.04 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.90; half-life in aerobic soil = NA days; half-life in water = >44,000 days.
* **p.p`-DDD:** log Kow = 5.5; log Koc (where Koc is in mL/g) = 5.0; water solubility = 0.05 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -0.194; half-life in aerobic soil = NA days; half-life in water = 10,000 days.
* **p.p`-DDT:** log Kow = 6.19; log Koc (where Koc is in mL/g) = 5.4; water solubility = 0.0055 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.37; half-life in aerobic soil = NA days; half-life in water = 5,000 days.
* **o.p`-DDE:** log Kow = 5.8; log Koc (where Koc is in mL/g) = 5.58; water solubility = 0.1 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.405; half-life in aerobic soil = NA days; half-life in water = NA days.
* **o.p`-DDD:** log Kow = 6.0; log Koc (where Koc is in mL/g) = 5.36; water solubility = 0.1 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -2.7; half-life in aerobic soil = NA days; half-life in water = NA days.
* **o.p`-DDT:** log Kow = NA; log Koc (where Koc is in mL/g) = NA; water solubility = 0.026 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -0.460; half-life in aerobic soil = NA days; half-life in water = NA days.

### Typical concentrations in drinking-water

DDT and its isomers were not detected in any of 230 samples from 212 supplies sampled in New Zealand between 1988 and 1992. Detection limits ranged from 0.00025 to 0.00004 mg/L (0.25 to 0.04 g/L) for this class of compounds.

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of DDT and its isomers (limit of detection = 0.0002 mg/L) (ESR 2001).

pp-DDT has been found in Otago groundwater at 0.00001 mg/L (MAF 2006).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). pp-DDT occurred at 0.01 µg/L, ie, 0.00001 mg/L

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). pp-DDT was detected in one well at a concentration of 0.033 µg/L, ie, 0.000033 mg/L.

In a study of surface water supplies in the United States between 1964 and 1968, the highest concentration of DDT recorded was 0.0008 mg/L. In Germany, concentrations were even lower, averaging 0.00001 mg/L (10 ng/L).

One water utility in the US reported detecting p,p’-DDT in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

One water utility in the US reported detecting p,p’-DDD in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

Two water utilities in the US reported detecting p,p’-DDE in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0003 mg/L.

### Removal methods

Specific information concerning the removal of DDT and its isomers from water is unavailable. However, its low solubility and attraction to soil particles makes it likely that removal by chemical coagulation and fine filtration processes is possible, maybe to as low as 0.0001 mg/L. However, USEPA (2008a) states that there is no evidence that DDE is substantially removed by conventional treatments, such as coagulation/ flocculation, sedimentation, and inert media filtration. Potential treatment technologies include activated carbon and reverse osmosis. WHO (2017) considers that 0.1 μg/L should be achievable using coagulation or GAC.

Isotherm adsorption data also indicate that removal by adsorption on to granular activated carbon should be possible.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction Gas Chromatographic/Mass Spectrometric Method (APHA 6410B).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6630B).

2. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

### Health considerations

DDT has a wide margin of safety when used judiciously, and few if any adequately documented cases of DDT poisoning in man have been fatal. It appears that the main toxicity to humans is related more to the solvent vehicle rather than the DDT itself (ICPS 1999).

Food is the major source of intake of DDT and related compounds for the general population.

Absorption of small doses of DDT, such as those found in food residues, is virtually complete and is facilitated by the presence of fat in food. It is stored preferentially in fat. Like most species, humans convert DDT to DDE, which is stored even more avidly than the parent compound. A small amount of DDD may also be found in tissues.

In humans, signs and symptoms reported following acute intoxication by DDT include nausea, vomiting, paraaethesia, dizziness, ataxia, confusion, tremor and, in severe cases, convulsions.

Occupational exposure of workers over 25 years at an average dosage of 0.25 mg/kg body weight per day resulted in no reported adverse effects. From epidemiological observations of humans, there is no firm evidence that DDT has any reproductive or teratogenic effects.

The JMPR 2000 meeting concluded that an acute RfD for DDT is unnecessary. This conclusion was based on a determination that the residues of this contaminant are unlikely to present an acute risk to consumers.

The oral RfD for DDT was calculated at 0.0005 mg/kg/d (USEPA (1996).

USEPA (2008) reports a benchmark value for health termed the Health Reference Level (HRL) for DDE of 0.0002 mg/L which considers the potential carcinogenic effects, and is based on the occurrence of liver tumours in mice following chronic exposures; no RfD is currently available for DDE.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for p,p’-DDT of:

* 0.0005 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.0005 mg/kg/day for intermediate-duration oral exposure (15–364 days).

The Tolerable Daily Intake (TDI) adopted in Australia for DDT is 0.002 mg/kg body weight, with a NOEL of 0.25 mg/kg bw from an epidemiological study. The NOEL is based on the absence of toxicological effects at this dose. The TDI incorporates a safety factor of 100, comprising 10 for intraspecies variation and 10 to take into account the uncertainty due to lack of detail in the study.

In most studies, DDT did not induce genotoxic effects in rodent or human cell systems, nor was it mutagenic in fungi or bacteria. DDT impaired reproduction in several species.

MfE (2011) states: DDT and its derivatives DDE and DDD are considered to be threshold contaminants, given the equivocal data on their genotoxicity. These substances enhance liver enzyme production, are weakly hormone disrupting, and act on the central nervous system. Ideally, toxicological criteria for DDT should be based on data regarding the effects of DDE, because it is the primary metabolite found in the environment. However, insufficient data is available to do so – other than to note that toxicologically the adverse effects of DDE and DDT are similar – hence criteria are set based on the effects of DDT. In line with a number of international agencies, an oral TDI of 0.5 µg/kg bw/day, based on hepatotoxicity in rats, is recommended for use in New Zealand. A dermal absorption of 0.018 (1.8 percent) is recommended for use. Dietary intake of DDT residues is considered to be the primary source of exposure. The dietary intakes of ∑DDT for a child aged 1–3 years are 0.0511 µg/kg bw/day and for an average adult 0.0193 µg/kg bw/day, while intake from drinking water is negligible.

DDT and p,p’-DDT are on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

INCHEM (2009) discusses carcinogenicity fully.

These chemicals appear on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. USEPA (1988) classified DDE and DDD as B2; probable human carcinogens. USEPA (1996) classified DDT as B2; probable human carcinogen. Based on animal studies DDE is likely to be carcinogenic to humans (USEPA 2008).

The International Agency for Research on Cancer (1991) concluded in an overall evaluation that, due to evidence of carcinogenicity in experimental animals, DDT is a possible human carcinogen (Group 2B). IARC (2017) revised this: there is now limited evidence in humans for the carcinogenicity of DDT. Positive associations have been observed between DDT and cancers of the liver and testis, and non-Hodgkin lymphoma. There is sufficient evidence in experimental animals for the carcinogenicity of DDT, DDE and DDD. Their overall evaluation was that DDT is probably carcinogenic to humans (Group 2A).

### Derivation of Maximum Acceptable Value

The MAV for DDT (plus its metabolites) was derived using the acceptable daily intake recommended by the Joint FAO/WHO Meetings on Pesticide Residues (JMPR) in 1984.

Because infants and children may be exposed to greater amounts of chemicals in relation to their body weight and because of concern over the bioaccumulation of DDT, a 10 kg child was used for the calculation of the MAV.

The MAV for DDT and its derivatives in drinking-water was derived as follows:

1 mg/kg body weight/day x 10 kg x 0.01 = 0.001 mg/L (1 g/L)

1 L/day x 100

where:

* acceptable daily intake is based on a NOAEL of 1 mg/kg of body weight per day for developmental toxicity in rats
* average weight of child = 10 kg
* average quantity of water consumed by an child = 1 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01
* uncertainty factor = 100.

The MAV exceeds the solubility of DDT of 0.001 mg/L (1 g/L). However, some of the DDT may be adsorbed on to the small amount of particulate matter present in drinking-water, so that the MAV could be reached under certain circumstances.

DDT is listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by drinking-water guidelines.

In the 1995 datasheet and the 1995 DWSNZ, the MAV for DDT and its derivatives in drinking-water had been derived as follows:

0.02 mg/kg body weight/day x 10 kg x 0.01 = 0.002 mg/L (2 g/L)

1 L/day

where:

* acceptable daily intake = 0.02 mg/kg body weight per day
* average weight of child = 10 kg
* average quantity of water consumed by an child = 1 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limits for DDD, DDE and DDT are 0.001 mg/L (for each).

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# Deltamethrin

CAS No. for deltamethrin is 52918-63-5. Deltamethrin is a synthetic dibromo-pyrethroid. Of the eight possible stereoisomers, only two isomers, 1R,3R,S(benzyl) and lR,3S,S(benzyl) have insecticidal activity. The commercial product, deltamethrin, contains only the former (cis) isomer; for this reason, deltamethrin, the [1R, cis, alpha-S]-isomer, is often referred to as cis-deltamethrin. products containing the latter, ie, lR,3S,S(benzyl) may be known as trans-deltamethrin. Deltamethrin has an α‑cyanogroup on the 3-phenoxybenzyl alcohol and is a type II pyrethroid.

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

WHO (2004) states that deltamethrin is unlikely to occur in drinking-water, so is excluded from guideline derivation. The 2005 DWSNZ had a provisional MAV for permethrin (qv), a synthetic (and most common) pyrethroid.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.04 mg/L for deltamethrin; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.0004 µg/L for deltamethrin in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Deltamethrin is a non-systemic insecticide belonging to the chemical class of pyrethroids. With the exception of deltamethrin, pyrethroids are a complex mixture of isomers.

One use of synthetic pyrethroids such as deltamethrin by the Australian wool industry is for control of the sheep louse Bovicola ovis. Another is on tamarillos.

Deltamethrin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Deltamethrin was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods in 2011 (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in tamarillos (<http://www.foodsafety.govt.nz/elibrary/industry/frsp2011-2012-quarter1-report.pdf>).

### Forms and fate in the environment

Pyrethrins and pyrethroids are only slightly soluble in water (most are <1 mg/L – see ATSDR 2003 – an exception is deltamethrin for which New York State 2007 quotes a solubility of 200 mg/L but they surely mean 0.002 mg/L; WHO (2012) quotes 0.0013 mg/L. Given the very high Koc and very short half-life, deltamethrin should not impact groundwater), and all adhere to particulate matter so do not readily leach to groundwater.

In soil, degradation occurs within 1–2 weeks and about 10 days after use, there are no deltamethrin residues observed on plants (EXTOXNET 1996). However, EFSA (2015) quotes the soil DT90 as ranging between 30 and 390 days.

Deltamethrin is not mobile in the environment because of its strong adsorption to particles, its lack of solubility in water, and the very low application rates used. Under laboratory conditions, deltamethrin was incubated in sand and organic soil at 28°C, approximately 52 percent and 74 percent, respectively, of the applied deltamethrin remained eight weeks after treatment (IPCS HSG 1989). Deltamethrin has little potential to leach into groundwater due to its strong tendency to bind to soil organic matter. Deltamethrin was stable to hydrolysis in aqueous solutions of pH 5 and 7; in a pH 9 solution, the average half-life was 2.5 days. Octanol-Water Partition Coefficient (Kow): 6.1. Henry’s constant: 1.2 x 10-4 to 5.0 x 10-5 atm·m3/mol. Soil Sorption Coefficient (Koc): ranges from 7.05 x 105 to 3.14 x 106 (NPIC).

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

USEPA (1998) developed a chronic RfD for deltamethrin of 0.01 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.01 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for deltamethrin is 0.10 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

Deltamethrin was evaluated by the FAO/WHO JMPR in 1977, 1980, 1992, 1994, 1995, 2000 and 2016. On the basis of residues data from a wide range of crops, the JMPR concluded that intake of residues of deltamethrin is unlikely to present a public health concern (JMPR 1995). In 2000/2016, the JMPR set an ADI of 0.01 mg/kg bw and an acute RfD of 0.05 mg/kg bw.

The EC (2002) quotes an ADI of 0.01 mg/kg/d and an ARfD of 0.05 mg/kg/d for deltamethrin. EFSA (2015) quotes an ADI of 0.01 mg/kg/d and an ARfD of 0.01 mg/kg/d.

IARC has classified deltamethrin, fenvalerate and permethrin as Class 3 (not classifiable as to its carcinogenicity to humans).

### Derivation of Maximum Acceptable Value

No MAV.

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# Desmedipham

CAS No. 13684-56-5. The IUPAC name for desmedipham is: ethyl 3‑phenylcarbamoyloxycarbanilate or ethyl 3-phenylcarbamoyloxyphenylcarbamate. The CAS name is ethyl [3-[[(phenylamino)carbonyl]oxy]phenyl]carbamate. Can be called ethyl m-hydroxycarbanilate carbanilate.

### Maximum Acceptable Value

Desmedipham does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Desmedipham is a non-systemic selective post-emergence contact carbanilate herbicide (carbamate), mainly used on beets to control annual broadleaf weeds and annual grasses. It seems to be sold in New Zealand as a mixture with phenmedipham (qv).

Desmedipham appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of desmedipham in soils ranges from 5 to 40 days and 2 to 13 days in water; no groundwater contamination is expected. The main environmental (soil and water) metabolite is ethyl-3-hydroxyphenyl carbamate (EHPC – CAS No. 7159-96-8) in both aerobic and anaerobic conditions; aniline forms as well.

The water solubility is about 7 mg/L.

NPIC (1994) quotes for desmedipham a soil half-life of 30 days, water solubility of 8 mg/L and a sorption coefficient (soil Koc) of 1500. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Desmedipham tends to concentrate in red blood cells where the half-life is about 100 hours. It is metabolised in the body, where 3- and 4-aminophenol may be of special toxicological concern.

Desmedipham shows no carcinogenic potential and no classification for mutagenicity is warranted (EC 2004). An ADI of 0.03 mg/kg was derived based on a two-year study using rats, and an acute reference dose (ARfD) of 0.1 mg/kg bw.

The USEPA RfD Committee recommended that a RfD for this chemical be based on a reproductive toxicity study in rats with a parental toxicity NOEL of 4 mg/kg/day. Effects seen were significant reduction of body weight, hemolytic anemia accompanied by significant increase in spleen weights and thyroid compensatory function at the next higher dose of 20 mg/kg/day, the middle dose level tested, and higher dose levels. An uncertainty factor (UF) of 100 was applied to account for the inter-species extrapolation and intra-species variability. On this basis, the RfD is 0.04 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.04 mg/kg/d, and an ARfD of 0.1 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for desmedipham is 1.00 mg/L.

EFSA (2014) established an ADI of 0.03 mg/kg/d and an ARfD of 0.1 mg/kg bw. These were revised (EFSA 2018): The acceptable daily intake (ADI) is 0.016 mg/kg bw per day based on the NOAEL of 3.2 mg/kg bw per day of the two-year rat study, and an uncertainty factor (UF) of 200 (an additional factor of two to allow for a sufficient margin of safety to the observed adenomas with a LOAEL of 5.8 mg/kg bw per day). The acute reference dose (ARfD) is set at 0.05 mg/kg bw, based on the NOAEL of 5.2 mg/kg bw per day from the 90-day study on rats where adverse effects on methaemoglobin were observed after 4 weeks and applying an uncertainty factor of 100.

In studies using laboratory animals, desmedipham generally has been shown to be practically non-toxic for acute oral toxicity, inhalation toxicity and dermal irritation, and has been placed in Category IV (the lowest of four categories) for these effects. Desmedipham is not considered a developmental toxicant or a mutagen. Its cancer classification is Group E (evidence of non-carcinogenicity for humans) pending receipt and evaluation of confirmatory data (USEPA 1996).

### Derivation of Maximum Acceptable Value

No MAV.

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# Diazinon

CAS No. 333-41-5. The IUPAC name for diazinon is: O,O-diethyl O-2-isopropyl-6-methylpyrimidin-4-yl phosphorothioate. The CAS name is O,O-diethyl O-[6-methyl-2-(1-methylethyl)-4-pyrimidinyl] phosphorothioate. Has also been called O,O-diethyl O‑(2-isopropyl-6-methyl-4-pyrimidinyl) phosphorothioate, and numerous trade names.

### Maximum Acceptable Value

WHO (2004 and 2011) states that diazinon is unlikely to occur in drinking-water, so did not establish a guideline value. Diazinon is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*.

In DWSNZ 2005, the provisional MAV for diazinon in drinking-water had been 0.01 mg/L.

The maximum acceptable concentration in Canada is 0.02 mg/L.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.001 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.004 mg/L, excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Diazinon is a non-systemic organophosphate insecticide that is used in both pesticides and veterinary medicines. Pesticides containing diazinon are applied to both fruit and vegetable crops including apples, kiwifruit, grapes, cereals, lettuce, tomatoes and onion and are also used as commercial insecticides on lawns and soil. Target pests include whitefly, aphids, caterpillars, nematodes and grass grubs. Diazinon is also used as an ectoparasiticide against fleas and ticks in cat and dog flea collars, sheep dips and dusting powders for sheep, dogs and horses.

Formulations containing diazinon have been registered for use in New Zealand since 1967. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). There are currently 32 products containing diazinon that are registered for use in New Zealand, including 14 insecticides and 18 veterinary medicines. From 1 July 2015, only approved handlers will be able to apply diazinon.

ERMA notes that 92 tonnes of diazinon were used in New Zealand in 2004, at an application rate of 2,400 grams of active ingredient per hectare.

Diazinon should not contain more than 2.5 g/kg of sulfotep.

### Forms and fate in the environment

Diazinon degrades in the field with a half-life of approximately 20–40 days. One study looked at 25 soils and found diazinon to be mobile in 80 percent of the soils tested, while another study found diazinon leached more in light-textured soils with low organic matter content (NPIC).

Diazinon degrades rapidly in aerobic aqueous conditions with a half-life of 7–15 days in natural river and pond water/soil systems. A predominant degradate is pyrimidinol.

The water solubility is 40–60 mg/L. Octanol-Water Partition Coefficient (Kow): 2.5 x 104. Henry’s constant: 1.4 x 10-6 to 1.1 x 10-7 atm·m3/mol. Soil Sorption Coefficient (Koc): 40 to 854.

NPIC (1994) quotes for diazinon a soil half-life of 40 days, water solubility of 60 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low (but see below).

USGS (2006) give the following values: log Kow = 3.3; log Koc (where Koc is in mL/g) = 2.76; water solubility = 60 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -1.39; half-life in aerobic soil = 39 days; half-life in water = 140 days.

The persistence and mobility of diazinon and its metabolites suggest the potential for groundwater contamination. Diazinon has been detected in groundwater samples collected in the United States and Canada.

Its low vapour pressure (9 x 10-5 mm Hg at 25°C) suggests little volatilisation from soil is expected. The low Henry’s Law constant (1.13 x 10-7 atm m3 per mol) suggests little volatilisation from water surfaces is expected. The octanol-water partition coefficient (log Kow) is 3.81. Diazinon is moderately mobile in some soils so has the potential to leach to groundwater. From IARC (2015).

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 342 zones, did not find any detectable concentrations of diazinon (limit of detection = 0.0003 mg/L) (ESR 2001).

Diazinon can move through the soil and contaminate groundwater. Diazinon has been found eight times in groundwaters in the Poverty Bay, Tasman, Canterbury and Southland areas ranging from 0.00001 to 0.00003 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Diazinon occurred at 0.01 to 0.03 µg/L, ie, up to 0.00003 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Diazinon occurred at 0.021 to 0.023 µg/L, ie, up to 0.000023 mg/L.

Diazinon was found in one bore during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.000062 mg/L. The bore was in the Bay of Plenty region.

In surveys of municipal and private water supplies conducted from 1971 to 1986 across Canada, diazinon was detected in only two (both were private wells) of 620 samples analysed (detection limits 0.000001 to 0.0005 mg/L).

Two water utilities in the US reported detecting diazinon (spectracide) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.169 mg/L. This result is something of an outlier – the next highest was 0.00028 mg/L.

### Removal methods

Reverse osmosis, granular activated carbon adsorption, and ozonation have been reported to remove diazinon from water with efficiencies ranging from 75 to 100 percent. Some oxidation processes can result in the formation of unwanted by-products, therefore a by-product management plan is also recommended before implementing any oxidation processes.

### Recommended analytical techniques

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector or Flame Photometric Detector (HMSO 1986).

### Health considerations

Diazinon is a reactive organophosphorus compound, and many of its toxic effects are similar to those produced by other substances of this class. Characteristic effects include inhibition of acetyl cholinesterase and central nervous system depression. Organophosphates are absorbed readily through the skin, and through the respiratory and gastrointestinal tracts.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.001 mg/kg body weight, with a NOEL of 0.02 mg/kg bw from a short-term (37–43 days) human study. The NOEL was based on inhibition of plasma cholinesterease. The ADI incorporates a safety factor of 20. The ARfD is 0.01 mg/kg bw based on a NOEL of 0.2 mg/kg bw/day from a human study. The NOEL was based on red blood cell cholinesterase inhibition after a single dose of diazinon. The ARfD incorporates a safety factor of 20.

The chronic reference dose or RfD (USEPA 2004/2006/2009/2011) is 0.0002 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.007 mg/L. The acute reference dose (aRfD) is 0.0025 mg/kg/day (USEPA 2006a).

Diazinon was evaluated by the JMPR in 1993, 1999 and 2001 when an ADI of  
0–0.002 mg/kg bw and ARfD of 0.03 mg/kg bw were established, and a number of maximum residue levels were estimated. The 2006 meeting increased the ADI to  
0–0.005 mg/kg/d. JMPR (2016) reaffirmed the ARfD, and established a new ADI of  
0–0.003 mg/kg bw, based on the overall NOAEL of 0.3 mg/kg bw per day from all repeated-dose toxicity studies, and using a safety factor of 100. This ADI was supported by the NOAEL of 0.03 mg/kg bw per day, the highest dose tested, identified in repeated-dose studies that involved a limited number of male volunteers, with application of a safety factor of 10.

The ADI for New Zealand is 0.0002 mg/kg/d.

As at September 2008, the USEPA has classified diazinon as Group D: “not likely to be carcinogenic to humans”.

IARC (2015) reports that there is limited evidence in humans for the carcinogenicity of diazinon. A positive association has been observed for non-Hodgkin lymphoma, leukaemia, and cancer of the lung. Their overall evaluation is that diazinon is probably carcinogenic to humans (Group 2A).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.006 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.002 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0007 mg/kg/day for chronic-duration oral exposure (>364 days).

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for diazinon since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

WHO (2004 and 2011) states that diazinon is unlikely to occur in drinking-water, so did not establish a guideline value. Diazinon is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*.

In DWSNZ 1995, 2000 and 2005, the provisional MAV for diazinon had been calculated by the New Zealand Ministry of Health as follows:

0.002 mg/kg x 70 kg x 0.2 = 0.014 mg/L (rounded to 0.01 mg/L)

2 L

where:

* acceptable daily intake = 0.002 mg/kg body weight
* average weight of adult = 70 kg
* proportion of acceptable daily intake allocated to drinking-water = 0.2
* average quantity of water consumed by an adult = 2 L/day.

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# 1,2-dibromo-3-chloropropane

CAS No. 96-12-8. The IUPAC name for 1,2-dibromo-3-chloropropane is (RS)-1,2-dibromo-3-chloropropane. The CAS name is 1,2-dibromo-3-chloropropane. Also called DBCP and dibromochloropropane.

### Maximum Acceptable Value

Based on health considerations, the concentration of 1,2-dibromo-3-chloropropane in drinking-water should not exceed 0.001 mg/L (1 g/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.0002 mg/L.

WHO (2017) states that DBCP has taste and odour thresholds of 0.01 mg/L each; however, it is not an aesthetic determinand in the DWSNZ.

### Sources to water

1,2-Dibromo-3-chloropropane may enter source waters due to its use as a nematocidal soil fumigant. In a survey of drinking-water wells near locations where DBCP had been used within the previous two years, it was found at low (μg/litre) levels. In wells not used for drinking-water, it has been detected at levels of up to 0.02 mg/L (WHO 2003).

1,2-Dibromo-3-chloropropane has never been registered for use in New Zealand. Commercial production is believed to have ceased worldwide (ATSDR 1992).

### Forms and fate in the environment

1,2-Dibromo-3-chloropropane is expected to volatilise from surface water. It is highly persistent in soil and has been shown to remain there for more than two years. It is mobile in soil and may migrate to groundwater.

Degradation of 1,2-dibromo-3-chloropropane in natural waters is a slow process. It volatilises from surface waters before significant degradation can occur. Hydrolysis of 1,2-dibromo-3-chloropropane in natural waters is unlikely to be an important removal process. The rate constant corresponds to half-lifes for hydrolysis of 38 years and 140 days at pH 7 and 9, respectively. Direct photolysis of 1,2-dibromo-3-chloropropane is not likely to occur in environmental waters.

1,2-Dibromo-3-chloropropane is highly soluble in water.

NPIC (1994) quotes for DBCP a soil half-life of 180 days, water solubility of 1,000 mg/L and a sorption coefficient (soil Koc) of 70. This resulted in a pesticide movement to groundwater rating of very high.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 332 zones, did not find any detectable concentrations of 1,2-dibromo-3-chloropropane (limit of detection = 0.0005 mg/L) (ESR 2001).

A limited survey overseas found levels of up to a few micrograms per litre in drinking-water. 191 water utilities in the US reported detecting 1,2-dibromo-3-chloropropane (DBCP) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.006 mg/L.

### Removal methods

No information is available on technologies capable of removing 1,2-dibromo-3-chloropropane from water. However, isotherm adsorption data indicate that removal by adsorption on to granular activated carbon should be possible. WHO (2017) states that 0.001 mg/L should be achievable using air stripping followed by GAC.

### Recommended analytical techniques

#### Referee method

Purge and Trap Capillary Column Gas Chromatographic/Mass Spectrometric Method (APHA 620D, EPA 524.2).

#### Some alternative methods

1. Purge and Trap Capillary-Column Gas Chromatographic Method (EPA 502.2).

2. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6231B).

3. Liquid/Liquid Extraction and Gas Chromatography.

### Health considerations

Absorption of dibromochloropropane is expected to be high following ingestion and distribution is primarily to the liver and kidneys. Dibromochloropropane can probably cross the placenta. Urine is the predominant route for elimination of metabolites.

The USEPA (1991) does not have a Reference Dose for Chronic Oral Exposure (RfD); this reference has a lot of information related to inhalation exposure.

The USEPA (2009/2011) quotes a health advisory of 0.003 mg/L for dibromochloropropane, representing a 10-4 cancer risk.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of 0.002 mg/kg/day for intermediate-duration oral exposure (15–364 days) to 1,2-dibromo-3-chloropropane.

Workers occupationally exposed to dibromochloropropane were reported to have reduced spermatogenesis. This condition was reported to be reversible although permanent damage of germinal epithelium was reported in a follow-up of exposed workers. No chromosomal aberrations were identified in men who were affected, nor were there increases in abortions and malformations in offspring.

No association was found between dibromochloropropane contamination in drinking-water and incidences of gastric cancer and leukaemia.

On the basis of data from studies on rats and mice, dibromochloropropane was determined to be carcinogenic in both sexes by ingestion, inhalation and skin contact. It was also determined to be a reproductive toxicant in humans and several species of laboratory animals. The International Agency for Research on Cancer (IARC) has classified dibromochloropropane in Group 2B (possible human carcinogen). Recent epidemiological evidence suggests an increase in cancer mortality in individuals exposed to high levels of dibromopropane.

Dibromochloropropane appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

1,2-Dibromo-3-chloropropane is one of the Substances from the Carcinogenic Potency Database which are of particular concern even if ingested at doses at or below 0.0025 μg/kg body weight per day (EFSA 2016).

### Derivation of Maximum Acceptable Value

The linearised multistage model was applied to the data on the incidence of stomach, kidney and liver tumours in the male rat in a 104-week dietary study. The concentration of dibromochloropropane associated with an excess lifetime cancer risk of one per 100,000 (10-5) is 0.001 mg/L (1 g/L). This MAV should be protective for the reproductive toxicity of dibromochloropropane.

1,2-Dibromo-3-chloropropane has a taste and odour threshold in water of 0.01 mg/L.

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# 1,2-dibromoethane

CAS No. 106-93-4. The IUPAC name for 1,2-dibromoethane is ethylene dibromide. The CAS name is 1,2-dibromoethane. Also called EDB or ethylenedibromide.

### Maximum Acceptable Value (Provisional)

Based on health considerations, the concentration of 1,2-dibromoethane in drinking-water should not exceed 0.0004 mg/L.

WHO (2004 and 2011) states that their guideline value is provisional due to serious limitations of the critical studies.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.00005 mg/L.

1,2-Dibromoethane is one of the “priority pollutants” under the US Clean Water Act. It also appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

### Sources to water

Ethylene dibromide may enter source waters as a result of its use as an insecticidal soil, grain and fruit fumigant, and as a lead scavenger in tetra-alkyl lead petrol and antiknock preparations. It has been used in New Zealand in the past as a fumigant. It has been a problem overseas in groundwater as a result of petrol spills and agricultural use. Ethylene dibromide can also be used as an industrial solvent. Also, 1,2‑dibromoethane appears to be formed naturally by microalgae growth and has been detected in ocean waters and air.

1,2-Dibromoethane does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It appears as 1,2-dibromoethane.

### Forms and fate in the environment

Volatilisation is the most important removal process for 1,2-dibromoethane released to surface waters. Volatilisation half-lifes of 1 to 16 days have been estimated for flowing and standing surface waters. Evaporated ethylene dibromide in the atmosphere reacts with photochemically produced hydroxyl radicals with half-lifes of 32 days. Ethylene dibromide is very stable in groundwater, especially under anaerobic conditions, where half-lifes of around 20 years are estimated; the presence of hydrogen sulfide increases the rate of hydrolysis from several years to approximately two months.

1,2-Dibromoethane exhibits low-to-moderate soil adsorption, with experimental Koc values ranging from 14 to 160, indicating that 1,2-dibromoethane will leach quickly into groundwater. 1,2-Dibromoethane volatilises readily from surface soil as predicted by its relatively high vapour pressure (11.2 mm Hg at 25°C). 1,2-Dibromoethane is very stable towards hydrolysis (half-life, T1/2 = 13.2 years at pH 7 and 20°C) and is more likely to undergo aerobic biodegradation in the soil rather than abiotic degradation. After eight weeks under anaerobic conditions in the presence of denitrifying bacteria, no biodegradation was observed compared with 97 percent degradation to ethylene under aerobic conditions. Hydrolysis of ethylene dibromide to bromide, ethylene, ethylene glycol and carbon dioxide takes place in the soil.

The water solubility of ethylene dibromide is 4,200 mg/L.

NPIC (1994) quotes for ethylene dibromide (EDB) a soil half-life of 100 days, water solubility of 4,300 mg/L and a sorption coefficient (soil Koc) of 34. This resulted in a pesticide movement to groundwater rating of very high.

### Typical concentrations in drinking-water

No data are available on the concentration of ethylene dibromide in New Zealand drinking-water supplies. Overseas results indicate that in agricultural areas, ethylene dibromide is found in groundwaters at concentrations of 0.00001 mg/L (0.01 g/L) to 0.015 mg/L.

It has been detected in groundwater following its use as a soil fumigant at concentrations as high as 0.1 mg/L (WHO 2004).

Seventy-nine water utilities in the US reported detecting ethylene dibromide (EDB) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00015 mg/L.

### Removal methods

No information is available on methods of removing ethylene dibromide from water. WHO (2017) states that 0.0001 mg/L should be achievable using GAC.

### Recommended analytical techniques

#### Referee method

Liquid/liquid extraction gas chromatographic APHA method 6231B uses a microextraction and capilliary columns.

WHO (2004) states a limit of detection 0.01 mg/L by microextraction GC/MS; 0.03 mg/L by purge and trap GC with halogen-specific detector; 0.8 mg/litre by purge-and-trap capillary column GC with photoionisation and electrolytic conductivity detectors in series.

#### Some alternative methods

Ethylene dibromide is also analysed by the purge and trap GC/MS, APHA methods 6200B and C.

### Health considerations

Animal studies have shown that ethylene dibromide is absorbed readily following oral, inhalation and skin exposure. Following ingestion, the highest level of metabolites was found in the liver and kidney.

The reference dose or RfD (USEPA 2004 and 2006/2009/2011) is 0.009 mg/kg/d, based on a total uncertainty factor of 3,000 and a LOAEL of 27 mg/kg-day. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.3 mg/L.

1,2-Dibromoethane has induced an increased incidence of tumours at several sites in all carcinogenicity bioassays identified in which rats or mice were exposed to the compound by gavage, ingestion in drinking-water, dermal application and inhalation. However, many of these studies were characterised by high early mortality, limited histopathological examination, small group sizes or use of only one exposure level.

Following long-term inhalation studies in mice and rats ethylene dibromide produced adenomas and carcinomas of the nasal cavity, haemangiosarcomas of the spleen and mammary tumours in both species. Ethylene dibromide induced skin and lung tumours in mice after skin application.

In humans, prolonged contact with ethylene dibromide causes skin irritation. Long-term occupational exposure to ethylene dibromide affects semen quality. Statistically significant decreases in sperm count ejaculate, the percentage of viable and motile sperm, and increases in the proportion of sperm with morphological abnormalities were observed among the exposed men compared with controls.

Ethylene dibromide induced sister chromatid exchange, mutations and unscheduled DNA synthesis in both human and rodent cells in vivo.

In 1987, the International Agency for Research on Cancer (IARC) concluded that the evidence for carcinogenicity in humans was inadequate, but that animal studies were sufficient to establish carcinogenicity and classed ethylene dibromide in Group 2A (probably carcinogenic to humans).

USEPA (2004) states that 1,2-dibromoethane is considered “likely to be carcinogenic to humans” based on strong evidence of carcinogenicity in animals and inconclusive evidence of carcinogenicity in an exposed human population. This weight-of-evidence carcinogenicity characterisation replaces the previous classification of “B2; probable human carcinogen”, entered on IRIS on 7 September 1988. The new classification and slope factor estimates are based on a review of newer data and a re-analysis of the data used in the earlier assessment. Based on the consistent findings of several studies reporting increased incidences of a variety of tumours in rats and mice of both sexes by different routes of administration at both the site of application and at distant sites, it can be concluded that there is strong evidence of the carcinogenicity of 1,2‑dibromoethane in animals. The available evidence further supports a conclusion that 1,2-dibromoethane is a genotoxic carcinogen based on evidence from a variety of in vitro and in vivo test systems.

Ethylene dibromide chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. The USEPA (2009/2011) quotes a health advisory of 0.002 mg/L for ethylene dibromide, representing a 10-4 cancer risk.

### Derivation of Maximum Acceptable Value

The 0.0004 mg/L provisional MAV for 1,2-dibromoethane is the lower end of the range (and thus more conservative estimate) of lifetime low-dose cancer risks calculated by linearised multistage modelling of the incidences of haemangiosarcomas and tumours in the stomach, liver, lung and adrenal cortex (adjusted for the observed high early mortality, where appropriate, and corrected for the expected rate of increase in tumour formation in rodents in a standard bioassay of 104 weeks) of rats and/or mice exposed to 1,2-dibromoethane by gavage.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for 1,2-dibromoethane is 0.000004 mg/L.

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# Dicamba

CAS No. 1918-00-9. The IUPAC and CAS name for dicamba is 3,6-dichloro-2-methoxybenzoic acid. IUPAC also calls it 3,6-dichloro-o-anisic acid. CAS No. 2300-66-5 refers to the dimethylamine form. Other salts or esters may be possible.

### Maximum Acceptable Value

Dicamba is not mentioned in the DWSNZ or in the WHO Guidelines.

The maximum acceptable concentration (MAC) for dicamba in drinking-water in Canada is 0.12 mg/L (120 µg/L).

The USEPA (2006/2009/2012) established a lifetime health advisory of 4 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Dicamba is a pre- and post-emergent systemic broad-spectrum benzoic acid (or chlorophenoxy) [herbicide](http://en.wikipedia.org/wiki/Herbicide) used since the 1960s to control annual and perennial broadleaf weeds and woody plants in grain crops and grasslands, and it is used to control brush and bracken in pastures. It is available in many forms: salts and esters. It is sometimes mixed with other products. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Dicamba is very mobile in most soils and significant leaching to groundwater is possible; it has been considered a Priority A chemical with respect to potential for groundwater contamination by the USEPA. The pKa of dicamba is 1.97, indicating that it will exist almost entirely in the anion form in the environment; anions generally do not adsorb to particulate matter. Volatilisation of dicamba from soil surfaces is not expected to be an important fate process; aerobic microbial degradation is important.

If released to water, microbial degradation appears to be the important dicamba removal process; photolysis may contribute to its removal from water. Aquatic hydrolysis, volatilisation, adsorption to sediment, and bioconcentration are not expected to be significant. A predominant degradate is 3,4-dichlorosalicylic acid (DCSA – CAS No. 320-72-9). See JMPR (2010) for details of other metabolites.

The half-life in aerobic soils is dependent on water content and temperature, and can vary from 3 to 20 weeks. DCSA is the predominant metabolite, and this breaks down to DCGA (2,5-dichloro-3,6-dihydroxy-benzoic acid, also called 3,6-dichlorosalicylic acid – CAS No. 3401-80-7); basically dicamba and DCSA were shown to be not persistent in soil in the field (JMPR 2010).

Water solubility of dicamba is about 4,500 mg/L (as the acid form) and about 72 percent (as the dimethylamine). Octanol-Water Partition Coefficient (Kow): 1.9. Henry’s constant: 1.0 x 10-4 Pa·m3/mol; 5.1 x 10-13 atm mole/m3. Soil Sorption Coefficient (Koc): 2.

NPIC (1994) quotes for dicamba salt a soil half-life of 14 days, water solubility of 40 percent and a sorption coefficient (soil Koc) of 2. This resulted in a pesticide movement to groundwater rating of very high.

USGS (2006) give the following values: log Kow = 2.21; log Koc (where Koc is in mL/g) = 1.11; water solubility = 4500 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -3.66; half-life in aerobic soil = 28 days; half-life in water = >200 days.

The potential for groundwater exposure from the representative uses by dicamba or the metabolite DCSA was concluded to be low (EFSA 2011).

### Typical concentrations in drinking-water

The USEPA monitored samples from 68,824 wells in 45 states from 1971 to 1991; dicamba was detected in 3,172 wells in 24 states. A recent study conducted by the US Geologic Survey found dicamba in 0.11 percent to 0.15 percent of the groundwaters surveyed. The maximum level detected was 0.0025 mg/L. There was no apparent correlation between the prevalence of dicamba in groundwater from agricultural areas (0.11 percent) compared with non-agricultural urban areas (0.35 percent).

Dicamba was not found in municipal water supplies in Alberta, but it was detected on two occasions (out of 48 analyses) in municipal water supplies in Manitoba and in about 6 percent of private wells monitored in southern Ontario, with a maximum recorded concentration of 0.002 mg/L (Health Canada 1987).

Thirty-four water utilities in the US reported detecting dicamba in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.018 mg/L.

### Removal methods

Granular activated carbon adsorption is reported to be a possible technique for removal of dicamba from drinking water. Some newer advanced oxidation processes are quite effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Dicamba is suspected of being a human teratogen. No teratogenic effects have been shown in lab animals such as rabbits and rats. Dicamba has not been shown to be a mutagen. The USEPA as at September 2008 describes dicamba as not classifiable (Group D) as to human carcinogenicity.

Estimated exposure to dicamba and its residues of concern for all population subgroups is well below the level of concern. When considering food alone, or food and water, the most highly exposed subgroup is children, aged 1–2, at 6.5 percent and 6.6 percent of the cPAD (chronic population adjusted dose) respectively USEPA (2006).

The reference dose or RfD for dicamba (USEPA 2006/2009/2012) is 0.5 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2012) is 18 mg/L. The oral RfD had previously been 0.03 mg/kg/d (USEPA 1992/2002).

EC (2008) quotes an ADI and ARfD of 0.3 mg/kg/d. These values were confirmed in EFSA (2011 and 2013).

Toxicological studies provided for the metabolite 5-OH-dicamba indicate that this metabolite is not of higher toxicity than the parent compound, and therefore the reference values of dicamba can also be applicable to this metabolite. With regard to the metabolite DCSA, the available toxicological information was limited but sufficient to support an ADI of 0.01 mg/kg bw/day (EFSA 2011).

The relevant short-term oral NOAEL is 50 mg/kg bw/day (90-day dog study). In long-term studies with mice and rats, the maximum tolerable dose (MTD) was not reached. The only adverse effect observed in mice was the slightly reduced body weight gain at 364 mg/kg bw/day, with the NOAEL being 121 mg/kg bw/day. In rats, no adverse effects were observed up to the dose level of 120 mg/kg bw/day. No carcinogenic potential is attributed to dicamba. Fertility and overall reproductive performance was not impaired. The parental NOAEL is 105 mg/kg bw/day, the offspring NOAEL is 35 mg/kg bw/day, and the reproductive NOAEL is set at 350 mg/kg bw/day. In the developmental toxicity studies, there was no evidence of teratogenicity, and the relevant maternal NOAELs are 160 mg/kg bw/day for rats and 30 mg/kg bw/day for rabbits; the developmental NOAELs are 400 and 150 mg/kg bw/day, respectively for rats and rabbits (EFSA 2011).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw from a short-term (developmental toxicity) study. The NOEL is based on maternal toxicity (decreased bodyweight) in rabbits. The ADI incorporates a safety factor of 100.

The 2010 JMPR meeting established an acceptable daily intake (ADI) of 0–0.3 mg/kg bw on the basis of a NOAEL of 30 mg/kg bw per day in a rabbit developmental toxicity study, based on maternal toxicity (behavioural changes) at 150 mg/kg bw per day. A safety factor of 100 was applied. The ADI is supported by a postnatal developmental NOAEL of 35.1 mg/kg bw per day in the rat multigeneration study, on the basis of reduced pup body weights at 105 mg/kg bw per day. This ADI would also be protective against the equivocal increase in the incidences of malignant lymphoma and thyroid parafollicular cell carcinoma in male rats at 107 mg/kg bw per day. The meeting established an acute reference dose (ARfD) of 0.5 mg/kg bw based on a NOAEL of 50 mg/kg bw per day in the 13-week dog study, based on behavioural effects observed shortly after dosing at 300 mg/kg bw per day. A safety factor of 100 was applied. These ADI and ARfD values were reaffirmed in JMPR (2013).

The USEPA established a Lifetime Health Advisory (LHA) level of 0.20 mg/L for dicamba in drinking-water. This means that USEPA believes that water containing dicamba at or below this level is acceptable for drinking every day over the course of one’s lifetime, and does not pose any health concerns. However, consumption of dicamba at high levels well above the LHA level over a long period of time has been shown to cause adverse health effects in animal studies, including changes in the liver and a decrease in body weight (EXTOXNET 1993).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for dicamba is 0.2 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

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# Dichlobenil

CAS No. 1194-65-6. The IUPAC and CAS name for dichlobenil is 2,6‑dichlorobenzonitrile.

The metabolite 2,6-dichlorobenzamide CAS No. is 2008-58-4; also called BAM, and sometimes DCBA.

### Maximum Acceptable Value

Dichlobenil is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*. The final report has not been published as at 2011.

### Sources to water

The benzonitrile systemic herbicide dichlobenil is used to kill perennial weeds in shrub beds, orchards, and berry fields. It is also used to kill roots in sewers and drains. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

It was approved in the UK (MAFF 1985) for direct application to water to control submerged weeds and some rooted floating weeds, with a maximum permitted water concentration of 3 mg/L. See also CEH (2004). The only species of algae controlled are Chara species.

A total of 1,592 samples, 850 surface water and 742 groundwater, were tested from sites in California, Idaho, Oregon and Washington. The limits of detection ranged from 0.00002 to 0.00012 mg/L, but were generally 0.00002 mg/L. Thirty-six samples had estimated detections ranging from 0.0003 mg/L to 0.0012 mg/L. The median value was 0.00004 mg/L, and the seven highest detections ranged from 0.00012 to 0.0012 mg/L.

### Forms and fate in the environment

Dichlobenil is remarkably persistent in soil and residues have been measured five years after application. Dichlobenil was found in groundwater for three years under an industrial site in Ireland that had been treated with dichlobenil over an 18-month period.

The calculated DT50 for dichlobenil in sandy loam soil is 13 weeks. Most of the loss of dichlobenil in soil is due to volatilisation rather than metabolism (JMPR 2014).

Four studies of ponds treated with dichlobenil found that persistence varies from 63 to 189 days, with an average of 130 days.

Dichlobenil volatilises (vaporises into the air) readily and was the most commonly detected herbicide in monitoring of rainwater in Italy.

Dichlobenil is hydrolytically stable in pH 5, 7 and 9 unsterilised buffers at 22 ±1°C, with half-lifes >150 days. Aqueous photolysis (sterile pH 7 buffer): 10 days under spring/summer sunlight at 40°N latitude. The octanol/water partition coefficient (log10POW) = 2.7 at pH 3, 22°C (JMPR 2014).

Dichlobenil water solubility is about 20 mg/L at 20°C; JMPR (2014) states 25 mg/L at 25°C.

NPIC (1994) quotes for dichlobenil a soil half-life of 60 days, water solubility of 21.2 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of moderate.

The metabolite 2,6-dichlorobenzamide (BAM) forms in soil and is more persistent than the parent. It has a water solubility of 2,700 mg/L (20-25°C). The octanol/water partition coefficient (log10POW) = 0.77. BAM was not photolysed or hydrolysed over 31 days (JMPR 2014), which also discusses the metabolites.

### Typical concentrations in drinking-water

2,6-Dichlorobenzamide, a persistent metabolite from the herbicide 2,6‑dichlorobenzonitrile (dichlobenil) and chlorthiamid, is the pesticide residue most frequently detected in Danish groundwater. These herbicides were banned for use in Denmark in 1997, but BAM is still the main pesticide residue in Danish groundwater, with 19.7 percent of the abstraction wells analysed in 2003 having detectable BAM concentrations and 8.1 percent of the wells containing BAM concentrations exceeding the EC threshold limit of 0.0001 mg/L for drinking water. Similar results were reported in 2003 in a monitoring program from Sweden, and BAM has additionally been detected in groundwater in The Netherlands, Germany, and Italy (Sorensen et al 2007).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

As at September 2008 the USEPA has classified dichlobenil in Group C: a possible human carcinogen. In laboratory studies, dichlobenil has caused increases in the incidence of cancer in three species of animals: rats, hamsters and mice.

Rats were given dichlobenil in the diet for 13 weeks at doses of 0, 5, 50, 150 mg/kg/day (subchronic study). Compound-related effects included increased absolute and relative liver and kidney weights; there was also hepatic degeneration without significant necrosis. The NOEL was 5 mg/kg/day. Groups of beagle dogs were given dichlobenil in the diet for two years (chronic study) at dosing levels of 0, 0.5, 1.25, or 8.75 mg/kg/day. The NOEL for systemic toxicity was 1.25 mg/kg/day (USEPA 1998). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.50 mg/kg/d for dichlobenil. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dichlobenil is 1.485 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1.25 mg/kg bw.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0045 mg/kg/d and an ARfD of 0.03 mg/kg/d for the metabolite 2,6‑dichlorobenzamide (BAM). BAM appears to be less toxic than dichlobenil (USEPA 2007). The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for BAM is 0.99 mg/L.

The toxicological profile of dichlobenil was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.01 mg/kg bw per day and 0.45 mg/kg bw, respectively. Toxicological reference values were also established for 2,6-dichlorobenzamide (BAM), the main metabolite of dichlobenil in plant and livestock matrices: the ADI was set at 0.05 mg/kg bw per day and the ARfD, at 0.3 mg/kg bw (EFSA 2013). BAM is also a major metabolite of fluopicolide (qv).

JMPR (2014) reports an ADI of 0.01 mg/kg bw, and an ARfD of 0.5 mg/kg bw (for women of childbearing age only) for dichlobenil. JMPR (2014) reports an ADI of 0.05 mg/kg bw, and an ARfD of 0.3 mg/kg bw (for women of childbearing age only) for 2,6-dichlorobenzamide.

USEPA (2015) found that based on weight of evidence considerations, there was no convincing evidence of potential interaction with the estrogen or thyroid pathways. The weight of evidence suggests that dichlobenil may potentially interact with the androgen pathway.

### Derivation of Maximum Acceptable Value

No MAV. Dichlobenil has an odour threshold of about 0.02 mg/L, which is unaffected by chlorination.

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# Dichlofenthion

CAS No. 97-17-6. The IUPAC name for dichlofenthion is O-2,4-dichlorophenyl O,O‑diethyl phosphorothioate. The CAS name is O-(2,4-dichlorophenyl) O,O-diethyl phosphorothioate. Sometimes spelt diclofenthion and dichlophenthion.

### Maximum Acceptable Value

Dichlofenthion does not have a MAV in the DWSNZ, and is not mentioned in the WHO *Guidelines for Drinking-water Quality*.

### Sources to water

Dichlofenthion is a phenyl organothiophosphate insecticide and nematicide.

Dichlofenthion appears on EPA’s 27 June 2013 list of organophosphate and carbamate (OPC) pesticides which no longer are able to be manufactured in or imported into New Zealand. There did not appear to be any current usage of the product in New Zealand.

Surface waters in the Hogeveense Polder, The Netherlands, sampled from August 1989 to January 1990, contained from 0.1 to 0.3 ug/L dichlofenthion (NIH, accessed June 2016).

### Forms and fate in the environment

Dichlofenthion has a relatively short half-life of only a few minutes in both water and soils. Because the sorption to soil and sediment is considered high, dichlofenthion is not a highly mobile compound. The estimated half-life of dichlofenthion in water, soil, and sediment is less than a few minutes.

An estimated Koc of 15,000 suggests that dichlofenthion will be immobile in soil. Volatilisation from moist soil surfaces may occur based on an estimated Henry’s Law constant of 9.5 x 10-4 atm-cu m/mol, but not from dry soil surfaces based on a measured vapour pressure. Dichlofenthion is expected to adsorb to suspended matter in water based on its Koc value. This compound should volatilise from water surfaces given its estimated Henry’s Law constant. Estimated half-lifes for a model river and model lake are seven hours and eight days, respectively (NIH, accessed June 2016).

It is stable to hydrolysis except under strongly alkaline conditions.

Dichlofenthion water solubility is about 0.25 mg/L at 25°C. The octanol-water partition coefficient at pH 7, 20°C = LogP = 5.14. The adsorption coefficient (Koc) is 18.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Dichlofenthion is a cholinesterase inhibitor. The oral LD50 for rats is 172 mg/kg.

NIH refers to some studies, two of which are:

In 90 day feeding trials cholinesterase activity was not significantly reduced nor was there evidence of abnormal pathology or disturbance in rat receiving 0.75 mg/kg daily.

Feeding to dogs at 0.75 mg/kg body wt/day for 90 days causes no significant reduction in cholinesterase activity nor any symptoms of illness; mixed product toxic to fish; mixed products not toxic to bees when used as prescribed.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

NIH. Accessed June 2016. *Dichlofenthion*. Compound summary CID 7328. <https://pubchem.ncbi.nlm.nih.gov/compound/dichlofenthion>

# Dichlofluanid

CAS No. 1085-98-9. The IUPAC name for dichlofluanid is N-dichlorofluoromethylthio-N′,N′-dimethyl-N-phenylsulfamide. The CAS name is 1,1-dichloro-N-[(dimethylamino)sulfonyl]-1-fluoro-N-phenylmethanesulfenamide.

### Maximum Acceptable Value

Dichlofluanid does not have a MAV in the DWSNZ, and is not mentioned in the WHO *Guidelines for Drinking-water Quality*.

### Sources to water

Dichlofluanid is a broad spectrum phenylsulfamide acaricide/fungicide commonly used on vegetables and some fruits, controlling scab and botrytis. Dichlofluanid has been used as a fungicide in approved agricultural pesticides since 1965, in wood preservative products since 1978 and as a ‘booster biocide’ in antifouling products since before 1987. The antifouling products are approved for use on vessels of any size plus structures below the waterline. Dichlofluanid may also be used in aquaculture (DEFRA 2003).

Dichlofluanid does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (see <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It also appears on the pesticide transfer list. Dichlofluanid is a component of anti-fouling paints, at timber preservative, and pesticide approved for use in New Zealand by ERMA. Also see EPA (2013).

Dichlofluanid is one of 320 pesticides to be withdrawn by the European Commission in July 2003 for use on crops. See tolylfluanid.

### Forms and fate in the environment

Dichlofluanid was observed to hydrolyse in water instantly at pH 9, so rapidly that no parent compound could be detected. At pH 7 and 20°C, a half-life of 26 hours was calculated. Further hydrolysis studies with the primary metabolite, dimethylaminosulfanilide, indicated that half-lifes were in excess of one year at all pHs tested.

Dichlofluanid is not often found in the water phase in and near marinas, but is often detected in the sediments.

The degradation of dichlofluanid in soil was investigated in a number of studies. Aerobic and anaerobic studies resulted in degradation of dichlofluanid to the primary metabolite dimethylaminosulfanilide and in anaerobic studies, degradation to a further metabolite methylaminosulfanilide was noted. Half-lifes of two to five days were calculated for aerobic conditions. Anaerobic half-lifes were not calculated. Several mobility studies confirmed that dichlofluanid was immobile. However, the primary metabolite dimethylaminosulfanilide was classified as immobile to slightly mobile.

Dichlofluanid hydrolyses rapidly to DMSA (N,N-dimethyl-N’-phenylsulfamide). It is also inherently biodegradable and, in biologically active soils, is degraded to DMSA with a half-life of less than one day. Leaching studies in soil showed that dichlofluanid was not mobile but was rapidly degraded under the conditions of the available studies, whereas DMSA was shown to be mobile (water solubility about 1,300 mg/L) and susceptible to degradation with time. It is non-volatile.

Dichlofluanid water solubility is about 1 to 3 mg/L at 20°C. DMSA solubility is 1,300 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The most consistent findings were cranial osteosclerosis in the rat, and findings consistent with fluorosis in a two-year mouse study. A detailed assessment of cranial osteosclerosis was performed in a rat two-year study, in which a LOEL was established at 10 to 14 mg/kg/d. A clear increase in the incidence of cranial osteosclerosis was observed in the low- and middle-dose groups, with almost all animals affected at the top dose. No evidence of fluorosis was observed in the dog studies.

Dichlofluanid is unlikely to pose a genotoxic hazard to man. Overall, it can be concluded that dichlofluanid is a non-genotoxic rat thyroid follicular cell carcinogen, but it is considered unlikely that the rat thyroid studies are of relevance to human health. Dichlofluanid is a suspected endocrine disruptor.

N,N-Dimethyl-N’-phenylsulfamide (DMSA) is a precursor to the formation of dichlofluanid, an impurity in the technical dichlofluanid and a metabolite formed from the breakdown of dichlofluanid. As it is formed from the degradation of dichlofluanid in the environment it is considered in the environmental risk assessment for the active substance. It is not an issue for the human health risk assessment as the in vivo data provide information on the effects from dichlofluanid and any metabolites that are formed. NDMA may be potentially formed as a result of the ozonation of dimethylsulfamide, a metabolite of the fungicide, tolyfluanid; dichlofluanid is structurally similar DWI (2008).

An ADI of 0.3 mg/kg bw was derived (IPCS 1974) based on no toxicological effects from the diet on rats at 75 mg/kg/d, and dogs at 25 mg/kg/d.

EC (2006) established an ADI of 0.35 mg/kg/d; they stated that an ARfD was not required for dichlofluanid in wood preservatives.

The Acceptable Daily Intake (ADI) adopted in Australia for dichlofluanid is 0.03 mg/kg body weight, with a NOEL of 2.7 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# 3,4-Dichloroaniline and 3,5-Dichloroaniline

3,4-Dichloroaniline: CAS No. 95-76-1. Also called 3,4-DCA, 1-amino-3,4-dichlorobenzene or 3,4-dichlorobenzenamine. The IUPAC name is 3,4‑dichlorophenylamine. Refer also to the datasheet for chloroanilines in the organic chemicals section.

3,5-Dichloroaniline: CAS No. 626-43-7. Also called 3,5-DCA, 1-amino-3,5-dichlorobenzene or 3,5-dichlorobenzenamine. The IUPAC name is 3,5‑dichlorophenylamine. Refer also to the datasheet for chloroanilines in the organic chemicals section.

The other dichloroanilines are:

* 2,3-Dichloroaniline: CAS No. 608-27-5. Appears on the USEPA List of Potentially Toxic Inerts/High Priority for Testing (USEPA 1989).
* 2,4-Dichloroaniline: CAS No. 554-00-7. Appears on the USEPA List of Potentially Toxic Inerts/High Priority for Testing (USEPA 1989).
* 2,5-Dichloroaniline: CAS No. 95-82-9.
* 2,6-Dichloroaniline: CAS No. 608-31-1. Appears on the USEPA List of Potentially Toxic Inerts/High Priority for Testing (USEPA 1989).

### Maximum Acceptable Value

There are no MAVs in the DWSNZ and the WHO Guidelines do not refer to 3,4‑dichloroaniline or 3,5-dichloroaniline.

3,4-Dichloroaniline is not a pesticide, but is an impurity in diuron (qv), linuron (qv) and propanil (qv). It is also a biodegradation product of several phenylcarbamates, phenylurea and acylanilide herbicides.

3,5-Dichloroaniline is not a pesticide, but is an impurity or metabolite of iprodione (qv), vinclozolin and procymidone (qv) (USEPA 1998).

### Sources to water

3,4-Dichloroaniline is exclusively used as an intermediate in the chemical industry for the synthesis of 3,4-dichlorophenylisocyanate, the herbicide propanil and an azo dye for polyester fabrics. There are no direct uses of 3,4-DCA without chemical transformation. It is used for the production of phenylurea herbicides (diuron, linuron) and the bactericide trichlorocarbanilide. Trichlorocarbanilide is used as a deodorant and soap bactericide in household products.

Neither 3,4-dichloroaniline nor 3,5-dichloroaniline appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2014 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register).

### Forms and fate in the environment

3,4-Dichloroaniline is very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. 3,4-Dichloroaniline is moderately lipophilic (log Pow of 2.7). Accordingly, 3,4-DCA has a low tendency to bioaccumulate (IUPAC 2003).

3,4-Dichloroaniline shows no volatilisation because of the low Henry’s Law constant, no hydrolysis, slow photolysis in surface waters (estimated half-life of 18 days), no significant biodegradation occurs in WWTPs and surface waters, and reacts with humic substances in soils and sediments. The reaction product accumulates due to the very low biodegradation (estimated half-life of 1,000 days). The partition coefficient (log Pow) is 2.7. Based on a Henry’s Law constant of 0.05 Pa.m3/mol 3,4-DCA is not expected to volatilise from the water column and neither is it expected to undergo hydrolysis. However, it is likely to be susceptible to photolysis with half-lives ranging from 0.4 hours to six days. On release to the aquatic environment 3,4-DCA forms covalent bonds with the organic fraction of sediments and suspended matter, removing it from the water column. Proposed PNECs (predicted no-effect concentrations) derived for 3,4-DCA range from 0.2 to 5.4 μg/L in environmental waters and 0.1 mg/kg dw (0.04 mg/kg ww) in sediments (UKTAG 2008).

If released to soil, 2,3-dichloroaniline is expected to have high mobility based upon an estimated Koc of 120. Based on the Henry’s Law constant, the volatilisation half-life from a model river (1 m deep, flowing 1 m/s, wind velocity of 3 m/s) is estimated as approximately 711 hours. The volatilisation half-life from a model lake (1 m deep, flowing 0.05 m/s, wind velocity of 0.5 m/s) is estimated as approximately 219 days. 2,3‑Dichloroaniline has been detected in European rivers up to 0.4 µg/L (TOXNET).

2,4-Dichloroaniline present in soil biodegrades relatively slowly. However, 2,4‑dichloroaniline does not sorb on to soil particles very well and as a result may leach into the groundwater (EAWAG 2012).

If released to soil, 3,5-dichloroaniline is expected to have moderate mobility based upon a Koc of 309. 3,5-Dichloroaniline may undergo covalent chemical bonding with humic materials, which can result in its chemical alteration to a latent form and tight adsorption. Incubation of 3,5-dichloroaniline in covered beakers containing a sandy loam soil for 14 days yielded the azo compound 3,3’,5,5’-tetrachloroazobenzene. Volatilisation from moist soil surfaces is expected to be an important fate process based upon an estimated Henry’s Law constant of 1.58 x 10-4 atm-cu m/mole. If released into water, 3,5-dichloroaniline is expected to adsorb to suspended solids and sediment in the water column based upon the Koc. Using the Closed Bottle screening test, a 0 percent theoretical BOD (Biological Oxygen Demand) was observed over a 30‑day inoculation period using a sewage inoculum. Volatilisation from water surfaces is expected to be an important fate process based on its estimated Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 30 and 219 days, respectively. When covalently bound in this latent form, leaching in soil systems is not generally expected to occur. An estimated BCF of 94 suggests the potential for bioconcentration in aquatic organisms is moderate. Hydrolysis is not expected to occur due to the lack of hydrolysable functional groups (EAWAG accessed February 2015).

Water solubilities:

* 3,4-dichloroaniline: 580 mg/L
* 3,5-dichloroaniline: 600 mg/L
* 2,3-dichloroaniline: 1,200 mg/L
* 2,4-dichloroaniline: 620 mg/L
* 2,5-dichloroaniline: 56 mg/L
* 2,6-dichloroaniline: 1,600 mg/L.

### Removal methods

Its strong association with humic substances and soil suggests that 3,4-dichloroaniline should be removed in water treatment plants designed for colour and turbidity removal. 3,5-Dichloroaniline is probably similar.

Causserand et al (2005) evaluated the performance of two nanofiltration membranes in removing dichloroaniline at concentrations from 1 to 10 ppb. They reported that the two membranes, made of different materials but having the same nominal cut-off, retained dichloroaniline to very different extents and by different mechanisms.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

3,4-Dichloroaniline and the 2,4- and 2,5-isomers are substances that produce methaemoglobin, the primary toxic effect.

Whereas no carcinogenicity data are available on 2,5-dichloroaniline, 2-chloroaniline and 3-chloroaniline, 4-chloroaniline are carcinogenic in rats and mice. Structural similarity of 4-chloroaniline may give some concern that 3,4-dichloroaniline may have carcinogenic properties too. Related to carcinogenicity, there are no data from long-term studies on 3,4-dichloroaniline available. In vivo genotoxicity data did not give concern on carcinogenic properties of 3,4-dichloroaniline itself. In the absence of further supporting data, it is concluded that the database is not sufficient for classification of 3,4-dichloroaniline as a category 3 carcinogen. For 3,4-dichloroaniline no significant adverse effects on embryonic/foetal development were revealed from a OECD Guideline teratology study in rats. From this study the following values were derived:

* NOAEL (embryo-/fetotoxicity) 25 mg/kg bw/day
* NOAEL (maternal toxicity) 5 mg/kg bw/day.

The total daily intake of 3,4-dichloroaniline for oral exposure via drinking water and fish and from plants has been calculated to amount up to about 0.004–0.010 mg/kg bw/day.

The European Commission (2006) concluded that 3,4-dichloroaniline should cause no concern in relation to reproduction and developmental toxicity, and a risk of carcinogenicity (via a genotoxic mechanism) is not expected.

IUPAC (2003) describes 3,4-DCA as having an intrinsic endocrine potential. 3,4-DCA acts as a competitive antagonist at the androgen receptor in mammals. However, there is also evidence that 3,4-DCA may disturb the endocrine system in fish. Inhibitory effects were observed at 0.2 mg/L on the synthesis and metabolism of androgens in breeding males of sticklebacks.

### Derivation of Maximum Acceptable Value

No MAV.

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# 4,5-dichloro-2-octyl-3(2h)-isothiazolone

CAS No. 64359-81-5. Also called 4,5-dichloro-2-n-octyl-3(2H)-isothiazolone, 4,5‑dichloro-2-n-octyl-4-isothiazolin-3-one, DCOI or DCOIT; a common trade name is Sea-nine 211, or colloquially just sea nine.

The parent chemical, 5-chloro-2-methyl-4-isothiazolin-3-one, is also registered as a pesticide overseas, CAS No. 26172-55-4.

Many of the chemicals in this group have synonyms, eg, the widely used 2-methyl-4-isothiazolin-3-one (CAS No. 2682-20-4) is also called 2-methyl-3(2H)-isothiazolin-3-one, 2-methyl-3-isothiazolin-3-one, 2-methyl-2,3-dihydroisothiazol-3-one, 2-methyl-3-isothiazolone, 2-methylisothiazol-3-one, methyl-3(2H)-isothiazolone, methylisothiazolinone, or even MIT or MI. This compound is also available as the hydrochloride, as listed in the table below. Because of the large number isothiazolinones and their wide range of uses, a datasheet for methylisothiazolinone has been added to the Organic Chemicals section.

The USEPA re‑registration eligibility decision (RED) for the pesticide methylisothiazolinone, includes the active ingredients 5-chloro-2-methyl-3(2H)-isothiazolone (CAS No. 26172-55-4) and 2-methyl-4-isothiazolin-3-one (CAS No. 2682‑20-4).

Several other isothiazolones (sometimes called isothizolinones) exist, many of which have a similar use (copied from [http://chemicalland21.com/lifescience/phar/4,5-dichloro-2-octyl-3(2h)-isothiazolone.htm](http://chemicalland21.com/lifescience/phar/4,5-DICHLORO-2-OCTYL-3(2H)-ISOTHIAZOLONE.htm)) as follows:

|  |  |
| --- | --- |
| **Some other isothiazolones** | **CAS No.** |
| (4-chlorobenzyl)-3(2H)-isothiazolone | 26530-09-6 |
| 1,2-benzisothiazolin-3-one | 2634-33-5 |
| 2-butyl-1,2-benzisothiazolin-3-one | 4299-07-4 |
| 2-methyl-4,5-trimethylene-4-isothiazolin-3-one | 82633-79-2 |
| 2-methyl-3-isothiazolone hydrochloride | 26172-54-3 |
| 2-methyl-4-isothiazolin-3-one | 2682-20-4 |
| 2-octyl-3(2H)-isothiazolone | 26530-20-1 |
| 4,5-dichloro-2-cyclohexyl-4-isothiazolin-3-one | 57063-29-3 |
| 4,5-dichloro-2-octyl-3(2H)-isothiazolone (DCOIT) | 64359-81-5 |
| 4-chloro-2-octyl-3(2H)-isothiazolone | 64359-80-4 |
| 5-chloro-2-(4-chlorophenylmethyl)-3(2H)-isothiazolone | 66159-95-3 |
| 5-chloro-2-methyl-3(2H)-isothiazolone, calcium chloride complex | 57373-19-0 |
| 5-chloro-2-methyl-2H-isothiazol-3-one hydrochloride | 26530-03-0 |
| 2-methyl-4-isothiazolin-3-one calcium chloride | 57373-20-3 |

Plus mixtures of these materials.

### Maximum Acceptable Value

Isothiazolones do not have MAVs in the DWSNZ, and are not mentioned in the WHO *Guidelines for Drinking-water Quality*.

EPA established an environmental exposure limit of 0.00004 mg/L (0.04 µg/L) for 4,5‑dichloro-2-n-octyl-3(2H)-isothiazolon in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

4,5-Dichloro-2-octyl-3(2H)-isothiazolone is an isothiazolinone biocide whose mechanism of action is poorly understood. Isothiazolinones containing sulfur atom, nitrogen, oxygen at 3 position and hydrogen can find application for making broad-spectrum biocides and preservatives such as antiseptic agents, bactericides, slimicides and fungicides. The biggest application is in paint industry especially marine antifouling agent. They are also used in adhesives, cutting oils, water systems (eg, cooling towers), cosmetics, household goods, liquid soaps, wet-wipes and wound protectant for pruning cuts. They are also used as pulp and wood impregnating agents as well as in leather, fur and polymer process.

4,5-Dichloro-2-octyl-3(2H)-isothiazolone, [5-chloro-2-methyl-4-isothiazolin-3-one](http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC35405) and 2-methyl-4-isothiazolin-3-one do not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, they are listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …). See also EPA (2013).

4,5-Dichloro-2-octyl-3(2H)-isothiazolone (DCOIT) is sold in New Zealand as a mixture with carbendazim; [5-chloro-2-methyl-4-isothiazolin-3-one](http://www.pesticideinfo.org/Detail_Chemical.jsp?Rec_Id=PC35405) and 2-methyl-4-isothiazolin-3-one are sold as a mixture with or without didecyl dimethyl ammonium chloride (or bromide, qv) and iodocarb (qv). Some formulations of DCOIT contain copper salts.

2-Methylisothiazol-3(2H)-one (MIT) is a metalworking fluid (MWF) preservative used to control the growth of a variety of micro‑organisms in MWFs in their action of cooling, lubricating and flushing away metal shavings (or swarf). The biocidal product is added directly to the sump of a metalworking operation in closed system. Use in industrial processes and by the general public is not envisaged (ECHA 2014).

1,2-Benzisothiazolin-3-one at 0.041 percent is used as a preservative in tralkoxydim.

### Forms and fate in the environment

DCOI degrades rapidly in aquatic microcosms with a half-life of less than an hour, but has a half-life of one to two weeks in sterile water. Degradation of the isothiazolonone biocides is an effective mechanism of detoxification since the metabolites are four to five orders of magnitude less toxic than the parent. Briefly, the isothiazolinone ring is cleaved between the labile N-S bond yielding N-methyl malonamic acid or N-(n-octyl) malonamic acid. Oxidation continues resulting in the formation of the respective amine and carbon dioxide; taken from ERMANZ HSNO Chemical Classification Information Database.

Of the two chemicals (5-chloro-2-methyl-3(2H)-isothiazolone and 2-methyl-3(2H)-isothiazolone) that make up methylisothiazolinone, only 5-chloro-2-methyl-3(2H)-isothiazolone was susceptible to hydrolysis and only at alkaline pH. 5-Chloro-2-methyl-3(2H)-isothiazolone is very mobile in most soils (USEPA 1998).

The main emission route of 2-methylisothiazol-3(2H)-one through its use in the representative biocidal product is via wastewater to sewage water treatment plants and subsequent release via effluents to surface water and sediment. There are no direct emissions to surface water or sediment, and aquatic or sediment organisms are not directly exposed to the active substance. Direct exposures of the environment via the pathways air, soil or groundwater are considered to be negligible.

The main emission route of C(M)IT/MIT (see Health Considerations, below) through its use in the representative biocidal product is via the wastewater to sewage water treatment plants and subsequent release via effluents and sludge to surface water, soil and groundwater (ECHA 2015).

Water solubility of 4,5-dichloro-2-octyl-3(2H)-isothiazolone is about 6 mg/L.

### Typical concentrations in drinking-water

4,5-Dichloro-2-octyl-3(2H)-isothiazolone is not mobile in soils so is not likely to leach to groundwater.

### Health considerations

DEFRA (2000) considered that the main toxicological concerns related to point of contact exposure. Isothiazolinones are moderately to highly toxic by oral administration.

Kathon 886 (CAS No. 55965-84-9)\* administrated in the drinking water to rats for three months produced slight gastric irritation at a dose of 20 mg/kg/day; the no effects level (NOEL) was 8 mg/kg/day. Dermal application of Kathon 886 at doses up to 0.4 mg/kg/day for three months produced no systemic toxicity in rabbits. The highest allowed concentration of Kathon in cosmetics is 15 ppm according to the cosmetic directive (Danish EPA 2001).

\* The biocide Kathon 886 is a trade name for a commercial mixture (in the ratio 1:3) of 2-methyl-4-isothiazolin-3-one and 5-chloro-2-methyl-4-isothiazolin-3-one. Sometimes called C(M)IT/MIT (ECHA 2015).

2-Methylisothiazol-3(2H)-one is not genotoxic, mutagenic, reproductive or a developmental toxicant (ECHA 2014).

Developmental and chronic feeding/carcinogenicity studies in rats resulted in no significant effects and the USEPA classified methylisothiazolinone as a Group D chemical, not classifiable as to human carcinogenicity. A RfD was not established for methylisothiazolinone because it is currently registered for non-food use applications only, outside the FDA regulated uses in paper and adhesives which may contact food. Also, chemicals such as methylisothiazolinone, used as disinfectants, microbiocides, microbiostats, and sanitiser have not been reviewed by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR). Results from mutagenicity studies were equivocal (USEPA 1998).

### Derivation of Maximum Acceptable Value

No MAV.

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# Dichlorophen

CAS No. 97-23-4. The IUPAC name for dichlorophen is 4,4′-dichloro-2,2′-methylenediphenol. The CAS name is 2,2′-methylenebis[4-chlorophenol]. Also called [4‑chloro-2-(5-chloro-2-hydroxy-benzyl)phenol](http://www.chemindustry.com/chemicals/079349.html). Called dichlorophene or dichlorphen sometimes too.

### Maximum Acceptable Value

Dichlorophen does not have a MAV in the DWSNZ, and is not mentioned in the WHO *Guidelines for Drinking-water Quality*.

### Sources to water

Dichlorophen is a bridged diphenyl fungicide, antihelmintic (for the treatment of tapeworms), algicide and bactericide. It is used against footrot in farm animals. It is used to control moss in turf and driveways. It is used as an ingredient in deodorants, shampoos, soaps and cosmetics.

Dichlorophen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Dichlorophen should not contain more than 20 g/kg of 4-chlorophenol.

HSE (2007) stated:

“In February 2004 the Pesticides Safety Directorate (PSD) was advised that the active substance dichlorophen was not being supported in the EU review programme. PSD consulted with relevant members of the MUN and other specialists and as a result of this essential use applications were sought. In June 2004 the Standing Committee on the Food Chain and Animal Health agreed the following essential use derogations in the UK for dichlorophen:

* liverworts and mosses on ornamentals
* control of fungi and other plant pathogens on glasshouses surfaces and in nurseries on crop standing areas
* moss control on managed amenity turf and hard surfaces.”

### Forms and fate in the environment

The half-life of dichlorophen in soil is about 13 days, and it does not readily leach to groundwater. It is quite toxic to aquatic life with long lasting effects. Water solubility is about 30 mg/L. The octanol-water partition coefficient at pH 7 and 20oC (ie, logP) is 3.23. Henry’s Law constant at 25oC (Pa m3 mol-1) is 1.17 x 10-07 so is considered non-volatile.

### Recommended analytical techniques

#### Some alternative methods

See <http://apvma.gov.au/node/2981>.

### Health considerations

The California Environmental Protection Agency Office of Environmental Health Hazard Assessment considers dichlorophen is known to cause reproductive toxicity: developmental toxicity was evidenced by an increased incidence of microphthalmia, delayed ossification, reductions in body weight and length, and increased resorption frequency (OEHHA 1999).

Dichlorophen appears on some lists of endocrine disruptors (IEH 2005).

### Derivation of Maximum Acceptable Value

No MAV.

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# 1,2-dichloropropane

CAS No. 78-87-5. The IUPAC and CAS name is 1,2-dichloropropane. Also called propylene dichloride, chloromethylchloride and dichloro-1,2-propane. Occasionally called PDC or 1,2-DPC.

### Maximum Acceptable Value (Provisional)

Based on health considerations, the concentration of 1,2-dichloropropane in drinking-water should not exceed 0.05 mg/L.

WHO (2004/2011) states that the guideline value is provisional owing to limitations of the toxicological database.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.005 mg/L.

The odour threshold is 0.01 mg/L; however, 1,2-dichloropropane is not an aesthetic determinand in the DWSNZ.

1,2-Dichloropropane is one of the “priority pollutants” under the US Clean Water Act.

### Sources to water

1,2-Dichloropropane may have entered source waters as a result of its use as a soil and grain fumigant, often in combination with 1,3-dichloropropene (qv). It had also been used as a lead scavenger for antiknock fluids.

It is used for a variety of industrial purposes, including as a chemical intermediate, rubber making and vulcanisation, and in dry-cleaning, metal-degreasing, paint remover and as a solvent for oils and fats.

1,2-Dichloropropane does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (see <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It appears as propylene dichloride. It was registered as a component of Shell DD soil fumigant.

“D-D” was the internationally registered trademark for a mixture of chlorinated hydrocarbons containing not less than 50 percent 1,3-dichloropropene (the cis- and trans-isomers), 20–35 percent 1,2-dichloropropane, and 15–30 percent 3,3‑dichloropropene, 2,3-dichloropropene, and other related chlorinated hydrocarbons. It sometimes also contained 1 percent epichlorohydrin as a stabiliser.

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008; it has not been used in the US since 1989.

Note that 1,3-dichloropropene is still registered (as at 2009) for use as a soil fumigant to control nematodes and fungi; the datasheet is included in this section.

DWI (2014) states: Concentrations of 1,2-dichloropropane in drinking water range from 0.01 to 21 μg/L, in groundwater from 0.01 to 1200 μg/L, in fresh surface water from 0.007 to 300 μg/L, in marine surface water <0.1 μg/L and in sewage effluents from 0 to 210 μg/L.

### Forms and fate in the environment

Most of the 1,2-dichloropropane released into the environment finally ends up in the air or groundwater. Breakdown in both the air and groundwater is slow. 1,2‑Dichloropropane volatilises from surface waters and is degraded in air by photochemically produced hydroxyl radicals with a half-life of 23 days or more. Little or no degradation in soil has been reported. It is mobile in soil and could migrate to groundwater, where its half-life is estimated to be between six months and two years.

1,2-Dichloropropane is resistant to hydrolysis, with an estimated hydrolysis half-life of 25–200 weeks. Most studies indicate that 1,2-dichloropropane is also resistant to biotransformation.

NPIC (1994) quotes for 1,2-dichloropropane a soil half-life of 700 days, water solubility of 2,700 mg/L and a sorption coefficient (soil Koc) of 50. This resulted in a pesticide movement to groundwater rating of very high. DWI (2014) quotes log Kow = 1.99, Koc = 68, Henrys law constant = 0.00282 atm m3/mole at 25°C.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 332 zones, did not find any detectable concentrations of 1,2-dichloropropane (limit of detection = 0.0005 mg/L) (ESR 2001).

Detected in groundwater and drinking-water, usually at concentrations below 0.02 mg/L, although levels as high as 0.44 mg/L have been measured in well water (WHO 2004/2017).

Analyses of groundwater by the US Geological Survey for the period 1986–1999 point to concentrations in the range <0.0002–0.019 mg/L, with the large majority (1,911 out of 1,926 total samples) containing no detectable PDC (limit of detection 0.0002 mg/L); taken from OECD (2007).

104 water utilities in the US reported detecting 1,2-dichloropropane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.0078 mg/L.

### Removal methods

WHO (2004/2011/2017) considers 0.001 mg/L should be achievable using GAC.

DWI (2014) reported studies that found that a powdered activated carbon (PAC) dose of 30 mg/L is required to reduce a concentration of 10 μg/L of 1,2-dichloropropane to 1 μg/L. Ozonation of an unspecified (but in the range 50 to 384 μg/L) concentration 1,2-dichloropropane gave removals of 0 percent, 0 percent and 5 percent for applied ozone doses of 2, 6 and 20 mg/L, respectively. Studies using reverse osmosis, gave reported removals of 10 percent, 61 percent and 90 percent using cellulose acetate, polyamide and thin film composite membranes, respectively. Studies on the effectiveness of a range of nanofiltration membranes at removing a 1.25 mg/L solution of 1,2-dichloropropane during drinking water treatment gave variable results, from 10 to 68 percent removal. Studies examining the effectiveness of air stripping have reported removal efficiencies of 50 to 90 percent.

WRF (2014) reports that 1,2-dichloropropane is characterised with a low Henry’s Law constant (0.088 dimensionless air/water). However, the results showed that low profile air stripping is effective for 1,2-dichloropropane removal. 1,2-Dichloropropane was almost completely removed at the three temperatures and air to water ratio of about 150. Slightly lower removal efficiencies (99.2 percent and 97.2 percent) were observed at lower air to water ratios (72 and 70) and lower temperatures (12°C and 4°C). It is noticeable that the removal efficiency is not very sensitive to the temperature variation at high air to water ratios (>150). The effect of lower temperatures started to become significant at low air to water ratios (around 53) and the removal efficacy varied significantly among the three temperature (98 percent, 95.7 percent and 83.0 percent for 20°C, 12°C and 4°C).

### Recommended analytical techniques

#### Some alternative methods

Purge and Trap Capillary-Column Gas Chromatographic Method (EPA 502.2). And see IARC (2017).

### Health considerations

Animal studies have shown that 1,2-dichloropropane is absorbed readily from the gastrointestinal tract with subsequent excretion in urine (major route of elimination). The highest levels were detected in the liver, kidney and blood.

Clinical symptoms following the ingestion of 1,2-dichloropropane in humans involve effects on the gastrointestinal system (nausea, burning and vomiting), central nervous system (dizziness, disorientation, headache and coma), kidney failure and liver necrosis. Effects on the respiratory system, heart and blood have also been described.

The liver is a target organ in rodents exposed repeatedly to PDC, with a chronic oral NOAEL of 62 to 125 mg/kg bw/d in rats (LOAEL 125 to 250 mg/kg bw/d) and a chronic LOAEL of 125 mg/kg bw/d in mice (no NOAEL established); centrilobular congestion, fatty change, hepatocytomegaly, and necrosis were among the changes described, along with decreased body weights. No functional or histopathological changes were reported in brain or nervous tissue from rats given PDC at doses up to 200 mg/kg bw/d by gavage as part of a 13-week neurotoxicity study (OECD 2007). DWI (2014) quotes a LOAEL of 100 mg/kg/d based on haematological changes.

The USEPA (2009/2011) quotes a health advisory of 0.06 mg/L for 1,2-dichloropropane, representing a 10-4 cancer risk. 1,2-Dichloropropane appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

DWI (2014) quoting WHO data derived an oral tolerable daily intake (TDI) of 14 μg/kg bw/day (rounded).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.1 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.07 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.09 mg/kg/day for chronic-duration oral exposure (>364 days).

There is a relatively limited data base on the toxicity of 1,2-dichloropropane, but it is mutagenic in some short-term assays in vitro. DWI (2014) states: The in vitro genotoxicity studies have given mixed results, although there appears to be genotoxic activity in mammalian cell assays. The majority of in vivo studies located have been negative, indicating that 1,2-dichloropropane is unlikely to be genotoxic in vivo.

When administered orally, 1,2-dichloropropane produced statistically significant increases in the incidence of hepatocellular adenomas and carcinomas in both sexes of mice. There was marginal evidence of carcinogenicity in female rats. The International Agency for Research on Cancer (IARC 1999) classified 1,2-dichloropropane as a Group 3 carcinogen (not classifiable as to its carcinogenicity to humans), as there are no human data and only limited data from animal studies.

IARC (2017) stated that there is sufficient evidence in humans for the carcinogenicity of 1,2-dichloropropane. 1,2-Dichloropropane causes cancer of the biliary tract (confirmed as cholangiocarcinoma). Their overall evaluation was that 1,2-dichloropropane is carcinogenic to humans (Group 1).

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the provisional MAV for 1,2-dichloropropane in drinking-water. The lowest-observable-adverse-effect level used in the derivation is based on a variety of systemic effects in a 13-week oral study in rats of changes in haematological parameters.

The MAV (provisional) for 1,2-dichloropropane in drinking-water was derived as follows:

100 x (5/7) mg/kg body weight/day x 70 kg x 0.1 = 0.05 mg/L

2 L/day x 5,000

where:

* lowest-observable-adverse-effect level = 100 mg/kg body weight per day on the basis of a variety of systemic effects in a 13-week oral study in rats (normalised for five days/week dosing in the derivation)
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 5,000; 100 for inter- and intra-species variation; 10 for the use of a LOAEL instead of a NOAEL, and 5 to reflect limitations of the database, including the limited data on in vivo genotoxicity and use of a subchronic study).

In the 1995 datasheet and the 1995 DWSNZ, the provisional MAV for 1,2‑dichloropropane in drinking-water had been derived as follows:

100 x (5/7) mg/kg body weight/day x 70 kg x 0.1 = 0.02 mg/L

2 L/day x 10,000

where:

* lowest-observable-adverse-effect level = 100 mg/kg body weight per day on the basis of a variety of systemic effects in a 13-week oral study in rats (normalised for five days/week dosing in the derivation)
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 10,000; 100 for inter- and intra-species variation; 10 for the use of a LOAEL instead of a NOAEL, and 10 to reflect the limited evidence of carcinogenicity in animals and a limited toxicity database, particularly for reproductive effects.

The MAV was provisional because of the use of such a large uncertainty factor.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for 1,2-dichloropropane is 0.005 mg/L.

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# 1,3-dichloropropane

CAS No. 142-28-9. The IUPAC and CAS name is 1,3-dichloropropane. Also called chloroallylchloride.

### Maximum Acceptable Value

There are insufficient data to derive a MAV for 1,3-dichloropropane in drinking-water. WHO (2004/2011/2017) states that the available data are considered insufficient to permit recommendation of a guideline value.

### Sources to water

1,3-Dichloropropane may have entered source waters due to its presence as a by‑product in D-D soil fumigant; this product does not appear on ERMA’s list of registered trade name pesticides as at August 2005. 1,3-Dichloropropane is also used in the chemical synthesis industry.

1,3-Dichloropropane has never been registered for use in New Zealand. However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (see <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It appears as 1,3-dichloropropane.

Note that 1,3-dichloropropene is still registered (as at 2009) for use as a soil fumigant to control nematodes and fungi; the datasheet is included in this section.

### Forms and fate in the environment

1,3-Dichloropropane volatilises from both soil and surface waters to the atmosphere where it can be degraded photochemically. It is mobile in soils.

### Typical concentrations in drinking-water

No data are available on the concentration of 1,3-dichloropropane in New Zealand drinking-water supplies, nor are data available on levels in drinking-waters overseas. Measurements in the Ohio River, USA, however, showed detected levels to be below 0.0008 mg/L (0.8 g/L). 9 water utilities in the US reported detecting 1,3‑dichloropropane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.167 mg/L.

### Removal methods

No information is available on technologies capable of removing 1,2-dichloropropane from water. It should behave in a similar manner to 1,2-dichloropropane.

### Recommended analytical techniques

#### Referee method

A referee method cannot be selected for 1,3-dichloropropane because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for 1,3-dichloropropane for the above reason. See WHO 2003 for further information. Also, the following information may be useful:

1,3-Dichloropropane in drinking-water may be analysed by purge and trap gas chromatography with mass spectrometry detection (Method APHA 620 or EPA Method 524.2). The detection limit is 0.0001 mg/L (0.1 g/L).

### Health considerations

1,3-Dichloropropane is of low acute toxicity.

Short-term animal studies have shown that 1,3-dichloropropane induced mild dermatitis on the shaved skin of mice. Peripheral blood changes, including an increased number of white blood cells and reticulocytes (newly formed red blood cells) were observed in dermally exposed animals.

There is some indication that 1,3-dichloropropane may be genotoxic in bacterial systems.

### Derivation of Maximum Acceptable Value

No short-term, long-term, reproductive or developmental toxicity data pertinent to exposure via drinking-water could be located for this compound. The available data are considered to be insufficient to recommend a MAV for 1,3-dichloropropane in drinking-water (WHO 2017).

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# 1,3-dichloropropene

Isomer mixture CAS No. 542-75-6. The IUPAC name for 1,3-dichloropropene is (EZ)‑1,3-dichloropropene. The CAS name is 1,3-dichloro-1-propene. The components are:

* *cis*-isomer: CAS No. 10061-01-5 the cis-isomer is also called the Z-isomer
* *trans*-isomer: CAS No. 10061-02-6 the trans-isomer is also called the E-isomer.

Also called 1,3-D, dichloro-1,3-propene, 3-chloroallyl chloride, alpha-chloroallyl chloride, gamma-chloroallyl chloride, 3-chloropropenyl chloride, 1,3‑dichloropropylene, alpha, gammadichloropropylene, 1,3-dichloro-1-propene, DCP, and the trade name Telone II.

### Maximum Acceptable Value

Based on health considerations, the concentration of 1,3-dichloropropene in drinking-water should not exceed 0.02 mg/L.

1,3-Dichloropropene is one of the “priority pollutants” under the US Clean Water Act.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

1,3-Dichloropropene may enter source waters as a result of its application as a broad spectrum soil fumigant, used for nematode control. It is often used in combination with 1,2-dichloropropane. The commercial product is a mixture of the cis and trans isomers.

It is was once registered in New Zealand as a component of Shell D-D soil fumigant, and still appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 and 2017 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), but as a Dow AgroSciences’ product called Telone.

1,3-Dichloropropene is the primary component of numerous formulations used as a nematicide. The current formulations contain approximately 92 percent by volume of cis- and trans-1,3-dichloropropene and epoxidised soybean oil. Previous formulations of 1,3-dichloropropene used in agriculture also contained 1,2-dichloropropane, epichlorohydrin, chloropicrin, 2,2-dichloropropene, 3,3-dichloropropene, methylisothiocyanate, 1,1,2-trichloroethane and other related chlorinated hydrocarbons and hexenes (USEPA data, quoted in ICPS 1997, and EFSA 2018).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

1,3-Dichloropropene volatilises from both soil and surface waters to the atmosphere where it can be degraded photochemically. Hydrolysis and microbial degradation can also occur. The estimated average half-life in soil and in water is about 10 days.

Water solubility ranges from 1,500 to 2,800 mg/L and the sorption coefficient is 32 mL/g. Due to its high mobility in soils, migration to shallow groundwater is possible.

NPIC (1994) quotes for 1,3-dichloropropene a soil half-life of 10 days, water solubility of 2,250 mg/L and a sorption coefficient (soil Koc) of 32. This resulted in a pesticide movement to groundwater rating of moderate.

If released to soil, cis-1,3-dichloropropene is expected to have very high mobility based upon a range of Kocs from 20 to 42. Volatilisation from moist soil surfaces is expected to be an important fate process based upon a Henry’s Law constant of 2.7 x 10-3 atm-cu m/mole for the cis form and 8.7 x 10-4 atm-cu m/mole for the trans form. Both cis- and trans-1,3-Dichloropropene may volatilise from dry soil surfaces based on their vapour pressures. The half-life of 1,3-dichloropropene (cis and trans isomers) in 13 aerobic soils at 20°C ranged from 6–17 days and the average half-life in anaerobic soils was reported as 8.4 days at 15°C and 2.4 days at 25°C. Hydrolysis in moist soils and water is expected based upon hydrolysis half-lifes of 51, 11 and 3.1 days at 10°C, 20°C and 30°C, respectively. If released into water, neither 1,3-dichloropropene is expected to adsorb to suspended solids and sediment based upon the Kocs. Volatilisation from water surfaces is expected to be an important fate process based on their Henry’s Law constants. Estimated volatilisation half-lifes for a model river and model lake are 1.3 and 102 hours (cis form) and 2 hours and 4.5 days (trans form). An estimated BCF of 8 suggests the potential for bioconcentration in aquatic organisms is low. cis-1,3-Dichloropropene degrades by chemical hydrolysis; at pH values of 5, 7, 9, the half-life of 1,3-dichloropropene was 13.5 days at 20°C (EAWAG accessed February 2015).

(EZ)-3-chloroallyl alcohol exhibits very low persistence in soil. (EZ)-3-chloroacrylic acid exhibits low to moderate persistence. (EZ)-1,3-dichloropropene and metabolites (EZ)‑3-chloroallyl alcohol and (EZ)-3-chloroacrylic acid exhibit high to very high mobility in soil. In sterile conditions and at pH 7 (EZ)-1,3-dichloropropene hydrolysed with a DT50 of 2.7 days (Z-isomer) and 4.8 days (E-isomer) with the major isomer being (EZ)-3-chloroallyl alcohol. This, and (EZ)-3-chloroacrylic acid, were stable to hydrolysis. (EZ)-1,3-dichloropropene is stable to aquatic photolysis, and is not biodegradable (EFSA 2018).

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 332 zones, did not find any detectable concentrations of 1,3-dichloropropene (limit of detection = 0.0005 mg/L) (ESR 2001).

1,3-Dichloropropene is probably formed as a disinfection by-product under certain conditions. It has been found in surface water and groundwater at concentrations of a few micrograms per litre (WHO 2004).

Ten water utilities in the US reported detecting 1,3-dichloropropene in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.13 mg/L. This result is something of an outlier – the next highest was 0.005 mg/L.

Thirteen water utilities in the US reported detecting cis-1,3-dichloropropene in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.0018 mg/L. Five water utilities in the US reported detecting trans-1,3-dichloropropane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.167 mg/L. This latter result is something of an outlier – the next highest was 0.0005 mg/L.

Groundwater exposure assessments show that the limit of 0.1 µg/L would be exceeded for all five scenarios relevant for tomato use by the parent and the two metabolites (EZ)-3-chloroallyl alcohol and (EZ)-3-chloroacrylic acid (EFSA 2018).

### Removal methods

No information is available on methods of removing 1,3-dichloropropene from water. There is no evidence that 1,3-dichloropropene is substantially removed by conventional treatments, such as coagulation/flocculation, sedimentation, and inert media filtration; the fairly high Henry’s Law constant suggests air stripping has potential (USEPA 2008, 2008a). However, isotherm adsorption data indicate that removal by adsorption on to granular activated carbon should be possible.

### Recommended analytical techniques

#### Some alternative methods

WHO (2003) states that USEPA Methods 524.2 and 502.2, which are standard purge-and-trap capillary-column gas chromatographic techniques for volatile organic compounds in water, should be suitable for the analysis of 1,3-dichloropropene. The detection limits for the compound are believed to range from 0.00002 to 0.00005 mg/L.

EFSA (2018) states (E-) and (Z-)-1,3-dichloropropene and metabolites (EZ)-3-chloroallyl alcohol and (EZ)-3-chloroacrylic acid can be monitored by GC-MS with LOQs of 0.05 µg/L (E-) and (Z-)-1,3-dichloropropene, and 3-chloroacrylic acid (each isomer), and a LOQ of 0.1 µg/L for 3-chloroallyl alcohol (each isomer).

### Health considerations

1,3-Dichloropropene is absorbed through the skin and respiratory and gastrointestinal systems. Oral administration of 1,3-dichloropropene in rats resulted in approximately 90 percent absorption of the administered dose. 1,3-Dichloropropene and its metabolites are excreted principally in urine.

The only known human fatality following accidental ingestion of a D-D mixture of unknown dosage occurred within a few hours. Symptoms were abdominal pain, vomiting, muscle twitching and pulmonary oedema. Inhalation of 1,3-dichloropropene at concentrations above 1,500 ppm resulted in gasping, coughing, substernal pain and respiratory distress.

ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.04 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.03 mg/kg/day for chronic-duration oral exposure (>364 days).

The reference dose or RfD (USEPA 2000 and 2006/2009/2011) is 0.03 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 1 mg/L.

NHMRC, NRMMC (2011) states that currently no acceptable daily intake (ADI) or acute reference dose (ARfD) values have been established for 1,3-dichloropropene, since these are required only for pesticides with residues in food. There are no detectable residues in crops when 1,3-dichloropropene is used as a pre-plant soil fumigant.

EFSA (2013) states that the toxicological profile of 1,3-dichloropropene was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.025 mg/kg bw per day and 0.2 mg/kg bw, respectively.

Mutagenicity tests on bacteria have indicated that 1,3-dichloropropene is a direct-acting mutagen.

It has been shown to produce forestomach tumours following long-term oral gavage exposure in rats and mice. Tumours were also found in the bladder and lung in female mice and liver in male rats. Long-term inhalation studies in the rat were negative, whereas inhalation studies in mice showed some benign lung tumours.

The International Agency for Research on Cancer concluded that there was sufficient evidence for the carcinogenicity of 1,3-dichloropropene in experimental animals to classify it in Group 2B (possibly carcinogenic to humans).

In 1987 the USEPA classified Telone in Group B: a probable human carcinogen. Later, USEPA (2000) stated that 1,3-dichloropropene is clearly a rodent carcinogen and is “likely to be carcinogenic to humans.” This characterisation is based on tumours observed in chronic animal bioassays for both inhalation and oral routes of exposure. The USEPA (2009/2011) quotes a health advisory of 0.04 mg/L for 1,3-dichloropropene, representing a 10-4 cancer risk.

1,3-Dichloropropene appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

Based on lung and bladder tumours observed in female mice in a two-year gavage study, and using the linearised multistage model, the concentration of 1,3‑dichloropropene (the sum of cis and trans) associated with an excess lifetime cancer risk of one per 100,000 (10-5) is 0.02 mg/L.

The USEPA has determined that exposure to 1,3-dichloropropene in drinking-water at concentrations of 0.03 mg/L for 1 or 10 days is not expected to cause any noncancerous adverse effects in a child.

An intermediate-duration (15–364 days) oral MRL (minimal risk level) of 0.04 mg/kg/day was derived by dividing the BMDL10 of 3.6 mg/kg/day by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

An MRL of 0.03 mg/kg/day has been derived for chronic-duration (>364 days) oral exposure to 1,3-dichloropropene.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for 1,3-dichloropropene is 0.002 mg/L.

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# Dichlorprop

CAS No.:120-36-5. The IUPAC name for dichlorprop is (RS)-2-(2,4-dichlorophenoxy)propionic acid. The CAS name is 2-(2,4-dichlorophenoxy)propanoic acid. Also called 2,4-DP, 2,4-DP-p or 2,4-dichlorophenoxypropionic acid. Also sold as the dimethylammonium salt and the ethylhexyl ester. Sometimes called dichloroprop (possibly in error).

Dichlorprop‐P‐2‐ethylhexyl (dichlorprop‐P 2‐EHE) is the modified ISO common name for (2RS)‐2‐ethylhexyl (2R)‐2‐(2,4‐dichlorophenoxy)propionate (IUPAC), a variant of dichlorprop‐P.

The (R)-isomer of this substance has the common name [dichlorprop-P](http://www.alanwood.net/pesticides/dichlorprop-p.html) or 2,4‑dichlorprop-P (CAS No. 15165-67-0, ie (R)-2-(2,4-dichlorophenoxy)propionic acid).

### Maximum Acceptable Value

Based on health considerations, the concentration of dichlorprop in drinking-water should not exceed 0.1 mg/L. Dichlorprop is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; excursions above this level even for a relatively short period are of concern as the health-based guideline is based on short- to medium-term effects.

2,4‐Dichlorophenol (2,4‐DCP) is considered a relevant impurity with a maximum content of 5 g/kg. Polychlorinated dibenzo‐p‐dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs) are also considered relevant, expressed as a sum of 2,3,7,8‑tetrachlorodibenzo‐p‐dioxin (TCDD) toxic equivalents (TEQs) at a maximum content of 0.01 mg/kg (EFSA 2018).

### Sources to water

Dichlorprop, like mecoprop and fenoprop, is a chlorophenoxy (or phenoxyproponic acid) selective, systemic, foliar hormone herbicide, which may enter source waters as a result of its use for the post-emergent control of annual and perennial broadleaved weeds; brush control; control of broadleaved aquatic weeds and chemical maintenance of embankments and roadside verges. It is used applied as various esters or salts. Dichloprop is a plant growth regulator (a synthetic hormone in the auxin family).

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The total annual usage of dichlorprop in New Zealand in the late 1980s was 35,000 kg, all of it in the North Island with the greatest usage being in Rangitikei (9,800 kg).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

If released to soil, dichlorprop is expected to have very high to high mobility based upon Koc values of 34–129. The pKa of dichlorprop is 3.1, indicating that it will exist almost entirely in the anion form in the environment; anions generally do not adsorb strongly to particulate matter. Volatilisation from moist soil surfaces is not expected to be an important fate process for the same reason. The half-life for degradation of dichlorprop to 2,4-dichlorophenol in soil is estimated to be 8 to 12 days and the recommended average half-life is 10 days.

Several aquatic aerobic studies have reported degradation of dichlorprop in five months or less. Degradation products of 2,4-DP-p include 2,4-dichlorophenol, 2,4‑dichloroanisole, and carbon dioxide, which are all common degradates to 2,4-D as well. USEPA (2007) states that all residues other than 2,4-D are not of risk concern due to low occurrence under environmental conditions, comparatively low toxicity, or a combination thereof.

In laboratory incubations in dark aerobic natural sediment water systems, dichlorprop‐P exhibited moderate persistence.

The water solubility of the acid is 350 mg/L with lower solubility for the ester (50 mg/L) and much higher solubility for salts (660,000 to 900,000 mg/L).

NPIC (1994) quotes for dichlorprop a soil half-life of 10 days, water solubility of 50 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

The potential for groundwater exposure above the parametric drinking water limit of 0.1 μg/L consequent to the uses assessed, was assessed as low for dichlorprop‐P‐2‐ethylhexyl, dichlorprop isomers and their soil metabolites 2,4‐dichlorophenol and 2,4‑dichloroanisole identified (EFSA 2018).

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, did not find any detectable concentrations of dichlorprop (limit of detection = 0.0001 mg/L) (ESR 2001).

Chlorophenoxy herbicides are not frequently found in drinking- water; when detected, concentrations are usually no greater than a few micrograms per litre (WHO 2004/2017).

### Removal methods

No specific information is available on methods of removing dichlorprop from water, but chlorophenoxy acids have been reported to be oxidised by ozone. Some types of activated carbon are likely to be effective.

### Recommended analytical techniques

#### Some alternative methods

1. High Performance Liquid Chromatography with a Photoiodide Array Ultraviolet Detector (EPA 555).

Also, see WHO (2003) for further information.

### Health considerations

Dichlorprop has appeared as the older racemic 2,4-DP and the enriched isomer 2,4‑DP-p. The older toxicity studies used 2,4-DP, while the newer toxicity studies were conducted with 2,4-DP-p. Available toxicity profiles comparing 2,4-DP-p and the older racemic 2,4-DP showed no significant differences in toxicity between the two isomeric forms (USEPA 2007).

In general, chlorophenoxy herbicides are absorbed rapidly from the gastrointestinal tract and evenly distributed throughout the body. Accumulation in human tissues is not expected and a steady-state level in the human body will be achieved within three to five days of exposure. Elimination occurs primarily in the urine, mostly in the unchanged form. Biological half-lifes of chlorophenoxy herbicides in mammals range from 10 to 33 hours. Metabolic conversions occur only at high doses. The salt and ester forms are hydrolysed rapidly and follow the same pharmacokinetic pathways as the free acid forms. Dichlorprop has been shown to cross the placenta.

Rats fed diets containing high doses of dichlorprop had slight liver hypertrophy. Long-term exposure studies in rats reported symptoms including effects on the liver, kidneys and blood. In dietary studies in rats, slight liver hypertrophy was observed in a three-month study, and effects in a two-year study included hepatocellular swelling, mild anaemia, increased incidence of brown pigment in the kidneys (possibly indicative of slight degeneration of the tubular epithelium) and decreased urinary specific gravity and protein. As a result, USEPA (2007) quotes a chronic dietary RfD of 0.036 mg/kg/d, and a NOAEL of 3.6 mg/kg/d. As at May 2014, their <http://water.epa.gov/drink/standards/hascience.cfm> includes an ARfD of 0.05 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight for dichlorprop (R and S isomers), based on a no-observed-effect level (NOEL) of 3.1 mg/kg bw/day from a 13-week study in dogs. The NOEL was based on changes in clinical chemistry and kidney discolouration. The ADI incorporates a safety factor of 100.

The Acceptable Daily Intake adopted in Australia is 0.03 mg/kg body weight for dichlorprop-p, based on a NOEL of 6 mg/kg bw/day in an 18-month mouse dietary study. The NOEL is based on chronic necropathy. The ADI incorporates a safety factor of 200. The ARfD for 2,4-dichlorprop-P is 0.2 mg/kg bw, based on a NOEL of 20 mg/kg bw/day from a developmental study in rats. The ARfD incorporates a safety factor of 100. In February 2017 APVMA decided that an ARfD was unnecessary for dichlorprop-P due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EFSA (2011/14) quotes an ADI of 0.06 mg/kg bw/day and an ARfD of 0.5 mg/kg bw. The provisional residue definition was established as “the sum of dichlorprop-P, its salts and conjugates, expressed as dichlorprop-P”. Both toxicological reference values were established for dichlorprop-P but they can also apply to dichlorprop which was demonstrated to have the same toxicity as dichlorprop-P. These values were not changed in 2017 (see <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4834/full>) The ARD was still 0.06 mg.kg/d in EFSA (2018), but the ARfD was revised to 0.2 mg/kg based on the NOAEL of 20 mg/kg bw per day for decreased food consumption and body weight/body weight gain observed at 80 mg/kg bw per day in the developmental toxicity study in rats. An uncertainty factor of 100 was applied.

Chlorophenoxy herbicides as a group, including 2,4-D and MCPA, have been classified by the International Agency for Research on Cancer in Group 2B (possibly carcinogenic to humans). However, based on the available data from studies on exposed populations and on animals, it is not possible to assess the carcinogenic potential of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects.

This chemical was removed from the State of California EPA list of chemicals known to cause cancer or reproductive toxicity in January 2002. The USEPA has classified 2,4‑DP‑p for potential carcinogenicity as “not likely to be carcinogenic to humans”.

EFSA (2018) stated that the weight of evidence suggests that dichlorprop‐P induced polyploidy in vitro but it is unlikely to be genotoxic in vivo. Dichlorprop‐P and dichlorprop showed no carcinogenic potential in mice and rats, respectively. No specific human data is available concerning epidemiological evidence for a carcinogenic potential of dichlorprop‐P and/or dichlorprop.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV for dichlorprop in drinking-water. The no-observable-adverse-effect level used in the derivation is for renal toxicity based on a two-year study in rats.

The MAV for dichlorprop in drinking-water was derived as follows:

3.64 mg/kg body weight/day x 70 kg x 0.1 = 0.127 mg/L (rounded to 0.1 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 3.64 mg kg body weight per day for renal toxicity based on a two-year study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter and intra-species variation).

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# Dichlorvos

CAS No. 62-73-7. The IUPAC name for dichlorvos is 2,2-dichlorovinyl dimethyl phosphate. The CAS name is 2,2-dichloroethenyl dimethyl phosphate. Also known as O,O-dimethyl O-(2,2-dichlorovinyl)phosphate or DDVP. Has also been called chlorvinphos.

### Maximum Acceptable Value

No MAV. WHO (2017) does not have a Guideline Value because dichlorvos occurs in drinking-water or drinking-water sources at concentrations well below those of health concern.

WHO (2017) established a health-based value for dichlorvos of 0.02 mg/L, and an acute health-based value of 3 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.005 mg/L; excursions above this level even for a short period are of concern, as the health-based guideline is based on short-term effects.

EPA established an environmental exposure limit of 0.000001 mg/L (0.001 µg/L) for dichlorvos in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Dichlorvos is a broad spectrum organophosphate pesticide which has been used since the early 1960s; it combines both contact and stomach action and has a marked vapour action. It is used in the control of both crawling and flying insects, often in food storage areas, and for parasite control in livestock and pets. Dichlorvos has both agricultural and public health uses. It is also used to control parasites in fish farming.

ln the past, 2 to 4 percent epichlorohydrin was added to stabilise the technical-grade product; other stabilisers may now be used in some products, but improved technology and purity has largely eliminated the need for them (IARC 1991). Dichlorvos should not contain more than 5 g/kg of chloral.

Formulations containing dichlorvos have been registered for use in New Zealand since 1968. Dichlorvos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). There are four products containing dichlorvos that are currently (2008) registered for agricultural use in New Zealand. As at 2011, ERMA is assessing whether this pesticide should continue to be approved for use in New Zealand.

### Forms and fate in the environment

Dichlorvos is a metabolite of trichlorfon (qv), which has a similar hazard profile and is also available in pesticide formulations in New Zealand.

Dichlorvos is not expected to persist in aquatic or soil environments mainly due to its fast breakdown and evaporation. It has a half-life of less than two days in aerobic soil. Dichlorvos is very soluble in water (about 19,000 mg/L or 1.9 percent at 10°C, 16,400 mg/L at 20°C, 15,700 mg/L at 30°C) (JMPR 2012).

Dichlorvos shows little sign of adsorbing to organic matter or sediments. The predominant degradation mechanism is hydrolysis, and dichlorvos is hydrolysed into dichloroethanol, dichloroacetaldehyde, dichloracetic acid, dimethyl phosphate and dimethyl phosphoric acid; these are considered to present fewer health concerns than the parent compound.

NPIC (1994) quotes for dichlorvos a soil half-life of 0.5 days, water solubility of 1 percent and a sorption coefficient (soil Koc) of 30. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

Given the physico-chemical profile of dichlorvos, contamination of groundwater is a possibility, although it is noted that the substance is not persistent. As at October 2017, there are no records of dichlorvos in New Zealand waters.

### Removal methods

At an elevated pH (>9) for a brief time during treatment, combined with the ample opportunities for hydrolysis degradation before the treated water reaches end users, virtually eliminates any exposure possibilities to dichlorvos in treated drinking water.

A dichlorvos concentration of 220 mg/L was reduced to 0 mg/L within 20 minutes by batch treatment with ozone at 1 mg/L, but the dichlorvos molecule was not destroyed completely. In the presence of microporous silica, which caused ozone to decompose to form hydroxyl radicals, destruction was more complete.

This compound belongs to a group of organophosphorus pesticides that have generally been shown to be amenable to treatment by coagulation (10 to 20 percent removal), activated carbon and chlorine.

Some newer advanced oxidation processes are promising.

WHO (2017) states that removal by membranes depends on membrane type and operational conditions. Removal by nanofiltration membranes has variable effectiveness (removal rates from 4 to 60 percent). Reverse osmosis would be expected to be effective (removal rates >85 percent) based on removal studies and predictions.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Dichlorvos is used as an anthelminthic in humans. Dichlorvos is absorbed rapidly by all routes of exposure and degraded rapidly. The metabolic pathways of dichlorvos are similar in mammalian species, including humans. Metabolites are excreted rapidly or incorporated into natural enzymatic pathways.

FAO/WHO (confirmed in 2011) set an Acceptable Daily Intake (ADI) value for dichlorvos of 0.004 mg/kg body weight, based on the NOAEL of 0.04 mg/kg bw per day for the inhibition of erythrocyte AChE activity in a 21-day study in male volunteers. The ADI was previously based on the NOAEL of 0.033 mg/kg bw per day in a 28-day study in male volunteers for the same end-point and before that on the NOAEL of 0.37 mg/kg bw per day in a 90-day study in dogs for the inhibition of brain ChE activity. The meeting established an acute reference dose (ARfD) of 0.1 mg/kg bw, based on the NOAEL of 1 mg/kg bw for erythrocyte AChE inhibition in the acute oral study in male volunteers and using a 10-fold intraspecies safety factor. The NOAEL is supported by observations in two other volunteer studies in which no erythrocyte AChE inhibition occurred 1 day after dosing at 0.5 and 0.1 mg/kg bw, respectively. The ADI of 0.004 mg/kg/d and ARfD of 0.1 mg/kg were reaffirmed in JMPR (2012) and FAO/WHO (2013).

The oral RfD was calculated at 0.0005 mg/kg/d (USEPA 1994). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0005 mg/kg/d, and an ARfD of 0.008 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dichlorvos is 0.08 mg/L.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.004 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.003 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0005 mg/kg/day for chronic-duration oral exposure (>364 days).

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand is 0.001 (0.0005 pre-2004) mg/kg body weight, with a NOEL of 0.014 mg/kg bw from a short-term (28-day) human study. The NOEL is based on plasma cholinesterase inhibition. The ADI incorporates a safety factor of 10. The ARfD is 0.1 mg/kg bw based on a NOEL of 1 mg/kg bw/day from a single oral dose study in human males. The ARfD incorporates a safety factor of 10.

The dichlorvos acute health-based value of 3 mg/L was based on an ARfD of 0.1 mg/kg bw, based on a NOAEL of 1 mg/kg bw for erythrocyte acetylcholinesterase inhibition in an acute oral study in male volunteers, application of a safety factor of 10, and 100 percent allocation to water (WHO 2017).

Several carcinogenicity studies in mice and rats using routes other than gavage were negative, even when doses causing signs of toxicity were used. It should be noted that two squamous cell carcinomas of the oesophagus were observed in treated mice in one study. IARC has classified dichlorvos in Group 2B, possibly carcinogenic to humans. A three-generation reproduction study in rats was negative at doses up to 235 mg/kg in the diet, equivalent to 12 mg/kg of body weight per day.

Dichlorvos is described by the USEPA (as at September 2008) to show “suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential”. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

Based on the JMPR ADI of 0–0.004 mg/kg of body weight (NOAEL of 0.04 mg/kg bw per day) and assuming a 60-kg adult drinking 2 litres of water per day with an allocation of 20 percent of the ADI to drinking-water, a health-based value for dichlorvos in drinking-water of 0.02 mg/L (rounded value) can be derived (WHO 2016/2017). This was based on inhibition of erythrocyte acetylcholinesterase activity in a 21-day study in male volunteers, application of a safety factor of 10, and 20 percent allocation from water.

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# Dicloran

CAS No. 99-30-9. The IUPAC name for dicloran is 2,6-dichloro-4-nitroaniline. The CAS name is 2,6-dichloro-4-nitrobenzenamine. Dicloran is a common spelling, but it often appears as dichloran. Sometimes called DCNA.

### Maximum Acceptable Value

Dicloran does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

#### 1 To source waters

Dicloran is an aromatic nitroaniline fungicide used to control the fungi Botrytis, Monilinia, Rhizopus, Sclerotinia and Sclerotium spp. on fruits and vegetables during the growing stages and/or post-harvest.

Dicloran appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Dicloran is no longer authorised within the EU.

### Forms and fate in the environment

The estimated half-life of the irradiated dicloran in soil based on first-order kinetics was 123 hours, and that of dicloran in the dark control 1932 hours. The half-life estimated from the net photolysis rate constant was 132 hours (FAO 1998). DCNA has low volatility and is expected to be persistent and have low mobility in soil, although mobility will be increased in coarser soils (USEPA 2006). Some sources quote 400–600 days.

4-Amino-3,5-dichlorophenol, 4-amino-2,6-dichloroaniline, 4-amino-3,5-dichloroacetoanilide, 2,6-dichloro-4-nitrophenol, 4-amino-2,6-dichlorophenol, 3,5-dichloro-4-hydroxyacetanilide, 2-chloro-6-hydroxy-4-nitroaniline, 2,6-dichlorophenol\* and 2,6-dichloroaniline\* are the main metabolites (FAO 1998).

\* 2,6-Dichlorophenol is discussed in the 2,4-dichlorophenol datasheet in Volume 3, Part 2.5: Aesthetic determinands. 2,6-Dichloroaniline is discussed in the chloroanilines datasheet in Part 2.2: Organic chemicals.

Water solubility of dicloran is about 6 mg/L.

NPIC (1994) quotes for DCNA a soil half-life of 60 days, water solubility of 7 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

A temporary ADI of 0 to 0.03 mg/kg bw was established by JMPR in 1974 on the basis of the results of a two-year study in dogs and short- and long-term studies in rats. The 1977 Meeting established an ADI of 0 to 0.03 mg/kg bw on the basis of these studies, after examination of further data on oculotoxicity in dogs, metabolism and pharmacokinetics in pigs, and the effects of dicloran on liver microsomal enzymes.

This ADI was revised in 1998 to 0.01 mg/kg bw (IPCS 1998), and an acute reference dose was considered unnecessary. The ADI was established on the basis of the NOAEL of 1.7 mg/kg bw per day for hepatic and haematological effects in the two-year study in dogs and a 200-fold safety factor. A larger than normal safety factor was used because of the inadequacy of the long-term studies in rats for assessing the carcinogenic potential of dicloran and because of the lack of a NOAEL for maternal and developmental toxicity in rats.

In an 18-month study of carcinogenicity in mice at dietary concentrations of 0, 50, 175, or 600 ppm, the NOAEL was 25 mg/kg bw per day on the basis of increased liver weights, centrilobular hepatocyte enlargement, centrilobular haemosiderosis, focal and single-cell liver necrosis, and vacuolation of centrilobular hepatocytes. There was no evidence of carcinogenicity in mice. The JMPR meeting concluded that dicloran is unlikely to be genotoxic. JPMR (2003) stated that the 1998 JMPR changed the ADI from 0–0.03 to 0–0.01 mg/kg body weight and concluded that an acute RfD was unnecessary.

For the chronic dietary assessment of dicloran, USEPA (2006) used a one-year chronic toxicity study in dogs. The USEPA used a NOAEL of 2.5 mg/kg/day based on clinical chemistry (increased alkaline phosphatase in both sexes and increased cholesterol in males), increased liver weights, hepatocyte hypertrophy, vacuolar alterations of the brain and spinal cord, prostate atrophy, degeneration of the seminiferous tubules, and hypospermia in the epididymides at the LOAEL of 25 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.50 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dicloran is 16.5 mg/L.

USEPA (2006) states:

* the target organs for DCNA include the kidney, liver, spleen and hematopoietic system, particularly red blood cells
* no reproductive effects were observed in studies with DCNA
* DCNA appears to elicit neuropathology (vacuolation in the brain)
* DCNA is classified as “Suggestive Evidence of Carcinogenic Potential,” but EPA concluded that no quantification of cancer risk is required.

The Acceptable Daily Intake (ADI) adopted for dicloran in Australia is 0.07 mg/kg body weight, with a NOEL of 7.5 mg/kg bw.

The toxicological profile of dicloran was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.005 mg/kg bw per day and 0.025 mg/kg bw, respectively. As some uncertainties remain regarding the specifications of dicloran used in the toxicological studies, EFSA (2013) does not consider these reference values as adequately supported by data.

### Derivation of Maximum Acceptable Value

No MAV.

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# Dicofol

CAS No. 115-32-2. The IUPAC name for dicofol is 2,2,2-trichloro-1,1-bis(4-chlorophenyl) ethanol, or α,α,α,4,4′-pentachloro-α-methylbenzhydryl alcohol. The CAS name is 4-chloro-α-(4-chlorophenyl)-α-(trichloromethyl)benzenemethanol. Has also been called di-(para-chlorophenyl)trichloromethylcarbinol or 1,1-bis(4-chlorophenyl)-2,2,2-trichloroethanol. A trade name is kelthane.

Dicofol as defined by ISO refers only to p,p’-dicofol while the technical material is normally a mixture of p,p’-dicofol and o,p’-dicofol (ratio in the range of 75-84:16-25).

### Maximum Acceptable Value

WHO (2017) states that it is not considered necessary to derive a formal guideline value for dicofol because it is unlikely to be found in drinking-water.

WHO (2017) introduced a health-based value for dicofol of 0.01 mg/L, and an acute health-based value for dicofol of 6 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.004 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Dicofol has been proposed to be added to the Stockholm Convention list of Persistent Organic Pollutants (POPs); see <http://chm.pops.int/>

### Sources to water

#### 1 To source waters

Dicofol is a persistent, broad spectrum contact, non-systemic, organochlorine acaricide/miticide. It is used in agriculture and horticulture to control spider mites and soft-bodied mites in apples, pears, soft fruit, cucumbers, tomatoes, hops, vines, lettuce and ornamentals.

Dicofol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Dicofol, which is manufactured from DDT, should not contain more than 1 g/kg of o,o′‑DDE, o,m′-DDE, o,p′-DDE, m,p′-DDE, p,p′-DDE, o,p′-chloro-DDT, or p,p′-chloro-DDT.

### Forms and fate in the environment

Dicofol is structurally very similar to DDT. It is cumulative in the environment. Dicofol in soil is expected to bind to organic matter and is not likely to leach to groundwater, although there are reports of dicofol in groundwater. However, residues in soil decrease rapidly. In surface water, dicofol is expected to adsorb to sediment and can hydrolyse to dichlorobenzophenone. Dicofol accumulates in body fat to a plateau level related to absorption. The USEPA persistence, bioaccumulation, toxicity (PBT) profiling model predicts dicofol to be persistent and bioaccumulative. A major metabolite is 2,2‑dichloro-1,1-bis(4-chlorophenyl)ethanol. EFSA (2011) lists some metabolites.

WHO (2007) states that dicofol is practically insoluble in water (about 0.8 mg/L).

NPIC (1994) quotes for dicofol a soil half-life of 45 days, water solubility of 0.8 mg/L and a sorption coefficient (soil Koc) of 5000. This resulted in a pesticide movement to groundwater rating of very low. Log Kow = 4.3.

### Typical concentrations in drinking-water

Levels in drinking-water would be expected to be very low. As at October 2017, there are no records of dicofol in New Zealand waters.

### Removal methods

The relatively low aqueous solubility and high octanol–water partition coefficient suggest that dicofol should be removed by adsorption on to activated carbon and should be removed during coagulation with particulate matter. Some oxidation processes (eg, chlorine and ozone) have been reported to break down some of the dicofol.

### Recommended analytical techniques

#### Referee method

None available.

#### Some alternative methods

See WHO 2007 for further information.

### Health considerations

Exposure of the public through foods such as pears, blackcurrants and strawberries can be higher than expected and may result in a breach of the ADI (WHO 2007).

Dicofol is extensively absorbed from the gastrointestinal tract. At near steady-state conditions, the highest tissue concentrations are found in adipose tissue, followed by the adrenal glands, thyroid and liver. The p,p′-dicofol isomer, the main component of technical dicofol, is more persistent in the body than the o,p′-isomer. Female rats tend to retain dicofol to a greater extent than males. Dicofol and DDT show a similar pattern of distribution and elimination. Dicofol is more polar and therefore less persistent in the body.

Dicofol has moderate acute oral toxicity. It produces signs of toxicity consistent with central nervous system depression. WHO has classified dicofol as slightly hazardous. USEPA (1998) reports results of a subchronic oral toxicity study in rats. Under the conditions of the study, dicofol produced a wide range of effects in both sexes of rats. Reduced body weights and food consumption were seen in rats of both sexes. Most of the other effects were associated with toxicity seen in the liver (increased liver weights, enhanced hepatic Mixed Function Oxidase (MFO) activity, and hepatocellular hypertrophy), adrenals (diffuse adrenal cortical cell vacuolation and decreased corticosterone levels), thyroid (hypertrophy of the thyroid follicular epithelium), and stomach (focal chief-cell hyperplasia in the fundic mucosa). The NOAEL was 0.07 mg/kg and the LOAEL was 0.64 mg/kg, based on an increase in the incidence of hypertrophy of the thyroid follicular epithelium.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.001 mg/kg body weight, with a NOEL of 0.12 mg/kg bw from a one-year dietary study in dogs. This NOEL is based on evidence of toxicity in the pituitary and liver. The ADI incorporates a safety factor of 100.

EFSA (2011) reports an ADI of 0.0022 mg/kg bw/d for dicofol, and an ARfD of 0.15 mg/kg bw.

FAO/WHO (2011) states that after evaluation of new information and re-evaluation of previous data, the meeting confirmed the ADI of 0–0.002 mg/kg bw derived from the NOAEL in the two-year toxicity and carcinogenicity study in rats of 0.22 mg/kg bw per day, based on histopathological changes in the liver and adrenal gland. A safety factor of 100 was applied. The ADI is supported by the NOAEL of 0.2 mg/kg bw per day from the 90-day neurotoxicity study in rats. There is a margin of 20,000 between the maximum ADI and the LOAEL for liver adenomas in the male mouse. An acute reference dose (ARfD) of 0.2 mg/kg bw was established on the basis of the NOAEL of 15 mg/kg bw in the acute neurotoxicity study in rats, based on decreased body weight and decreased feed intake at 75 mg/kg bw. This ARfD was supported by the NOAEL of 15 mg/kg bw in a single dose oral toxicity study in rats, based on decreased feed intake and hypertrophy of adrenal zona fasciculata at 75 mg/kg bw. Although these effects were mild, they were observed in two studies, and therefore 75 mg/kg bw was considered a marginal LOAEL. A safety factor of 100 was applied. The ADI of 0–0.002 mg/kg bw and ARfD of 0.2 mg/kg bw were reaffirmed in JMPR (2012) and FAO/WHO (2013).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes for dicofol a RfD of 0.0004 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dicofol is 0.50 mg/L.

The primary effects of dicofol after short- or long-term exposure of experimental animals were body weight reduction associated with decreased feed intake, and increased liver weight accompanied by changes in liver enzyme activities. Dicofol caused liver tumours in male mice at doses associated with significant enzyme induction and liver hypertrophy. However, on the basis of the absence of genotoxicity in an adequate range of in vitro genotoxicity and in vivo chromosomal aberration tests, the absence of carcinogenic effects in rats and the expectation that the adenomas present in mice will exhibit a threshold, dicofol is unlikely to pose a carcinogenic risk to humans at anticipated dietary exposure levels. There is a margin of 20 000 between the upper bound of the ADI and the LOAEL for liver adenomas in the male mouse (WHO 2017).

There was no evidence of carcinogenicity in a 78-week carcinogenicity study in rats. As at September 2008 the USEPA has classified dicofol in Group C: a possible human carcinogen. IARC (1983) stated that the available data are insufficient to evaluate the carcinogenicity of dicofol to humans (ie, Group 3).

After reviewing the available genotoxicity data, JMPR concluded that dicofol was not genotoxic, and after consideration of the liver tumours in male mice found in the long-term studies together with the genotoxicity data, that dicofol did not present a carcinogenic hazard for humans.

### Derivation of Maximum Acceptable Value

No MAV.

WHO (2017) considered it unnecessary to derive a formal guideline value for dicofol because it is not normally expected to occur in drinking-water. Nevertheless, in the event of a spill or similar event, it would be useful to have guidance on concentrations of dicofol in water that are not associated with adverse health effects, and so a health-based value of 0.01 mg/L is derived as follows:

An ADI of 0.002 mg/kg of body weight was allocated, based upon the NOAEL of 0.22 mg/kg of body weight per day for histopathological changes in the liver and adrenal gland in a two-year toxicity and carcinogenicity study in rats, using a safety factor of 100. The health-based value is based on a 60 kg adult drinking two litres of water, with an allocation of 20 percent of the ADI to drinking-water.

The acute health-based value for dicofol of 6 mg/L was derived from an ARfD of 0.2 mg/kg bw, based on a NOAEL of 15 mg/kg bw for decreased body weight and decreased feed intake in an acute neurotoxicity study in rats, and application of a safety factor of 100, 100 percent allocated to water, for a 60 kg adult drinking two litres per day (WHO 2016/17).

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# Dicyclanil

CAS No. 112636-83-6. The IUPAC name for dicyclanil is 4,6-diamino-2-cyclopropylaminopyrimidine-5-carbonitrile. The CAS name is 4,6-diamino-2-(cyclopropylamino)-5-pyrimidinecarbonitrile. Also called 2,4,6-triamino-5-pyrimidinecarbonitrile.

### Maximum Acceptable Value

Dicyclanil does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Dicyclanil is an insect growth regulator (ectoparasiticide) belonging to the group of pyrimidinamines (or pyrimidines), and is commonly used to control flies on sheep (fly strike). The recommended dose for dycyclanil for sheep is 30–100 mg/kg once per season, administered topically. Dicyclanil interferes with the chitin metabolism of the insect; treated larvae will therefore be unable to moult to the next stage.

Dicyclanil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

DEFRA (2011) found dicyclanil was one of the ten veterinary medicines in the UK, that based on consumption of either raw (environmental) water or conventionally treated water, were close to or exceeded ADI values. They predicted a groundwater concentration of 0.055 mg/L was possible.

### Forms and fate in the environment

The half-life of dicyclanil in sterile water in the dark may exceed a year; light can reduce this to about two months, but in the presence of humic material the half-life is less than a week. Dicyclanil is readily degradable (half-life <20 days) in soil under moist, aerobic conditions, but the principal metabolite formed, CGA 297107, is only slightly degradable (half-life in the range 60–180 days) under the same conditions. Dicyclanil is likely to have medium to high mobility in soil (APVMA 2006).

The most important metabolite is 2,4,6-triamino-pyrimidine-5-carbonitrile and is usually included with the parent compound in residue regulations. Also found are N‑(4,6-diamino-5-cyano-pyrimidin-2-yl)propionamide, 3-(4,6-diamino-5-cyanopyrimidin-2-ylamino)propionic acid (4 percent to 10 percent), and 2‑(4,6‑diamino-5-cyanopyrimidin-2-ylamino)-3-hydroxypropionic acid.

Water solubility of dicyclanil is 350 mg/L at pH 7 and 610 mg/L at pH 5.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

IPCS (2000) reports an ADI of 0.007 mg/kg body weight, on the basis of the NOEL of 0.71 mg/kg bw per day for increased plasma cholesterol concentrations in the one-year study of toxicity in dogs and a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for dicyclanil is 0.007 mg/kg body weight, with a NOEL of 0.7 mg/kg bw from a one year study in dogs with an uncertainty factor of 100 applied; there is no ARfD.

Dicyclanil is not considered to be carcinogenic or mutagenic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Didecyl dimethyl ammonium bromide

CAS No. 2390-68-3. Also called DDAB. The USEPA issued a notice clustering quaternary ammonium compounds as follows (see USEPA 2007 for more details):

* Group I: The alkyl or hydroxyalkyl (straight chain) substituted Quats.\*
* Group II: The non-halogenated benzyl substituted Quats (including hydroxybenzyl, ethylbenzyl, hydroxyethylbenzyl, naphthylmethyl, dodecylbenzyl, and alkyl benzyl).
* Group III: The di- and tri-chlorobenzyl substituted Quats.
* Group IV: Quats with unusual substitutes (charged heterocyclic compounds).

The USEPA also issued a document in 2006: Re‑registration Eligibility Decision for Alkyl Dimethyl Benzyl Ammonium Chloride (ADBAC with CAS No. 68424-85-1) EPA‑739‑R‑06-009. 126 pp. This group comprises 24 compounds. See: <http://www.epa.gov/pesticides/reregistration/status.htm>

EC (2009) and EFSA (2013) reviewed the use of didecyldimethylammonium chloride or DDAC (CAS No. 7173-51-5, sometimes written as didecyl dimethyl ammonium chloride). They stated that an IUPAC and ISO name could not be given because the active substance is a mixture of quaternary alkyl-ammonium salts with typical alkyl chain lengths of C8, C10 and C12.

### Maximum Acceptable Value

Didecyl dimethyl ammonium bromide does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.0013 mg/L (1.3 µg/L) for DDAC in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Didecyl dimethyl ammonium bromide is a quaternary ammonium microbiocide. The bromide form has been shown to be a more effective fungicide than didecyl dimethyl ammonium chloride (DDAC). The compound also acts as a wetting agent. Didecyl dimethyl ammonium bromide is an active ingredient in veterinary pharmaceuticals used as an antiseptic.

The only aliphatic alkyl quaternaries outdoor uses are as an algicide in decorative/ swimming pools, antisapstain wood preservative treatment, once-through cooling tower treatment, and oil field uses. The pond and oil field uses are considered to be contained. The other uses are not expected to significantly contaminate drinking water sources. Therefore, the aliphatic alkyl quaternaries contributions for drinking water exposure are considered to be negligible and are not quantified (USEPA 2007).

Didecyl dimethyl ammonium chloride is occasionally used (with polyhexamethylene biguanide hydrochloride and hydrogen peroxide in lightly loaded swimming pools as an algicide (NZS 5826:2010). Polyhexamethylene biguanide hydrochloride has a datasheet in the Organic Chemicals section.

Didecyl dimethyl ammonium bromide does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (see: <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …). It is sold in New Zealand as a mixture with carbendazim and diiodomethylsulfonyl toluene.

### Forms and fate in the environment

The environmental fate assessment for DDAC is based on the available data submitted to fulfil the reregistration data requirements (USEPA 2007). The available data indicates that DDAC is hydrolytically stable under abiotic and buffered conditions over the  
pH 5–9 range. The calculated half-lifes for DDAC were 368 days at pH 5, 194 days at pH 7 (TRIS), 175 days at pH 7 (HEPES), and 506 days at pH 9. DDAC is stable to photodegradation in pH 7 buffered aqueous solutions; even in the presence of a photosensitiser (acetone), degradation is minimal with a calculated half-life of 227 days. DDAC is photolytically stable in soil with a calculated half-life of 132 days.

Aquatic metabolism studies under aerobic and anaerobic conditions indicate that DDAC is stable to microbial degradation. The calculated aerobic and anaerobic half-lifes of DDAC in flooded river water are 180 days and 261 days, respectively.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The aliphatic alkyl quaternaries are corrosive, highly irritating to the eye and skin, with moderate acute toxicity by oral, dermal, and inhalation routes of exposure. These chemicals are classified as not likely to be a human carcinogen based on a negative carcinogenicity study in rats and mice feeding studies using doses above the limit. There is no evidence of these chemicals being associated with increased susceptibility to developmental toxicity or reproductive toxicity based on two developmental toxicity studies and a two-generation reproductive study. Lastly, they are negative for mutagenicity and neurotoxicity.

The acute RfD for DDAC = 0.1 mg/kg/day (for females age 13–50). The chronic RfD = 0.1 mg/kg/day (USEPA 2007). The short- and intermediate-term incidental oral NOAEL is 10 mg/kg/day from the dog chronic toxicity study and rat prenatal developmental toxicity studies that noted increased incidence of skeletal variations, increased incidence of clinical signs in males and females and decreased total cholesterol levels in females. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.1 mg/kg/d, and an ARfD of 0.1 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for DDAC is 3.30 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.44 mg/kg/d, but no ARfD for ADBAC.

The Acceptable Daily Intake (ADI) adopted in Australia for didecyl dimethyl ammonium chloride is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

EC (2009) reviewed the use of didecyldimethylammonium chloride and stated that and ADI and ARfD were not applicable because residues are not found in the food chain.

EFSA (2013) proposed an ADI of 0.1 mg/kg bw per day and an ARfD of 0.61 mg/kg bw; these should be considered as indicative only, as long as the concerns on the specifications of the active substance have not been solved.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Difenoconazole

CAS No. 119446-68-3. Sometimes misspelt(?) difenconazole. The IUPAC name for difenoconazole is 3-chloro-4-[(2RS,4RS;2RS,4SR)-4-methyl-2-(1H-1,2,4-triazol-1-ylmethyl)-1,3-dioxolan-2-yl]phenyl 4-chlorophenyl ether. The CAS name is 1-[2-[2-chloro-4-(4-chlorophenoxy)phenyl]-4-methyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole.

The ranges for the cis and trans isomers are the subject of a data gap. Information on the biological activity of the isomers is also the subject of a data gap. Toluene was considered as a relevant impurity, its maximum content in the technical material is 5 g/kg (EFSA 2011).

### Maximum Acceptable Value

Difenoconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Difenoconazole is a systemic conazole fungicide, often appearing with other fungicides, used for seed treatment and fungal control in many fruits, vegetables, cereals and other field crops. Conazoles act similarly in plants (fungi) by inhibiting ergosterol biosynthesis.

Difenoconazole is one of the five most commonly found agricultural chemical residues found in food in New Zealand (NZFSA 2007). Difenoconazole residues were also found during the December 2009 Food Residue Surveillance Programme. Difenoconazole exceeded the maximum residue limits in olive oil in 2011/2012.

Difenoconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Difenoconazole is a triazole-derived pesticide. Difenoconazole shares common metabolites with other triazole-derivative chemicals, including free triazole (1,2,4‑triazole) and triazole-conjugated plant metabolites (such as triazole alanine and triazole acetic acid). These common metabolites have been the subject of separate risk assessments (USEPA 2005). See EFSA (2012) for a list of metabolites.

Difenoconazole residues are reasonably persistent in soils and are expected to be present in the soil at harvest time for treated root and tuber crops. Difenoconazole slowly degrades in the soil with a maximum DT90 value observed in field studies of 879 days (EFSA 2011 and 2014). Difenoconazole residues are also expected to persist in the soil until the sowing of rotational crops. The confined rotational crops studies demonstrate that difenoconazole itself does not appear as a residue in the rotational crop. The water soluble and mobile metabolites triazolylalanine, triazolylacetic acid and triazolyl-lactic acid have been identified in the rotational crops.

Water solubility is about 3–5 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2011).

### Health considerations

A variable pattern of toxicological responses is found in conazoles. Some are hepatotoxic and hepatocarcinogenic in mice. Some induce thyroid tumours in rats. Some induce developmental, reproductive, and neurological effects in rodents. Furthermore, the conazoles produce a diverse range of biochemical events including altered cholesterol levels, stress responses, and altered DNA methylation.

Difenoconazole was included in the list of analytes examined in foods in the 20th Australian Total Diet Survey (FSANZ 2003). The dietary exposure for difenoconazole was estimated to be zero, because its concentration in the surveyed foods was less than the limit of detection (0.01 mg/kg).

A cancer dietary exposure assessment was not conducted by the USEPA for difenoconazole because the cancer NOAEL is higher than the chronic NOAEL; therefore, the chronic dietary risk estimate is more protective.

Difenoconazole was evaluated by the JMPR at the first time in 2007 when an ADI of  
0–0.01 mg/kg bw and ARfD of 0.3 mg/kg bw was established (FAO/WHO 2007). These values were reaffirmed in JMPR (2013 and 2017).

The USEPA established a chronic RfD of 0.1 mg/kg body weight in 1997. The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.01 mg/kg/d, and an ARfD of 0.25 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for difenoconazole is 2.5 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

EC (2008) established an ADI of 0.01 mg/kg/d and an ARfD of 0.2 mg/kg/d.

Difenoconazole appears on the EU list of endocrine disruptors. As at September 2008 the USEPA has classified difenoconazole in Group C: a possible human carcinogen.

EFSA (2012, confirmed 2014) quotes an ADI of 0.01 mg/kg bw per day and an ARfD of 0.16 mg/kg bw. EFSA defined toxicological reference values also for the triazole derivative metabolites (TDMs). TDMs are common metabolites of active substances belonging to the chemical class of triazoles. See datasheet for triazole metabolites for latest ADI and ARfD.

### Derivation of Maximum Acceptable Value

No MAV.

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# Difethialone

CAS No. 104653-34-1. The IUPAC name for difethialone is 3-[(1RS,3RS;1RS,3SR)-3-(4′-bromobiphenyl-4-yl)-1,2,3,4-tetrahydro-1-naphthyl]-4-hydroxy-1-benzothiin-2-one where the ratios of the racemates (1RS,3RS) to (1RS,3SR) lie within the ranges 0–15 to 85–100 respectively. The CAS name is 3-[3-(4′-bromo[1,1′-biphenyl]-4-yl)-1,2,3,4-tetrahydro-1-naphthalenyl]-4-hydroxy-2H-1-benzothiopyran-2-one. Has also been called superwarfarin and difethiarol.

### Maximum Acceptable Value

Difethialone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Difethialone is a second generation single-dose [anticoagulant](https://en.wikipedia.org/wiki/Anticoagulant) coumarin [rodenticide](https://en.wikipedia.org/wiki/Rodenticide), ie, with an anti-vitamin K mode of action. Difethialone is present as two diastereoisomers, with similar kinetics. Both diastereomers are active.

Difethialone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2015 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

In May 2008 the United States Environmental Protection Agency banned the use of difethialone in consumer-use rodenticide products and also for exterior use by commercial applicators.

### Forms and fate in the environment

If difethialone is released to soil, it is expected to have no mobility based upon an estimated Koc of 9.7 x 106. Volatilisation from moist soil surfaces may occur based on a Henry’s Law constant of 1.0 x 10-6 atm-cu m/mole; however, adsorption to soil is expected to attenuate volatilisation. Volatilisation from dry soil is not expected based on difethialone’s vapour pressure. If released into [water](http://pubchem.ncbi.nlm.nih.gov/compound/water), difethialone is expected to adsorb to suspended solids and sediment based on the estimated Koc. Volatilisation from [water](http://pubchem.ncbi.nlm.nih.gov/compound/water) surfaces may occur based on its estimated Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 85 and 630 days, respectively. However, volatilisation from [water](http://pubchem.ncbi.nlm.nih.gov/compound/water) surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the [water](http://pubchem.ncbi.nlm.nih.gov/compound/water) column. Difethialone may be susceptible to hydrolysis under environmental conditions, since it has a hydrolysable functional group. NIH (accessed 2015).

Difethialone is found to be neither aerobically (<6 percent after 28 days) nor anaerobically (<5 percent after 28 days) biodegradable. The active substance is slowly degraded in soil under aerobic conditions with half-lifes between 417 and 976 days at 12°C (mean value 635 days) (EU 2007; ECHA 2014).

Difethialone is practically insoluble in water, although solubility increases with pH: 0.03 mg/L at pH 5.2, 2.5 mg/L at pH 7.3, 84 mg/L at pH 9.3; all at 20°C (DoC 2005). Log Kow = 5.17 (which is high indicating it is highly lipophilic). Log Koc = 9.7 x 106; this value suggests that difethialone is expected to be immobile in soil. The hydrolysis half life at pH 7 is 175 days. NSW Government (2013) reports that difethialone is highly sensitive to photolysis in aqueous solutions.

### Typical concentrations in drinking-water

Difethialone is unlikely to leach to groundwater.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of difethialone.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In acute oral toxicity studies, difethialone was very toxic to rats and mice with the lowest LD50 to the male rat of 0.55 mg/kg bw and to the mouse 1.29 mg/kg bw. Difethialone is less toxic to dogs (11.8 mg/kg bw), cats (≥16 mg/kg bw, study of low reliability), with pigs showing a greater sensitivity (LD50 of 2.0 to 3.0 mg/kg bw) (EU 2007; ECHA 2014).

The repeat dose NOAEL established in 90-day dose oral studies were 2 μg/kg bw/day in the rat study and 10 μg/kg bw/day in the dog study. Difethialone was not mutagenic in a standard range of in vitro and in vivo test (EU 2007).

Death of all exposed animals due to anticoagulation effect of difethialone was observed in the 90-day rat study at levels greater than or equal to 0.016 mg/kg bw/day, with a LOAEL of 0.004 mg/kg bw/day. Deaths were attributable to haemorrhages seen at necropsy (ECHA 2014).

The Acceptable Daily Intake (ADI) adopted in Australia for difethialone is 0.0000006 mg/kg body weight, with a NOEL of 0.00125 mg/kg bw. The ARfD is 0.0005 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# Diflubenzuron

CAS No. 35367-38-5. The IUPAC name for diflubenzuron is 1-(4-chlorophenyl)-3-(2,6-difluorobenzoyl)urea. The CAS name is N-[[(4-chlorophenyl)amino]carbonyl]-2,6-difluorobenzamide.

### Maximum Acceptable Value

The WHO Guidelines (3rd addendum 2008) and 2011/2017 state that a guideline value is not considered appropriate for pesticides used for vector control in drinking-water.

The recommended dosage of diflubenzuron in potable water in containers should not exceed 0.25 mg/L (WHO 2011).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L; minor excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for diflubenzuron in fresh water (set by an approval under Part 5 of the HSNO Act) of 0.00037 mg/L (0.37 µg/L).

### Sources to water

Diflubenzuron is a halogenated benzoylphenylurea, an effective stomach and contact insecticide acting by inhibition of chitin synthesis and so interfering with the formation of the cuticle. It has no systemic activity in plants, and does not penetrate plant tissue, hence plant sucking insects are in general unaffected, forming the basis of its selectivity. It is used in public health applications against mosquito and noxious fly larvae, applied directly to plants or water. Diflubenzuron is approved for use as a veterinary drug in Norway and Chile in the treatment of sea lice (Lepeophtheirus salmonis and Caligus rogercresseyi) infestations in Atlantic salmon. Formulations for use as a vector control agent in drinking-water sources are specified by WHO.

Diflubenzuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Approved for use as sheep dip in New Zealand.

EC (2010) states that the manufacturing impurity 4-chloroaniline (PCA), is considered to be of toxicological concern and a maximum level of 0.03 g/kg is established.

### Forms and fate in the environment

Diflubenzuron is rapidly adsorbed to soil and particles and is immobile in soil. It will also adsorb rapidly to sediments and the sides of vessels and pipes, but it may also partition into the surface film because of its low water solubility (about 0.1 mg/L) and high Kow. In soils, over 90 percent is degraded by hydrolysis to 2,6-difluorobenzoic acid, 4-chlorophenylurea (CPU) and p-chloroaniline (4-chloroaniline). It is not volatile. The major route of dissipation appears to be biotic processes (half-life of approximately two days for aerobic soil metabolism). EFSA (2015) also refers to the metabolites 2,6‑difluorobenzamide (DFBAM) and 4-chloroacetanilide (PCAA).

Water solubility is about 0.1–0.3 mg/L for pH 4 to 10. In alkaline waters it is hydrolysed rapidly. The parent compound and 4-chlorophenylurea may persist on sediment for more than 30 days.

NPIC (1994) quotes for diflubenzuron a soil half-life of 10 days, water solubility of 0.08 mg/L and a sorption coefficient (soil Koc) of 10,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

Although exposure of the public through either food or drinking-water is negligible, there is a potential for direct exposure when it is applied directly to drinking-water storage containers.

### Removal methods

The low aqueous solubility (0.1 mg/L) and relatively high log Kow of 3.7 suggest that it may be amenable to adsorption by activated carbon. Diflubenzuron is fairly unstable in water; the half-life was reported to be approximately half-day for solutions exposed to natural sunlight in the laboratory.

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of diflubenzuron in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

1. WHO (2008) summarises a range of analytical techniques.

### Health considerations

Diflubenzuron is considered to be of very low acute toxicity, with oral LD50 in mice and rats of >4,500 mg/kg body weight.

It is reported that public exposure to diflubenzuron through either food or drinking-water is negligible. However, there is a potential for direct exposure through drinking-water when diflubenzuron is directly applied to drinking-water storage containers. The maximum dosage in drinking-water of 0.25 mg/l would be equivalent to approximately 40 percent of the upper limit of the ADI allocated to drinking-water for a 60 kg adult drinking two litres of water per day. For a 10 kg child drinking one litre of water, the exposure would be 0.25 mg, compared with an exposure of 0.2 mg at the upper limit of the ADI. For a 5 kg bottle-fed infant drinking 0.75 litre per day, the exposure would be 0.19 mg, compared with an exposure of 0.1 mg at the upper limit of the ADI. Diflubenzuron is unlikely to remain in solution at the maximum recommended applied dose, and the actual levels of exposure are likely to be much lower than those calculated. Consideration should be given to using alternative sources of water for bottlefed infants for a period after an application of diflubenzuron, where this is practical. However, exceeding the ADI will not necessarily result in adverse effects (WHO 2017).

The WHO panel of the 2001 JMPR 2001 considered that an acute RfD is unnecessary and therefore the 2002 JMPR concluded that the short-term intake of diflubenzuron residues is unlikely to present a public health concern. The 2001 and 2011 JMPR reconfirmed the previously established ADI of 0–0.02 mg/kg bw and that an acute RfD is unnecessary.

Young animals do not appear to be significantly more sensitive than adults so the assessment is based on a 60 kg adult. Where diflubenzuron is used for vector control in potable water this will involve less than life-time exposure. Under these circumstances the maximum dosage in drinking water of 0.25 mg/L would be equivalent to approximately 40 percent of the ADI allocated to drinking water. Exposure from food is considered to be low. However, in setting local guidelines or standards, health authorities should take into consideration the potential for higher rates of water consumption in the area or region under consideration.

USEPA (2002) quotes a chronic RfD of 0.02 mg/kg/d based on methaemoglobinemia and sulfhaemoglobinemia in a chronic dog study. An acute RfD was not applicable due to there being no appropriate endpoint. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.02 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for diflubenzuron is 0.14 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw from long-term dietary studies in rats and dogs. The NOEL is based on haematotoxicity and liver damage. The ADI incorporates a safety factor of 100.

EC (2010) established an ADI of 0.1 mg/kg/d; an ARfD was considered to be unnecessary. These values were confirmed in EFSA (2012).

Diflubenzuron is absorbed rapidly to a moderate extent (approximately 30 percent) from the gastrointestinal tract. Absorbed diflubenzuron is metabolised extensively with >90 percent excreted within 48 hours, mostly in the urine, although some biliary excretion and enterohepatic circulation occurs.

Diflubenzuron has been tested adequately for both genotoxicity and carcinogenicity, and there was no evidence that it is either genotoxic or carcinogenic. It was not fetotoxic or teratogenic, and did not show significant signs of reproductive toxicity. As at September 2008 the USEPA has classified diflubenzuron in Group E: evidence of non-carcinogenicity for humans. However, p-chloroaniline (PCA), a metabolite of diflubenzuron, is a probable (Group B2) human carcinogen (USEPA 1997). EFSA (2015) states that the lowest appropriate points of departure for PCA from animal carcinogenicity studies are 0.16 and 0.56 mg/kg body weight (bw) respectively for an extra 5 percent (benchmark dose lower limit BMDL5) and 10 percent (BMDL10) risk compared to the background (rat adrenal gland pheochromocytomas endpoint, log‑probit model). An acceptable daily intake (ADI) and acute reference dose (ARfD) cannot be set for an in vivo genotoxic carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Diflufenican

CAS No. 83164-33-4. The IUPAC name for diflufenican is 2′,4′-difluoro-2-(α,α,α-trifluoro-m-tolyloxy)nicotinanilide. The CAS name is N-(2,4-difluorophenyl)-2-[3-(trifluoromethyl)phenoxy]-3-pyridinecarboxamide. Sometimes called diflufenicanil.

### Maximum Acceptable Value

Diflufenican does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

#### 1 To source waters

Diflufenican is an anilide (or pyridine or carboxamide) residual and foliar herbicide used pre- and post-emergence mainly on cereals to control broad leaf weeds. It is often used mixed with other pesticides, eg, bromoxynil and isoproturon. Diflufenican appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). It is not registered for use in the US.

### Forms and fate in the environment

Diflufenican is highly persistent in soil with dissipation half-life values of 311 to 733 days, as well as in the water body with little hydrolysis over a range of pH levels at 22°C. This could lead to prolonged contamination of surface water due to run-off of soil containing residues. The major metabolite is [2-(3-trifluoromethylphenoxy)nicotinamide](http://sitem.herts.ac.uk/aeru/iupac/Reports/769.htm). In anaerobic conditions, 2,4-difluoroaniline may form.

According to the soil degradation studies evaluated in the framework of the peer review, DT90 values of diflufenican and its relevant soil metabolite AE 0542291 are all expected to range between 744–2063 days and 45–195 days respectively (EFSA 2013).

Diflufenican is unlikely to contaminate groundwater. Water solubility about 0.5 mg/L.

### Removal methods

None reported.

### Health considerations

EC (2008) derived an ADI of 0.2 mg/kg body weight based on the critical minimum effect level of 500 ppm (24 mg/kg bw/day), derived from the 24-month chronic dietary study in the rat or the multigeneration study in the rat and allows for a 100-fold safety factor. The observed effects included minimal reductions in body weight gain and a slight reduction in thymus weights at the 500 ppm dose level. An ARfD was said to be not required. Reaffirmed in EFSA (2013).

The Acceptable Daily Intake (ADI) adopted in Australia for diflufenican is 0.2 mg/kg body weight, with a NOEL of 16.3 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Diiodomethylsulfonyl toluene

CAS No. 20018-09-1. Synonyms include diiodomethyl p-tolyl sulfone, 4-tolyl diiodomethyl sulfone, 4-(diiodomethylsulfonyl)toluene, 2-(diiodomethylsulfonyl)toluene, and 1-((diiodomethyl)sulfonyl)-4-methyl benzene, and sometimes with diiodo spelt di-iodo. A trade name is amical-48.

### Maximum Acceptable Value

Diiodomethylsulfonyl toluene does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Diiodomethylsulfonyl toluene is an algicide, bactericide, and fungicide. Diiodomethyl p-tolyl sulfone products are used for: dry film mildewicide/algicide in paints, air duct coatings, and fire-retardant coatings; pigment dispersions, inks, emulsions, and extender slurries as fungal preservatives; adhesives, caulks, and sealants for dry film mildew control and as a fungal preservative; for wood preservation; rubber and plastic surface fungal protection; textile dry-film fungal protection; leather in-process fungal protection; paper production to protect pulp and slurries; paper/paperboard for dry-film fungal protection; wetlap storage as a fungal preservative; and nitrocellulose fungal preservative (USEPA 2008). When used as an antifungal preservative involving food wraps and containers, levels are not to exceed 0.3 percent by weight of the sealants and caulking materials (US FDA regulation for “indirect food additives”).

Diiodomethylsulfonyl toluene does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …). Sold in New Zealand mixed with carbendazim as an antisapstain.

### Forms and fate in the environment

Diiodomethyl p-tolyl sulfone is stable to hydrolysis at pH 5, but it degrades with half-lifes of 2 to four days at pH 7 and 9. Monoiodomethyl-p-tolylsulfone (loss of one iodo group) was the major degradate formed. Methyl-p-tolylsulfone (loss of both iodo groups) and p-toluene sulfonic acid (parent minus methyl group) reached minor concentrations. Soil photolysis half-lifes of 13 days (linear) and 5.3 days (non-linear) were observed for the parent compound. Diiodomethyl p-tolyl sulfone was found in equal portions in water and sediment.

Water solubility is about 10 mg/L. Dow quotes 0.1 mg/L.

### Health considerations

The chronic dietary risks from the combined use of diiodomethyl p-tolyl sulfone as an indirect food additive in the preservation of adhesives, can side-seam cements, and repeat-use rubber sealants were calculated using the chronic RfD of 0.002 mg/kg/day (USEPA 2008). The Acceptable Daily Intake (ADI) developed by the US FDA for diiodomethylsulfonyl toluene is 0.002 mg/kg body weight. The chronic RfD was established by using an oral NOAEL of 2 mg/kg/day, which is based on a 90-day oral dog study that observed decreased activity, dehydration, mucoid ocular discharge, weakened appearance, abnormal faeces, and thyroid degeneration. Although female dogs in the 90-day dog study had decreased mean body weight-gain from days 0 to 91 of at least 20 percent in comparison to the control value, the differences are within an acceptable range as is shown in historical control data. The NOAEL for the short-term incidental oral endpoint is 4 mg/kg/day. The NOAEL is based on a 30-day oral rabbit developmental toxicity study, which observed clinical signs of toxicity, reduced body weight gain, and reduced food consumption of maternal animals at a dose of 15 mg/kg/day. For the short-term incidental oral exposure, the target margin of exposure for diiodomethyl p-tolyl sulfone is 100 (10x inter-species extrapolation; 10x intra-species variation).

Based on the use patterns, the potential for diiodomethyl p-tolyl sulfone to impact drinking water sources is negligible and, therefore, a quantitative drinking water assessment was not conducted (USEPA 2008). Diiodomethyl p-tolyl sulfone has not been formally classified for carcinogenicity. The mutagenicity studies for diiodomethyl p-tolyl sulfone are negative and, therefore, diiodomethyl p-tolyl sulfone is not mutagenic.

### Derivation of Maximum Acceptable Value

No MAV.

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# Dimethenamid

CAS No. 87674-68-8. The IUPAC name for dimethenamid is (RS)-2-chloro-N-(2,4-dimethyl-3-thienyl)-N-(2-methoxy-1-methylethyl)acetamide. The CAS name is 2‑chloro-N-(2,4-dimethyl-3-thienyl)-N-(2-methoxy-1-methylethyl)acetamide.

The (S)-isomer of this substance has the ISO common name [dimethenamid-P](http://www.alanwood.net/pesticides/dimethenamid-p.html) (CAS No. 163515-14-8); the (R)-isomer is not biologically active. The IUPAC name for dimethenamid-P is S-2-chloro-N-(2,4-dimethyl-3-thienyl)-N-(2-methoxy-1-methylethyl)acetamide. The CAS name is 2-chloro-N-(2,4-dimethyl-3-thienyl)-N-[(1S)-2-methoxy-1-methylethyl]-acetamide.

Also called dimethamid.

### Maximum Acceptable Value

Dimethenamid does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

#### 1 To source waters

Dimethenamid is a new amide (chloroacetamide) herbicide used to control unwanted grasses and some important broad leaf weeds, often used in maize and potatoes. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Dimethenamid-P is stable in aqueous buffered solutions at pH 5, 7 and 9 (25°C in the absence of light) for at least 31 days. The leaching properties of dimethamid can result in contamination of groundwaters. Water solubility is about 1,450 mg/L with no dissociation so is not pH dependent.

The JMPR meeting received information on the comparative behaviour and fate of dimethenamid-P and dimethenamid in aerobic soil. No significant differences were observed in the degradation rates. EFSA (2013) states DT90 values of dimethenamid range between 11 and 115 days; nevertheless, DT90 values of two relevant soil metabolites (oxalamide (M23) and sulfonate (M27)) are expected up to 527 and 454 days respectively.

EFSA (2018) stated that dimethenamid‐P exhibited high to medium mobility in soil and metabolites M656H023, M656PH031 and M656PH027 exhibited very high mobility. Dimethenamid-P is a semi-volatile substance. The potential for groundwater exposure was concluded to be low. One monitoring study of groundwater in maize growing regions at 20 groundwater wells in Germany for the dimethenamid‐P metabolites found M656PH027 (maximum 1.680 μg/L, in five wells), the second most frequently observed was M656PH023 (maximum 0.379 μg/L, detected in three wells). etabolite M656PH047 was detected in four wells at concentrations up to 0.149 μg/L.

See JMPR (2004) and EFSA (2018) for a discussion on metabolites.

### Removal methods

None reported.

### Recommended analytical techniques

#### Some alternative methods

See JMPR (2004) and EFSA (2018).

### Health considerations

As at September 2008 the USEPA has classified dimethenamid in Class C: a possible human carcinogen. The chronic reference dose (cRfD) of 0.05 mg/kg/day used for risk assessment is based on non-cancer precursor effects in the liver; therefore, the cRfD is considered protective of both cancer and non-cancer effects. A separate cancer exposure assessment was not performed (USEPA 2007). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.75 mg/kg/d for dimethenamid and dimethenamid-P. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dimethenamid and dimethenamid-P is 24.8 mg/L.

Dimethenamid is at most a weak carcinogen. An intermediate dose showed marginally significant results (p = 0.056) with liver adenomas one species (rat) and one sex (males). The incidence of liver tumours was just slightly increased from the level in the historical control data. Higher doses did not demonstrate the occurrence of liver adenomas significantly different from the controls. No dose-related tumours were seen in the mouse carcinogenicity study, and a battery of mutagenicity studies with dimethenamid-P (90:10 S:R isomers) were negative or equivocal for genetic mutations including unscheduled DNA synthesis (USEPA 2004).

EC (2003) derived an ADI of 0.02 mg/kg body weight for dimethenamid-P, based on a one-year dog study, incorporating a safety factor of 100; the ARfD was 0.25 mg/kg/d. Reaffirmed by EFSA (2013). EFSA (2018) stated that applying the standard uncertainty factor (UF) of 100, the appropriate ADI is 0.04 mg/kg bw per day, and the ARfD is now 0.08 mg/kg. The toxicological dossier of dimethenamid‐P is based on studies performed on both dimethenamid as racemic mixture (50:50 R/S‐isomers) and on the S‐isomer alone that has been shown to retain the herbicidal activity. Comparison of acute, short‐term toxicity, genotoxicity and developmental toxicity performed on both substances has determined that they present a similar toxicological profile at equivalent dose levels and that all available studies for the racemic mixture could be considered in the hazard identification and characterisation of dimethenamid‐P.

The Acceptable Daily Intake (ADI) adopted in Australia for dimethenamid-P is 0.03 mg/kg body weight, with a LOEL of 5 mg/kg bw, and the ARfD is 0.25 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

The JPMR Meeting (2004) concluded that the toxicology of the S-enantiomer (dimethenamid-P) is not significantly different from that of the racemic mixture. An ADI of 0–0.07 mg/kg bw was established for dimethenamid-P and racemic dimethenamid based on the NOAEL of 7 mg/kg bw per day for bile-duct hyperplasia and reduced body-weight gain observed only in female rats in a 24-month study in rats given diets containing racemic dimethenamid, and a safety factor of 100. The meeting established an ARfD of 0.5 mg/kg bw for dimethenamid-P and racemic dimethenamid based on an overall NOAEL of 50 mg/kg bw for maternal clinical signs of toxicity and developmental toxicity (foetal body-weight deficits and increases in early deaths) in studies in rats, and a safety factor of 100.

### Derivation of Maximum Acceptable Value

No MAV.

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# Dimethoate

Dimethoate: CAS No. 60-51-5. The IUPAC name for dimethoate is O,O-dimethyl S-methyl-carbamoyl-methyl phosphorodithioate, or 2-dimethoxyphosphinothioylthio-N-methylacetamide. The CAS name is O,O-dimethyl S-[2-(methylamino)-2-oxoethyl] phosphorodithioate. Sometimes been called phosphamide.

Omethoate: CAS No. 1113-02-6. The IUPAC name for omethoate is 2‑dimethoxyphosphinoylthio-N-methylacetamide or O,O-dimethyl S‑methylcarbamoylmethyl phosphorothioate. The CAS name is O,O-dimethyl S-[2-(methylamino)-2-oxoethyl] phosphorothioate. Omethoate is also called demethoxon.

### Maximum Acceptable Value

Based on health considerations, the concentration of dimethoate in drinking-water should not exceed 0.008 mg/L (8 μg/L).

The maximum acceptable concentration of dimethoate in Canada is 0.02 mg/L.

The USEPA concluded on 22 September 2009 that dimethoate is known or anticipated to occur in PWSs and may require regulation. Therefore they added dimethoate to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L for dimethoate. Excursions above this level even for a short period are of concern, as the health-based guideline is based on short-term effects.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.001 mg/L for omethoate. Minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

#### 1 To source waters

Dimethoate is a broad-spectrum systemic and contact organophosphate (or organothiophosphate) insecticide and acaricide. It is used on cereal, fodder, fruit, lucerne, pasture and vegetable crops for the control of various pest insects including aphids, leafhoppers, leafminers, mealy bugs, scale crawlers, whiteflies and thrips. It is also used as a residual wall spray in farm buildings for house flies.

Formulations containing dimethoate have been registered for use in New Zealand since 1977. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The products containing dimethoate that are currently registered for agricultural use in New Zealand are Rogor E, Perfekthion S and Dimezyl 40EC. ERMA notes that 0.6 tonnes of dimethoate were used in New Zealand in 2004, at an application rate of 960 grams of active ingredient per hectare. Since 2014 omethoate is no longer able to be manufactured in or imported into New Zealand.

Dimethoate degrades (oxidises) to omethoate, which has a similar hazard profile. Dimethoate may also contain O,O,S-trimethyl phosphorodithioate. There are no formulations containing omethoate approved for use in New Zealand, although the active ingredient has an approval. Omethoate appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. Dimethoate should not contain more than 5 g/kg of O,O,O′,O′-tetramethyl dithiopyrophosphate. Omethoate should not contain more than 20 g/kg of trimethyl phosphate.

Formothion (qv) can be detected after use of dimethoate (IPCS 1989).

### Forms and fate in the environment

Dimethoate is biodegradable. It undergoes rapid degradation in soil and in sewage treatment plants. The major toxic degradate of dimethoate is omethoate which is more toxic, ie (O,O-dimethyl S-(N-methylcarbamoylmethyl) phosphorothioate) (USEPA 2006).

Because dimethoate is highly soluble in water (about 2.5 to 4 percent) and it adsorbs only very weakly to soil particles, it may be subject to considerable leaching. It may be subject to degradation by hydrolysis, especially in alkaline soils, and to evaporation from dry soil surfaces. Losses due to evaporation of 23 to 40 percent of applied dimethoate have been reported. Biodegradation may be significant, with 77 percent degradation reported for a non-sterile clay loam soil in two weeks reported.

Dimethoate does not persist. The half-life of dimethoate in different plants is between two and five days. Soil half-lifes can be 4 to 16 days, although as high as 122 days have been reported. Half-lifes between 2.5 and four days were reported during drought and moderate rainfall conditions. Dimethoate breaks down faster in moist soils. It is broken down rapidly by most soil micro-organisms.

In water, dimethoate is not expected to adsorb to sediments or suspended particles, nor to bioaccumulate in aquatic organisms. It is subject to significant hydrolysis, especially in alkaline waters, although it is relatively stable at pH 2 to 7. Hydrolysis half-lifes of 3.7 and 118 days at pH 9 and pH 7, respectively, have been estimated. Photolysis and evaporation from open waters is not expected to be significant. The half-life for dimethoate in raw river water was eight days, with disappearance possibly due to microbial action or chemical degradation. Dimethoate and its metabolites are very mobile in water. The potential for groundwater exposure from the representative uses by dimethoate above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios for dimethoate and these metabolites (EFSA 2018).

EFSA (2013) discusses several metabolites.

Health Canada (1986) states that dimethoate has a vapour pressure of 1.1 × 10-3 Pa at 25°C and reported log octanol-water partition coefficients are 0.78 and 0.79.

NPIC (1994) quotes for dimethoate a soil half-life of seven days, water solubility of 4 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

Dimethoate was not detected in 98 samples from municipal and private drinking water supplies in Nova Scotia, Quebec, Metropolitan Toronto and Manitoba surveyed from 1971 to 1986 (reported detection limits 0.0002 and 0.0006 mg/L). It was detected at trace levels in a private well in Nova Scotia (detection limit 0.00001 mg/L) (Health Canada 1986).

### Removal methods

Because dimethoate is highly soluble in water and it adsorbs only very weakly to soil, treatment processes that remove particulate matter should be ineffective at reducing the concentration of dimethoate and omethoate in water. Chlorination converts dimethoate into omethoate. Activated carbon and advanced oxidation processes seem to be the most promising removal process. Omethoate is expected to behave in a similar manner.

### Recommended analytical techniques

#### Some alternative methods

WHO (2004) states that dimethoate may be determined in water by extraction into dichloromethane and analysis by gas–liquid chromatography with flame photometric detection. The detection limit is 0.0005 mg/L.

### Health considerations

Dimethoate is moderately toxic by ingestion, inhalation and dermal absorption. As with all organophosphates, dimethoate is readily absorbed through the skin.

Dimethoate is metabolised rapidly by mammals. Rats excreted about 60 percent of an administered dose in urine and expired air within 24 hours. In another study, rats given a single oral dose, excreted 50 percent in the urine and 25 percent in the faeces within 24 hours. Nine days later, only 0.9 to 1.1 percent of the dose remained in the rats’ tissues. Human volunteers excreted 76 to 100 percent of administered dimethoate within 24 hours.

Omethoate, the oxygen analogue found in plants, insects, and mammals, is about 10 times more toxic and is a more potent inhibitor of cholinesterase activity than dimethoate (IPCS HSG 1988).

#### Acute poisoning

The oral LD50 for technical dimethoate in rats is 60 to 387 mg/kg, 60 mg/kg in mice, 400 mg/kg in dogs, 200 mg/kg in hamsters, 300 mg/kg in rabbits, 350 mg/kg in guinea pigs, and 100 mg/kg in cats.

The four-hour LC50 for dimethoate in rats is 1.2 mg/L. Dimethoate is highly toxic to fish and to aquatic invertebrates. The 96-hour LC50 for dimethoate in rainbow trout is 6.2 ug/L. The 48-hour LC50 in Daphnia magna, a small freshwater crustacean, is 2.5 ug/L.

Dimethoate showed no cholinesterase inhibition in an adult human who ingested 18 mg (about 0.26 mg/kg/day) of dimethoate/day for 21 days. No toxic effects and no cholinesterase inhibition were observed in individuals who ingested 2.5 mg/day (about 0.04 mg/kg/day) for four weeks. In another study with humans given oral doses of 5, 15, 30, 45 or 60 mg/day for 57 days, cholinesterase inhibition was observed only in the 30 mg/day or higher dosage groups.

#### Chronic exposure

Repeated or prolonged exposure to organophosphates may result in the same effects as acute exposure, including the delayed symptoms. Other effects reported in workers repeatedly exposed include impaired memory and concentration, disorientation, severe depressions, irritability, confusion, headache, speech difficulties, delayed reaction times, nightmares, sleepwalking and drowsiness or insomnia. An influenza-like condition with headache, nausea, weakness, loss of appetite, and malaise has also been reported.

When mice were given 60 ppm (9.5 to 10.5 mg/kg/day) dimethoate in their drinking water, there was decreased reproduction, pup survival, and growth rates of surviving pups. Adults in this study exhibited reduced weight gain, but their survival was not affected. In a three-generation study with mice, 2.5 mg/kg/day did not decrease reproductive performance or pup survival. Once in the bloodstream, dimethoate may cross the placenta.

Dimethoate is possibly a human teratogen. It was teratogenic in cats and rats. A dosage of 12 mg/kg/day given to pregnant cats increased the incidence of extra toes on kittens. The same dosage given to pregnant rats produced birth defects related to bone formation, runting and defects related to malfunction of the bladder. Dosages of 3 or 6 mg/kg/day were not teratogenic in cats or rats. The NOAEL for both cats and rats was 2.8 mg/kg/day. There were no teratogenic effects seen in the offspring of mice given 9.5–10.5 mg/kg/day dimethoate in their drinking water.

USEPA (1995) states: the USEPA has concluded that dimethoate poses no greater than a negligible cancer risk to humans; therefore, the Agency has chosen to use reference dose calculations to estimate dietary risk from dimethoate residues. The dietary risk exposure analysis used a Reference Dose (RfD) for dimethoate of 0.0005 mg/kg/body weight/day, based on a NOEL of 0.05 mg/kg/bwt/day for brain cholinesterase inhibition from a two-year feeding study in rats, and an uncertainty factor of 100. The oral RfD for dimethoate had previously been 0.0002 mg/kg/d (USEPA 1990). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0022 mg/kg/d, and an ARfD of 0.13 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dimethoate is 0.130 mg/L.

The 2003 JMPR meeting recommended a number of MRLs and established an acute reference dose (ARfD) of 0.02 mg/kg bw (JMPR 2008) for dimethoate (including its metabolite omethoate which is ten times more toxic).

The Acceptable Daily Intake (ADI) adopted in Australia for dimethoate is 0.02 mg/kg body weight, with a NOEL of 0.2 mg/kg bw from a short-term (57-day) human volunteer study. The NOEL is based on cholinesterase inhibition. The ADI incorporates a safety factor of 10.

The Acceptable Daily Intake (ADI) adopted in Australia for omethoate is 0.0004 mg/kg body weight, with a NOEL of 0.04 mg/kg bw from two-year dietary study in rats. The NOEL was based on inhibition of acetylcholinesterase. The ADI incorporates a safety factor of 100. The ARfD is 0.003 mg/kg bw based on a NOEL of 0.25 mg/kg bw/day from an acute neurotoxicity study in rats. The NOEL was based on inhibition of acetylcholinesterase activity. The ARfD incorporates a safety factor of 100. As at December 2015, the Acceptable Daily Intake (ADI) adopted in Australia for dimethoate is 0.001 mg/kg body weight, with a NOEL of mg/kg bw, and the ARfD is 0.02 mg/kg bw.

EC (2006) established an ADI for dimethoate of 0.001 mg/kg/d and an ARfD of 0.01 mg/kg/d. These values were reaffirmed by EFSA (2013 and 2018). EC (2006) added that the manufacturing impurities omethoate and isodimethoate are of toxicological concern and must not exceed respectively 2 g/kg and 3 g/kg in the technical material. In addition separate toxicological reference values were set for omethoate, a metabolite considerably more toxic than dimethoate (EFSA 2012).

The ADI for New Zealand is 0.001 mg/kg/d.

EFSA (2013) quotes an ADI of 0.0003 mg/kg/d for omethoate, and an ARfD of 0.002 mg/kg bw.

Dimethoate is possibly a mutagen. Mutagenic effects (dominant lethal) were more prominent in male mice given a single high dose of dimethoate than in male mice given one-twelfth of the same dose daily for 30 days. Dimethoate is not carcinogenic to rodents. JMPR concluded that although in vitro studies indicate that dimethoate has mutagenic potential, this potential does not appear to be expressed in vivo.

As at September 2008 the USEPA has classified dimethoate in Group C: a possible human carcinogen. EFSA (2013) states there is no evidence of carcinogenicity for dimethoate or omethoate.

USEPA (2015) found that based on weight of evidence considerations there was no convincing evidence of potential interaction between dimethoate and the estrogen or androgen signalling pathways in mammals or wildlife. There was evidence of potential interaction with the thyroid pathway.

### Derivation of Maximum Acceptable Value

An acceptable daily intake approach has been used for the derivation of the MAV for dimethoate in drinking-water. JMPR concluded that it was not appropriate to base the ADI on the results of the studies of volunteers, since the crucial end-point (reproductive performance) has not been assessed in humans. It was suggested that there may be a need to re-evaluate the toxicity of dimethoate after the periodic review of the residue and analytical aspects of dimethoate has been completed if it is determined that omethoate is a major residue.

The MAV for dimethoate was derived as follows:

1.2 mg/kg body weight per day x 70 kg x 0.1 = 0.0084 mg/L (rounded to 0.008 mg/L)

2 L x 500

where:

* no observable adverse effect level = 1.2 mg dimethoate per kg body weight per day identified on the basis of reproductive performance in a study of reproductive toxicity in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 500 to take into consideration concern regarding whether this could be a LOAEL.

The odour threshold of dimethoate is 0.00001 mg/L; however, it is not an aesthetic determinand in the DWSNZ.

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# Dimethomorph

CAS No. 110488-70-5. The IUPAC name for dimethomorph is (EZ)-4-[3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)acryloyl]morpholine. The CAS name is 4-[3-(4-chlorophenyl)-3-(3,4-dimethoxyphenyl)-1-oxo-2-propenyl]morpholine. It is a mixture of two isomers (E and Z) in approximately equal proportions but only the Z isomer (CAS No. 113210-98-3) has fungicidal activity. Sometimes called (misspelt?) dimetomorph and dimethmorph.

### Maximum Acceptable Value

Dimethomorph does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.0001 mg/L (0.1 µg/L) for dimethomorph in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Dimethomorph is a systemic morpholine (or cinnamic acid derivative) fungicide, often used to control downy mildew on vines, and to control late blight on tomatoes and potatoes, and on grapes. Dimethomorph is often mixed with other pesticides, eg, mancozeb. Its mode of action is the inhibition of sterol (ergosterol) synthesis.

Dimethomorph appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Dimethomorph has a low soil mobility and low leaching potential. Its half-life in aerobic soils has been reported to range from two to four months. EFSA (2013) states that in soil degradation studies a moderate persistency (maximum DT90 in field studies) of 203 days was observed. Water solubility is about 30–60 mg/L.

The primary route of degradation of dimethomorph is by microbial action. Degradation products in soil are not extractable in aqueous/organic solvents and slowly mineralise to CO2. No significant degradation products have been detected in four soils. The E‑isomer of dimethomorph appears to degrade faster in soil than the Z-isomer under aerobic conditions. Dimethomorph is slowly degraded in the soil under the influence of light to give two minor unidentified photolysis products.

Several metabolites are listed in EFSA (2011).

### Typical concentrations in drinking-water

The predicted dimethomorph surface water and groundwater concentrations are well below the USEPA’s drinking water level of concern.

### Health considerations

Two-year studies on rats and long-term studies of mice demonstrate that dimethomorph is unlikely to cause tumour development, and is not mutagenic (EXTOXNET 1995).

The Acceptable Daily Intake (ADI) adopted in Australia for dimethomorph is 0.06 mg/kg body weight, with a NOEL of 6 mg/kg bw.

The acceptable daily intake (ADI) (EXTOXNET 1995) is 0.1 mg/kg bw, based on a NOEL of 200 mg/kg (rat) and 450 mg/kg (dog).

The USEPA determined a reference dose (RfD) of 0.1 mg/kg/day based on the NOAEL of 11 mg/kg/day from the rat oncogenicity study and was supported by similar results in the rat chronic dietary study in which there were significant body weight decrement and liver effects in female rats at the LOAEL of 46.3 mg/kg/day. An uncertainty factor of 100 was applied to account for both the interspecies extrapolation and the intraspecies variability. The USEPA has classified dimethomorph as “not likely to be a human carcinogen” based on no increased incidence of neoplasms in the rat chronic or carcinogenicity studies or in the mouse carcinogenicity study (USEPA 1998). In 2003 USEPA quoted a RfD (and cPAD) of 0.09 mg/kg/d (sometimes rounded to 0.1); an acute Rfd was considered as not needed. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.10 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dimethomorph is 0.70 mg/L (no acute one-day value available.)

EC (2006) finalised an ADI of 0.05 mg/kg bw, and an acute reference dose (ARfD) of 0.6 mg/kg/d bw. These values were confirmed in EFSA (2011 and 2013).

The 2007 JMPR meeting established an ADI of 0–0.2 mg/kg bw based on a NOAEL of 15.2 mg/kg bw per day identified on the basis of the liver weight and clinical chemistry changes and prostate weight changes and prostate fibrosis observed at higher doses in the 13-week and the one-year studies in dogs. A safety factor of 100 was applied. The meeting established an ARfD of 0.6 mg/kg bw based on a NOAEL of 60 mg/kg bw per day identified on the basis of post-implantation losses at higher doses in the study of developmental toxicity in rats. A safety factor of 100 was applied (FAO/WHO 2007). These values were reaffirmed in JMPR (2014/2016).

### Derivation of Maximum Acceptable Value

No MAV.

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# Dinoseb

CAS No. 88-85-7. The IUPAC name for dinoseb is (RS)-2-(sec-butyl)-4,6-dinitrophenol. The CAS name is 2-(1-methylpropyl)-4,6-dinitrophenol. Has also been called binapacryl.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because dinoseb is unlikely to occur in drinking-water, a guideline value has not been derived.

The USEPA (2006/2009/2011) has set a MCLG for dinoseb at 0.007 mg/L because they believe this level of protection would not cause any of the potential health problems. The MCL and lifetime health advisory has been set at 0.007 mg/L too because USEPA believes, given present technology and resources, this is the lowest level to which water systems can reasonably be required to remove this contaminant should it occur in drinking water.

The maximum acceptable concentration in Canada is 0.01 mg/L.

A Public Health Goal of 0.014 mg/L has been adopted for dinoseb in drinking water in California.

Dinoseb appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see: <http://www.pic.int/home.php?type=s&id=77>

### Sources to water

Dinoseb is a dinitrophenol herbicide. Its greatest use is as a contact herbicide for post-emergence weed control in cereals, undersown cereals, seedling lucerne and peas. Dinoseb is also used as a corn yield enhancer and an insecticide and miticide. It does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register).

### Forms and fate in the environment

Dinoseb is degraded slowly by soil bacteria and binds weakly to soil. Therefore, leaching in soil is possible and dinoseb has been detected in groundwater. In water, dinoseb is mainly broken down by sunlight. It is not likely to accumulate in aquatic life.

Dinoseb is of low persistence regardless of the form (phenolic or salt). Reported field half-lifes for both types of dinoseb range from 5 to 31 days. Solubility: 52 mg/L of water at 25°C; tends to form salts which are highly soluble in water.

NPIC (1994) quotes for dinoseb a soil half-life of 30 days, water solubility of 52 mg/L and a sorption coefficient (soil Koc) of 30. This resulted in a pesticide movement to groundwater rating of high. Its GUS score is 3.80, indicating that it will leach to groundwater.

### Typical concentrations in drinking-water

Over a 10-year period, dinoseb was found to be one of three particularly persistent contaminants in Ontario wells. Entry to the wells was due to spills of concentrated and dilute herbicide, drift during spraying, and from storm run-off. Well water concentrations ranged from 0.00005 to 5 mg/L in these wells, and removal of dinoseb proved to be very difficult.

Thirty-three water utilities in the US reported detecting dinoseb in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0054 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Dinoseb was found in one sample, at 0.23 µg/L, ie, 0.00023 mg/L.

Water may be yellow if contaminated with more than 0.1 mg/L.

### Removal methods

The following treatment method has been approved by EPA for removing dinoseb: Granular activated charcoal.

### Health considerations

Long-term: dinoseb has the potential to cause the following effects from a lifetime exposure at levels above the MCL: decreased body and thyroid weight, degeneration of testes; thickening of intestinal lining. As at September 2008 the USEPA has classified dinoseb in Group C: a possible human carcinogen. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Dinoseb is readily absorbed through the skin, gastrointestinal tract, and lung surface. Esters of dinoseb are rapidly transformed into dinoseb, which is the active toxicant. The chemical is excreted in the urine and faeces and is metabolised in the liver. Breakdown products are found in the liver, kidneys, spleen, blood, and urine. Dinoseb can also pass through the placenta into the fetus of experimental animals.

There is inadequate evidence to state whether dinoseb has the potential to cause cancer from lifetime exposure in drinking-water.

The use of dinoseb was cancelled in the US in 1986, based on the potential risk of birth defects and other adverse health effects for applicators and other persons with substantial dinoseb exposure.

The reference dose or RfD (USEPA 1989/2006/2009/2011) is 0.001 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.035 mg/L.

### Derivation of Maximum Acceptable Value

A Public Health Goal of 0.014 mg/L was developed for dinoseb in drinking water in California. The PHG was calculated based on a lowest-observed-adverse-effect-level (LOAEL) of 1 mg/kg-day for cystic endometrial hyperplasia in female mice and hypospermatogenesis and atrophy/degeneration of the testes in male mice. This is the identical LOAEL used by the USEPA to promulgate its Maximum Contaminant Level (MCL) for dinoseb of 0.007 mg/L. The federal MCL is based upon a Drinking Water Equivalent Level (DWEL) of 0.035 mg/L (rounded by USEPA to 0.04 mg/L).

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# Diphacinone

CAS No. 82-66-6. The IUPAC name for diphacinone is 2-(diphenylacetyl)indan-1,3-dione. The CAS name is 2-(diphenylacetyl)-1H-indene-1,3(2H)-dione. The sodium salt CAS No. is 42721-99-3. Also called diphenadione, diphacin, dipazin, diphenacin, and ratindan.

### Maximum Acceptable Value

Diphacinone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Diphacinone is an indandione rodenticide used in bait for control of rats, mice, and other rodents, typically at 0.005 percent of the bait. Typically diphacinone, like other anticoagulants, takes several days to kill. It inhibits the production of vitamin K, which is required to clot blood, and death results from haemorrhaging. It may also be used as a anticonvulsant drug under the name of diphenadione.

Diphacinone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Diphacinone has a low potential to leach in soil. Diphacinone is rapidly decomposed in water by sunlight. The rodenticides are generally stable to hydrolysis, except for diphacinone at pH 5 (which has a half-life of 44 days), moderately persistent to persistent to aerobic soil degradation (half-lifes of 26 to 178 days) and, except for bromethalin can generally be considered to be immobile in the soil (Kds = 5.4 to 1,000, and found in the upper soil layer of column leaching studies). Generally the potential for these chemicals to reach groundwater is low. They probably reach surface waters through adsorption to eroding soil, as opposed to dissolution in run-off water. Because of their generally high adsorption coefficients and/or demonstrated lack of movement in soil leaching columns they would have a good probability of partitioning into the suspended and bottom sediments instead of the water column after reaching surface waters (USEPA 1998).

Water solubility is about 0.3 mg/L.

### Removal methods

Treatment methods that remove particulate matter should reduce the concentration of diphacinone.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The principal target of diphacinone is the blood (specifically the clotting factors), but effects on the liver, kidneys, heart, and musculature have been seen, probably as secondary effects. No permanent or life-threatening effects occurred in humans on recommended dose regimes of an initial 20 mg dose (ca. 0.29 mg/kg in a 70 kg human), followed by successive 2 to 4 mg daily doses (ca. 0.03 to 0.06 mg/kg/day in a 70 kg person) for several days to weeks. All test animals exposed at dietary levels of 0.1 and 0.2 mg/kg/day in a 21-day study showed fatal massive internal haemorrhaging, although at doses of 0.05 mg/kg/day, they were unaffected. In a 90-day study in which rats were given dietary doses of 0.002 to 0.025 mg/kg/day, single rats in each of the 0.003 and 0.013 mg/kg/day dose groups died from internal haemorrhage, but the others remained unaffected by treatment (EXTOXNET 1996).

The rat maternal toxicity NOEL = <10 μg/kg/day. The rat maternal toxicity LOEL = 10 μg/kg/day based on signs consistent with anticoagulant activity (USEPA 1998).

The Acceptable Daily Intake (ADI) and ARfD adopted in Australia for diphacinone is described as “not necessary”.

### Derivation of Maximum Acceptable Value

No MAV.

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# Diquat

CAS No. 2764-72-9. The IUPAC name for diquat is 9,10-dihydro-8a,10a-diazoniaphenanthrene, or 6,7-dihydrodipyrido[1,2-a:2′,1′-c]pyrazine-5,8-diium, or 1,1′‑ethylene-2,2′-bipyridyldiylium. The CAS name is 6,7-dihydrodipyrido[1,2-a:2′,1′-c]pyrazinediium.

The main commercial product, diquat dibromide is CAS No. 85-00-7. CAS No. 6385‑62‑2 refers to diquat dibromide monohydrate, 231-36-7 for the free diquat ion, and 4032‑26-2 for diquat dichloride).

### Maximum Acceptable Value

WHO (2017) states that diquat occurs in drinking-water or drinking-water sources at concentrations well below those of health concern.

WHO (2017) derived a health-based value for diquat of 0.03 mg/L (small exceedances above the HBV for a short period are unlikely to have an impact on health), and an acute health-based value of 20 mg/L; this acute HBV indicates the concentration of diquat in drinking-water that a person could consume for 24 hours without appreciable health risk.

In DWSNZ 2005, the provisional MAV for diquat in drinking-water had been 0.01 mg/L (10 μg/L); there was no MAV in the 2008 DWSNZ.

The maximum contaminant level or MCL of diquat dibromide (USEPA 2006/2009) is 0.02 mg/L. The maximum acceptable concentration for diquat (measured as the cation) in Canada is 0.07 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Diquat, a cyclic hydrocarbon or bipyridyl, is commonly sold as diquat dibromide and is available as liquids (ready to use) or as a soluble concentrate. It is a rapid acting, non-selective contact herbicide and crop desiccant. It is used to control crop weeds, and may also be used (at or below 1 mg/L) as an aquatic herbicide for the control of free-floating and submerged aquatic weeds in ponds, lakes and irrigation ditches. This use presents a direct route of entry into surface water systems. Diquat mode of action is interruption of the electron transport system in plant photosynthesis, resulting in the formation of hydrogen peroxide, which then desiccates green plant tissue.

On a global basis, pre-harvest desiccation to aid the harvesting of seed and fodder crops accounts for the use of two-thirds of the global volume of diquat, whereas one-third of the diquat sold is used as a weed killer (WHO 1998). Diquat is usually formulated as an aqueous solution or a compound product mixed with the herbicide paraquat.

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The soluble concentrate is available with diquat as the single active ingredient (trade names Reglone and Torpedo), or with paraquat as a second active ingredient (trade name Preeglone). Diquat should not contain more than 10 mg/kg of free 2,2′-bipyridyl or ethylene dibromide (USEPA 1995). However, JMPR (2008) quotes 750 mg/kg for 2,2′-bipyridyl, 10 mg/kg for ethylene dibromide, and 1 mg/kg for total terpyridines. Diquat treatment of aquatic weed beds first began in the Rotorua Lakes in 1960 and has been used there regularly for 45 years (Environment Waikato 2005).

No information is available on the annual usage of specific active ingredients in New Zealand, although diquat is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Diquat is very soluble in water of pH 5.2 to 9.2: 715 g/L (715,000 mg/L or 71.8 percent) (WHO 1998). The double positive charge on the diquat cation causes it to be adsorbed tightly to the negatively charged clay minerals present in the soil so is unlikely to leach to groundwater. It has a long half-life in sterile soil (250 days: Hort Research 2000 and >1,000 days: JMPR 2013). Diquat is rapidly and extensively degraded by soil micro-organisms normally found in soil pore water, in the absence of soil, to give a small number of non-volatile degradation products, with mineralisation to CO2. The DT50 for degradation in soil solution is rapid at <1 week, however sorbed diquat is not available to biological degradation processes with a half-life ranging from 1.2 to 41 years (JMPR 2013). Diquat is particularly persistent in anaerobic soil, with half-lifes reported as many years.

Diquat is adsorbed strongly to soil, is not taken up by plant roots, and is not metabolically degraded by plants. The rate of degradation in soil, although slow, was found to be sufficient to ensure that diquat residues would not accumulate indefinitely in soil but would reach a plateau level when the amount degraded each year was equal to the amount of new addition. In the presence of sunlight, rapid and extensive photochemical degradation occurs (WHO 1998). It is not volatile.

Following its use as an aquatic herbicide at normal application rates, diquat residues in water have been found to decrease rapidly to essentially undetectable levels within  
7–14 days (IPCS HSG 1991). When diquat is added to natural waters to control aquatic weeds, residues in the water decline rapidly, owing mainly to the absorption of diquat into the aquatic plants, where it is bound firmly until the decaying weeds disintegrate into the bottom mud. The diquat is then irreversibly bound to the soil particles, leaving the water free of diquat residues. Adsorbed diquat is persistent and immobile, and is not expected to be a groundwater contaminant. Half-lifes of diquat in natural waters are generally less than 48 hours (FAO/WHO 1995). Diquat will photodegrade in surface layers of water in 1–3 or more weeks when not adsorbed to particulate matter (USEPA Technical Factsheet on diquat). No major degradates were isolated from any of the environmental fate studies (USEPA 1995).

Sediment samples from five New Zealand lakes, some of which had been treated with diquat for years, were all free from residues of diquat (NIWA 2005).

Degradation in soil is very slow: no significant degradation after 32 days in aerobic soil, and withstands degradation anaerobically (EC 2001).

NPIC (1994) quotes for diquat dibromide a soil half-life of 1,000 days, water solubility of 72 percent and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

There is no information available regarding the greatest source of exposure to diquat for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

An absolute value for Henry’s Law Constant cannot be calculated since pure diquat dibromide has no measurable vapour pressure; its value is estimated to be less than 5 x 10–12 Pa/m3/mol. The partition coefficient n-octanol/ water = logPow = -0.46. The hydrolysis of diquat was studied in the dark in sterile, aqueous buffered solutions at pH 4, pH 7 and pH 9 at 50°C for five days; diquat was shown to be hydrolytically stable under all the conditions tested in this study. JMPR (2013), which tabulates some metabolites.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included diquat, and so typical concentrations in New Zealand drinking-waters are unknown.

Groundwater was analysed for diquat at two sites in Japan where the product had been used commercially for 5 and 15 years. No diquat was detected in the water, although the limit of detection was relatively high, being 0.1 mg/L (FAO/WHO 1995).

Thirty-seven water utilities in the US reported detecting diquat in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.010 mg/L.

### Removal methods

Diquat is adsorbed by activated carbon (Faust and Aly 1983). The pesticide’s high water solubility and low octanol–water partition coefficient suggest that a high carbon usage rate per volume of water treated would be needed (WHO 2016).

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of diquat in water.

Under alkaline conditions, chlorination removes diquat from water by oxidation; the rate of removal increases with a rise in pH. However, at pH 7 to 8, a relatively long contact time (two hours or more) is necessary to achieve reasonable removal. Chlorine dioxide acts extremely rapidly (within a few minutes) to oxidise diquat (Health Canada 1986).

Diquat can be oxidised by ozone. This is achieved most effectively at more alkaline pH values, or by a combination of ozone and UV light. Both of these methods produce hydroxyl radicals which are strong oxidising agents (Haag and Yao 1992). Use of activated carbon following ozonisation should be considered to adsorb oxidation products.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Recommended analytical techniques

#### Referee method

Liquid/solid extraction, HPLC with UV detection (EPA Method 549.2).

#### Some alternative methods

Acid hydrolysis and clean-up and concentration by ion exchange chromatography followed by reduction and measurement of the diquat reduction products by gas–liquid chromatography with a nitrogen–phosphorus detector. The limit of determination is 0.004 mg/L (WHO 2004).

### Health considerations

Diquat is an analogue of paraquat, which is a pesticide of high toxicity to humans. Diquat is considerably less potent than paraquat (qv), but nonetheless can cause severe acute and chronic poisoning. Paraquat is also registered for use in New Zealand.

Diquat poisoning is much less common than paraquat poisoning, so human reports and animal experimental data for diquat poisoning are less extensive than for paraquat (Reigart and Roberts 1999). Part of the reduced toxicity may be related to the fact that it is absorbed poorly from the gastrointestinal tract. A latency period of 24 hours is seen prior to visible acute toxic effects (Klaassen 1996).

The mode of action of diquat is not understood.

#### Acute poisoning

Following acute, high-dose exposure or chronic exposure of animals to diquat, the major target organs were the gastrointestinal tract, the liver, and the kidneys. Oral LD50 values in various species are of the order of 100 to 400 mg/kg (Klaassen 1996), which suggests a moderate level of acute oral toxicity when compared with other pesticides. The acute lethal dose of diquat dibromide is considered to be 6–12 g for humans (WHO 1994). It is considered that diquat can form free radicals, and that the tissue necrosis is associated with the same mechanism(s) of superoxide-induced peroxidation as observed with paraquat (Klaassen 1996).

In many human diquat poisoning cases (acute exposure), clinical signs of neurologic toxicity are the most important. These include nervousness, irritability, restlessness, combativeness, disorientation, nonsensical statements, inability to recognise friends or family members, and diminished reflexes. Neurologic effects may progress to coma, accompanied by tonic-clonic seizures, and result in the death of the patient (Vanholder et al 1981, Olson 1994, both cited in Reigart and Roberts 1999). Parkinsonism has also been reported following dermal exposure to diquat (Sechi et al 1992, cited in Reigart and Roberts 1999).

The kidney is the principal excretory pathway for diquat absorbed into the body. Renal damage is therefore an important feature of poisonings.

#### Chronic exposure

Chronic feeding studies resulted in an increased incidence of cataracts in both dogs and rats (Klaassen 1996 and WHO 1998). Numerous reproductive and developmental toxicity studies have been conducted and have shown reduced maternal and foetal weight gain at certain doses (WHO 1998).

In chronic feeding/carcinogenicity studies on rats, the systemic NOEL was 0.58 mg/kg/day for males and 0.72 mg/kg/day for females, expressed as diquat cation; and the systemic LOEL was 2.91 mg/kg/day for males and 3.64 mg/kg/day for females, expressed as diquat cation (USEPA 1995).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw from a long-term study. The NOEL is based on cataract formation in a two-year rat dietary study. The ADI incorporates a safety factor of 100. The acute reference dose (ARfD) of 0.05 mg/kg bw/day for diquat was established in 2002, based on a NOEL of 26.5 mg/kg bw/day from an acute dietary study in dogs. The ARfD incorporates a safety factor of 500.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.02 mg/L. The oral RfD had previously been 0.002 mg/kg/d (USEPA 1995).

EC (2001) stated that the ADI was 0.002 mg/kg/d for the diquat ion, and added that the ARfD was unnecessary. EFSA (2015) affirmed these values.

JMPR (2013) reports an Acceptable Daily Intake (ADI) of 0–0.006 mg/kg bw for diquat and an Acute Reference Dose (ARfD) of 0.8 mg/kg bw.

The International Agency for Research on Cancer (IARC) has not classified diquat, but the USEPA considers that there is inadequate evidence to state whether diquat has the potential to cause cancer from a lifetime exposure in drinking-water (USEPA Technical Factsheet on diquat). As at September 2008 the USEPA has classified diquat in Group E: evidence of non-carcinogenicity for humans. No carcinogenic or tumourigenic potential was reported for diquat in long-term feeding studies in rats and dogs (Health Canada 1989).

Diquat is not carcinogenic in mice or rats. In tests for genotoxicity, diquat gave equivocal or positive responses in the mammalian cell cytogenetic assay, but was negative in the in vivo mouse micronucleus assay and dominant lethal assay. No reproductive effects were observed in a two-generation reproductive toxicity study in rats, and diquat was not teratogenic in rats or rabbits (WHO 2017).

### Derivation of Maximum Acceptable Value

WHO (2004 and 2011) stated that diquat is not expected to occur in drinking-water (unless used as an aquatic herbicide), and it is therefore not necessary to establish a guideline value for diquat in drinking-water.

The health-based value of 0.03 mg/L is derived from the ADI of 0–0.006 mg/kg bw (expressed as the diquat ion), based on a NOAEL of 0.58 mg/kg bw per day for cataracts in a two-year toxicity and carcinogenicity study in rats and application of a safety factor of 100, with an allocation to water of 20 percent, for a 60 kg adult drinking two litres a day (WHO 2016/17).

The acute health-based value of 20 mg/L is derived from the ARfD of 0.8 mg/kg bw (expressed as the diquat ion), based on a NOAEL of 75 mg/kg bw for clinical signs and decreased body weight gain in the 1st week and decreased feed consumption in a neurotoxicity study in rats and application of a safety factor of 100, and 100 percent allocation from water (WHO 2016/17).

In DWSNZ 1995, 2000 and 2005, the provisional MAV had been derived as follows: an acceptable daily intake approach has been used for the derivation of the MAV for diquat in drinking-water. WHO (2011) states that this calculation could be used to establish a health-based value. The ADI was based on cataract formation at the next higher dose identified in a two-year study in rats and using an uncertainty factor of 100:

0.19 mg/kg body weight per day x 70 kg x 0.1 = 0.007 mg/L (rounded to 0.01 mg/L)

2 L x 100

where:

* no observable adverse effect level = 0.19 mg diquat ion per kg body weight per day identified on the basis of cataract formation at the next higher dose identified in a two-year study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

WHO (2004) states that it should be noted that the limit of detection of diquat in water is 0.001 mg/L, and its practical quantification limit is about 0.01 mg/L.

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# Dithianon

CAS No. 3347-22-6. The IUPAC name for dithianon is 5,10-dihydro-5,10-dioxonaphtho[2,3-b]-1,4-dithiine-2,3-dicarbonitrile. The CAS name is 5,10-dihydro-5,10-dioxonaphtho[2,3-b]-1,4-dithiin-2,3-dicarbonitrile. Also been called 2,3-dinitrilo-1,4-dithia-anthraquinone, 1,4-dithiaanthraquinone-2,3-dinitrile, and several others.

### Maximum Acceptable Value

Dithianon does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Dithianon is a broad spectrum quinone herbicide, used as a multi-site protective fungicide which inhibits spore germination. It is used on a range of fruits and vegetables, commonly apples, pears and grapes in New Zealand. Dithianon appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Dithianon is not particularly persistent in soil or water, and is not likely to leach to groundwater. Water solubility is about 0.25 mg/L.

JMPR (2013) reports a 20°C Henry’s Law constant of 1.347 x 10-7 Pa.m3/mol. The n‑octanol/water partition coefficient at 20°C = logPow = 3.2. Hydrolysis half-lifes are 10.7 days at pH 5, 0.6 days at pH 7 and 10 minutes at pH 9. Photolysis is rapid: DT50 is <0.05 days, with major metabolites being phthalic acid, phthaldialdehyde and 1,2‑benzenedimethanol.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Dithianon is classified by the USEPA as “having suggestive evidence of carcinogenic potential” based on the presence of renal adenomas and carcinomas in the female rat at doses that were adequate to assess carcinogenicity. This classification is based on several weight-of-evidence considerations.

USEPA (undated) reported an acute RfD of 0.02 mg/kg/d, and a chronic RfD of 0.006 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.006 mg/kg/d, and an ARfD of 0.02 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dithianon is 0.66 mg/L.

The 2010 JMPR meeting reaffirmed the ADI of 0–0.01 mg/kg bw for dithianon based on a NOAEL of 1 mg/kg bw per day for histopathological kidney lesions in females at 6 mg/kg bw per day in a two-year toxicity study of rats and using a 100-fold safety factor. The meeting established an acute reference dose (ARfD) of 0.1 mg/kg bw for dithianon, taking into account a NOAEL of 12 mg/kg bw and using a safety factor of 100. The NOAEL was based on a mechanistic study in which nephrotoxicity was assessed in rats following four and seven days of dosing. At these time points, a dietary intake of 60 mg/kg bw per day of dithianon induced repeated cellular degenerative/regenerative responses in kidney tubular cells of female rats. They concluded that dithianon was not genotoxic, and that dithianon did not pose a carcinogenic hazard for humans. These ADI and ARfD values also appear in JMPR (2013).

The 2010 JMPR meeting reaffirmed the ADI of 0–0.01 mg/kg bw for dithianon based on a NOAEL of 1 mg/kg bw per day for histopathological kidney lesions in females at 6 mg/kg bw per day in a two-year toxicity study of rats and using a 100-fold safety factor. The meeting also established an acute reference dose (ARfD) of 0.1 mg/kg bw for dithianon, taking into account a NOAEL of 12 mg/kg bw and using a safety factor of 100. The NOAEL was based on a mechanistic study in which nephrotoxicity was assessed in rats following four and seven days of dosing. At these time points, a dietary intake of 60 mg/kg bw per day of dithianon induced repeated cellular degenerative/regenerative responses in kidney tubular cells of female rats.

Dithianon does not pose a genotoxic risk and is not likely to be a genotoxic carcinogen (PMEP 1997). In 90-day oral studies in rats and dogs the NOELs were 15.5 mg/kg/day and 3.0 mg/kg/day, respectively. In the 24-month combined chronic toxicity and oncogenicity study in rats, the NOEL for chronic effects was 1.0 mg/kg/day. The carcinogenicity NOEL for females 6.0 mg/kg/day.

EFSA (2015) quotes an ADI of 0.01 mg/kg bw/d, and an ARfD of 0.01 mg/kg bw. Genotoxicity studies were provided on metabolites Reg. No. 31062, 4110904 and 4110933 indicating that these compounds are unlikely to be genotoxic.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.007 mg/kg body weight, with a NOEL of 0.66 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# Diuron

CAS No. 330-54-1. The IUPAC name for diuron is 3-(3,4-dichlorophenyl)-1,1-dimethylurea. The CAS name is N’-(3,4-dichlorophenyl)-N,N-dimethyl-urea.

### Maximum Acceptable Value (Provisional)

Based on health considerations, the concentration of diuron in drinking-water should not exceed 0.02 mg/L (20 μg/L). Diuron is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Word\www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has set (by an approval under Part 5 of the HSNO Act) a tolerable exposure limit (TEL) of 0.02 mg/L in drinking water and an environmental exposure limit (EEL) in fresh water of 0.0002 mg/L (0.2 µg/L).

The maximum acceptable concentration for diuron in Canada is 0.15 mg/L.

The USEPA concluded on 22 September 2009 that diuron is known or anticipated to occur in PWSs and may require regulation. Therefore they added diuron to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009a). The USEPA (2009) established a one day and a ten day health advisory for a 10 kg child of 1 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; excursions above this level even for a relatively short period are of concern as the health-based guideline is based on medium-term effects.

Its principal breakdown product 3,4-dichloroaniline (see datasheet) is more toxic than diuron itself. Two ‘dioxin-like’ compounds, 3,3’,4,4’-tetrachloroazobenzene (TCAB) and 3,3’,4,4’-tetrachloroazoxybenzene (TCAOB), are present in diuron preparations as contaminants from the manufacturing process.

### Sources to water

Diuron is used as a pre-emergence non-selective substituted urea-based herbicide. Its uses include control of vegetation in non-crop areas, including irrigation and drainage ditches. Diuron is mainly applied in non-agricultural areas such as sporting grounds and railroads. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is available in a wide variety of formulations, many containing other active ingredients including amitrole, bromacil, terbuthylazine and norflurazon. Trade names include: Agpro Diuron 800, Boundary, Chemagro Terminex-A, Fenican, Griffen Karmex 80 DF Herbicide.

After 1 July 2017 antifouling paints containing diuron will no longer able to be manufactured in or imported into New Zealand. See EPA (2013).

Diuron should not contain more than 2 mg/kg of 3,3′,4,4′-tetrachloroazoxybenzene, or 20 mg/kg of 3,3′,4,4′-tetrachloroazobenzene (TCAB).

Diuron is also registered for use as an anti-fouling paint for protection of appliances/structures used in an aquatic environment and many of these formulations have copper compounds as additional active ingredients. Trade names include: Alloy Antifouling, Coppercoat Extra, Cruiser Superior, Interclene 165 BWA 900 Bright Red, Intersmooth Tin Free SPC. Diuron is monitored in New Zealand harbour waters (ERMA undated).

No information is available on the annual usage of specific active ingredients in New Zealand, although diuron is understood to constitute approximately 60 percent of the Urea Derivatives class of pesticides used in the country (Holland, personal communication).

In the Japanese aquatic environment 86 percent of tested samples showed a 0.0035 mg/L concentration of diuron. In Dutch coastal waters a higher level than the permitted 430 ng/L was detected. According to the French Environmental Institute diuron is detected in 34.6 percent of surface waters in France where it was the fifth most frequently detected pesticides. It was also found in 6.4 percent of groundwater samples where it was the seventh most frequently detected pesticide. In the UK diuron is consistently one of the pesticides most frequently found exceeding the non-statutory Environmental Quality Standard of 0.0001 mg/L; however, it is no longer allowed to be used in the UK. Many other studies have reported contamination of water by diuron in antifouling paint (see Pesticide News 2005).

### Forms and fate in the environment

Diuron is moderately soluble in water: 42 mg/L (Merck & Co 1996).

The USEPA has ranked diuron fairly high, as a Priority B chemical, with respect to potential for groundwater contamination, and it also rates highly in Agriculture Canada’s ranking of potential leaching agents (Health Canada 1987/89). It has a half-life in soil of 65 days (Hort Research 2000), and a mobility (as Koc) of 530 was recorded from eight soils from Nelson, Marlborough and Hawkes Bay (Close et al 2001). This suggests that diuron is relatively easily adsorbed to organic soil and therefore not very mobile in those conditions, with half-lifes between 90 and 180 days. In water it is slowly degraded biologically. Photolytic degradation was also observed (IUPAC 2003). Health Canada (1987) states that its hydrolysis rate is negligible at neutral pH but increases under strongly acidic or alkaline conditions, and it has a log octanol-water partition coefficient of 2.6, which is considered low to moderate. It is adsorbed to soils to some degree, with a moderate soil-water partition coefficient of 485.

NPIC (1994) quotes for diuron a soil half-life of 90 days, water solubility of 42 mg/L and a sorption coefficient (soil Koc) of 480. This resulted in a pesticide movement to groundwater rating of moderate. Its GUS score is 3.40, indicating that it will leach to groundwater.

USGS (2006) give the following values: log Kow = 2.78; log Koc (where Koc is in mL/g) = 2.6; water solubility = 40 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -3.17; half-life in aerobic soil = 372 days; half-life in water = >500 days.

Metabolites of diuron include 3,4-DCA (3,4-dichloroaniline), plus 1-(3,4-dichlorophenyl)-3-methylurea, 1-(3,4,dichlorophenyl) urea, and N`-(3-chlorophenyl)-N,N-dimethyl urea. The latter is similar to monuron, which causes kidney and liver tumours in male rats (USEPA 2002).

There is no information available regarding the greatest source of exposure to diuron for New Zealanders (eg, dermal contact, inhalation, diet: food, water).

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included diuron, so typical concentrations in New Zealand drinking-waters are unknown.

Diuron has been found 10 times in groundwaters in the Waikato, ranging from 0.00003 to 0.0095 mg/L (MAF 2006).

Pesticide monitoring of groundwater conducted by Environment Canterbury has detected diuron on four occasions at one location in the Level Plain area in South Canterbury. The concentrations ranged from 0.00008–0.0003 mg/L (Close et al 2001).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Diuron occurred at 0.8 µg/L, ie, 0.0008 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Diuron was found in one sample at 0.21 µg/L, ie, 0.00021 mg/L.

Two water utilities in the US reported detecting diuron in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0049 mg/L.

### Removal methods

Diuron is adsorbed by activated carbon (Faust and Aly 1983), and is degraded well by ozone (Camel and Bermond 1998). Use of activated carbon following ozonisation should be considered to adsorb oxidation products. Chlorine also breaks down the diuron molecule.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Recommended analytical techniques

#### Referee method

Liquid/liquid extraction/liquid/solid extraction/high pressure liquid chromatography (EPA 553).

#### Some alternative methods

Liquid/liquid extraction/liquid/solid extraction/high pressure liquid chromatography–ultraviolet detection or high pressure liquid chromatography-mass spectrometer (EPA 8321B).

### Health considerations

Diuron is absorbed from the gastrointestinal and respiratory systems. In humans, it is metabolised within hours by hydroxylation and N-dealkylation, then excreted via the urine. Cows fed very low doses of diuron in their diets had small amounts of residues in whole milk. Cattle fed small amounts accumulated low levels of diuron in fat and muscle, liver, and kidney (EXTOXNET 1996).

#### Acute poisoning

Diuron is of low acute toxicity. Juveniles and animals on protein-deficient diets are more susceptible than adults to the toxic effects of diuron, based on LD50 results (Hayes 1982, cited in Health Canada 1989). The acute oral LD50 for rats is 3,400 mg/kg (RSocC 1987) which suggests a moderate to low acute oral toxicity when compared with other pesticides. Some signs of central nervous system depression have been noted at high levels of diuron exposure (EXTOXNET 1996).

#### Chronic exposure

Chronic effects attributed to moderate to high doses of diuron over time include changes in blood chemistry, increased mortality, growth retardation, abnormal blood pigment and anemia.

Daily low doses of diuron fed to female rats through three successive generations caused significantly decreased body weight of offspring in the second and third litters. The fertility rate remained unaffected. It is unlikely that diuron will cause reproductive effects in humans at expected levels of exposure.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.007 (0.006 pre-2005) mg/kg body weight, with a NOEL of 0.7 mg/kg bw from a 6-month dietary study in rats. This NOEL is based on reduced haemoglobin concentrations and increased reticulocytes. The ADI incorporates a safety factor of 100. The ARfD is 0.007 mg/kg bw based on a NOEL of 0.7 mg/kg bw/day from a six-month dietary study in rats. The ARfD incorporates a safety factor of 100. In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The reference dose or RfD (USEPA 2006/2009/2011) is 0.003 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.1 mg/L. The oral RfD had previously been 0.002 mg/kg/d (USEPA 1988).

EC (2008) established an ADI of 0.007 mg/kg/d and an ARfD of 0.016 mg/kg/d. EFSA (2011) reaffirmed these values.

Diuron is teratogenic at high doses but does not appear to be mutagenic. Limited evidence indicates that low level exposures to diuron does not cause cancer. Low doses of diuron over extended periods of time can cause enlargement to the liver and the spleen (EXTOXNET 1996). The USEPA calls diuron a known/likely human carcinogen. The USEPA (2009/2011) quotes a health advisory of 0.2 mg/L for diuron, representing a 10-4 cancer risk.

Diuron appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. The International Agency for Research on Cancer has not classified diuron for its potential to cause cancer.

For diuron there are no experimental data available that would support endocrine disruption properties of this pesticide. However, owing to the structural similarities between linuron and diuron and the common metabolite 3,4-DCA, an intrinsic endocrine potential may be expected (IUPAC 2003).

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used by the MoH for the derivation of the PMAV for diuron in drinking-water, as follows:

0.625 mg/kg body weight per day x 70 kg x 0.1 = 0.02 mg/L

2 L x 100

where:

* no observable adverse effect level = 0.625 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Dodine

CAS No. 2439-10-3. The IUPAC name for dodine is 1-dodecylguanidinium acetate. The CAS name is dodecylguanidine monoacetate.

Another active ingredient of similar chemical composition and properties, dodecylguanidine hydrochloride (DGH) – CAS No. 13590-97-1, has been included with some dodine products; DGH has only antimicrobial uses (USEPA 2005).

### Maximum Acceptable Value

Dodine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Dodine is an aliphatic nitrogen fungicide and bactericide, often used (first in 1955) to control scab on apples, pears and pecans, brown rot of peaches, and several foliar diseases of cherries, strawberries, peaches, and black walnuts, and for black spot on roses. It is also used as an industrial biocide and preservative. The compound works by changing the cell walls of the fungus, causing loss of the materials from within the cell (EXTOXNET 1993/1996).

Dodine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Dodecylguanidine hydrochloride (DGH) may be used in the treatment of paper that comes into contact with food, paint additives, and anti-bacterial treatment of diapers.

### Forms and fate in the environment

Dodine is quite soluble in water (about 900 mg/L). Despite its solubility, it binds strongly to soil so is unlikely to contaminate groundwater. Its soil half-life is 5 to 20 days. A significant metabolite is the natural product, creatine, and in some conditions, urea. Ultimately it mostly ends up as CO2.

Dodine is immobile and is generally not expected to persist in aerobic soils. Because of dodine’s high partitioning coefficient, the potential to reach drinking-water sources via run-off or leaching is limited. Based on a low estimated vapour pressure, volatilisation is an unlikely route of dissipation. Dodine may, however, be transported off-site to drinking-water sources as sediment or via spray drift during aerial, airblast or ground spray applications. Once in aquatic environments, dodine is resistant to hydrolysis and photolysis. In aerobic aquatic environments, dodine is likely to be moderately persistent. In anaerobic aquatic environments, dodine is likely to be very persistent. In the field, dodine was almost exclusively confined to the 0 to 6 inch depth of soils and is immobile in soil (sand, sandy loam, clay loam, and silt loam), regardless of organic matter content (USEPA 2005).

According to the laboratory degradation studies evaluated in the framework of the peer review, DT90 values of dodine ranges between 10.6–27.2 days (EFSA 2015).

NPIC (1994) quotes for dodine acetate a soil half-life of 20 days, water solubility of 700 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

None necessary, because no MAV.

### Health considerations

Dogs fed dodine for 12‑months exhibited histological changes in the thyroid indicative of thyroid stimulation. The NOEL in this study was 1.25 mg/kg. In a two-year feeding study, rats given dietary doses of 800 mg/kg exhibited slight retardation of growth, but no adverse effects on reproduction or lactation. Offspring of mice fed dodine in the diet exhibited decreased numbers of pups surviving to weaning (EXTOXNET 1993).

JMPR (IPCS 1974) derived an ADI of 0.01 mg/kg bw, based on the above dog study. The ADI was 0.01 mg/kg bw, and the RfD was 0.004 mg/kg/d (EXTOXNET 1996). The 2000 JMPR allocated an acceptable daily intake for humans of 0 to 0.1 mg/kg bw and an acute reference dose of 0.2 mg/kg bw (FAO 2003; JMPR 2003).

USEPA (2005) adopted a chronic dietary RfD of 0.02 mg/kg/d, based on a NOAEL of 2 mg/kg/d and an uncertainty factor of 100, based on body weight loss in female dogs. The oral RfD had previously been 0.004 mg/kg/d based on thyroid toxicity in a one-year dog feeding study (USEPA 1990). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.02 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for dodine is 0.14 mg/L (no acute one-day value available.)

EFSA (2013 and 2015) quotes an ADI of 0.1 mg/kg bw per day and an ARfD of 0.1 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted for dodine in Australia is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw.

Based on the weight of evidence it can be concluded that there is no evidence of carcinogenicity for dodine. In a mouse feeding study, females showed an increase in combined hepatocellular adenomas/carcinomas; however, when compared to historical controls the increase of incidence of combined tumours is marginal. In a rat feeding study there was no evidence of carcinogenicity (USEPA 2005).

Dodine does not appear to be mutagenic; the Ames test for mutagenicity was negative on five strains of bacteria.

### Derivation of Maximum Acceptable Value

No MAV.

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# Emamectin benzoate

CAS No. 155569-91-8, formerly 137512-74-4 and 179607-18-2. The IUPAC name is huge! The CAS name is (4″R)-4″-deoxy-4″-(methylamino)avermectin B1 benzoate (1:1).

The CAS No. for emamectin is 119791-41-2; formerly 137335-79-6 and 123997-28-4.

The minimum purity of emamectin benzoate as manufactured is 950 g/kg (sum of emamectin B1a benzoate and emamectin B1b benzoate), with a minimum content of emamectin B1a benzoate component of 920 g/kg and a maximum content of emamectin B1b benzoate component of 50 g/kg. At the moment no FAO specification exists. EFSA (2012) and EC (2013).

### Maximum Acceptable Value

Emamectin benzoate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Emamectin is the 4”-deoxy-4”-methylamino derivative of [abamectin](http://en.wikipedia.org/wiki/Abamectin), a 16-membered macrycyclic lactone produced by the fermentation of the soil [actinomycete](http://en.wikipedia.org/wiki/Actinomycete) Streptomyces avermitilis. It is generally prepared as the [benzoic acid](http://en.wikipedia.org/wiki/Benzoic_acid) [salt](http://en.wikipedia.org/wiki/Salt_(chemistry)). There is also a datasheet for [abamectin](http://en.wikipedia.org/wiki/Abamectin) (in the Bacteria section). The abamectin (also called avermectin) family of compounds exhibit toxicity for nematodes, arthropods, and several other pests, that acts by adversely affecting the nervous system. Emamectin has also shown promising applications in the eradication of fish lice and in fish farming.

Emamectin benzoate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Avermectin compounds, including emamectin, have proved useful in pharmaceutical applications such as treating human dermatological diseases.

### Forms and fate in the environment

Environmental effects are considered to be minimal due to the low application rate, as low as 6 g per acre.

Emamectin degrades very rapidly on a leaf surface to photo-metabolites. Emamectin benzoate soil half-life (in the dark) is 8 to 15 months (SITEM), and aqueous photolysis half-life is 4 to 11 days.

Fate and behaviour of emamectin benzoate B1a was investigated in two studies with three dark water sediment systems under aerobic conditions. Emamectin rapidly portioned to sediment in these experiments. Degradation was slow in both systems and no major metabolites were identified; EFSA (2012). The hydrolysis half-life of emamectin benzoate is 19.5 weeks at pH 9 and stable at pHs 5.2, 6.2, 7.2 and 8.2. Emamectin benzoate degraded on microbially active soil with a photolysis half-life of five days, degraded in natural water with an aqueous photolysis half-life of 3.6 days in summer sunlight, and 6.9 days in fall sunlight (PMEP 2000). Emamectin benzoate exhibits no mobility. Given the very low application rate, the short half-life for photolysis, the very high kocs and the results of the terrestrial field dissipation studies, it appears that this product will not impact groundwater.

See EFSA (2011) for metabolites.

Water solubility is about 20–40 mg/L.

### Recommended analytical techniques

#### Referee method

None necessary, because no MAV.

#### Some alternative methods

See EFSA (2011).

### Health considerations

The USEPA calculated an oral reference dose (RfD) for emamectin benzoate of 0.00025 mg/kg/d based on the no-observed-effect level (NOEL) from the subchronic neurotoxicity in mice (0.075 mg/kg/day) and an uncertainty factor of 300. This value has not yet been adopted by the USEPA’s *Integrated Risk Information System* (PMEP 2000). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.000075 mg/kg/d, and an ARfD of 0.00025 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for emamectin benzoate is 0.003 mg/L.

USEPA (2000) quotes an acute Rfd for avermectin B1 of 0.0025 mg/kg/d, and a chronic RfD (also = cPAD) of 0.0012 mg/kg/d.

NZFSA (2008) quotes an Acceptable Daily Intake (ADI) for emamectin benzoate of 0.002 mg/kg bw/day.

USEPA (2005) states that an acute reference dose (aRfD) for emamectin benzoate of 0.00025 mg/kg body weight/day for infants, children, and females 13 years and older was based upon a 0.075 mg/kg bwt/day NOAEL from a 15–day neurotoxicity study in mice, using an uncertainly factor of 100X. A chronic reference dose (cRfD) for emamectin benzoate of 0.000083 mg/kg bwt/day for infants, children, and females 13 years and older was based upon a 0.075 mg/ kg bwt/day NOAEL from a 15–day neurotoxicity study in mice, using an uncertainly factor of 100X.

The Acceptable Daily Intake (ADI) adopted in Australia for emamectin is 0.002 mg/kg body weight, with a NOEL of 0.25 mg/kg bw, and the ARfD is 0.0005 mg/kg bw.

The FAO/WHO 2011 JMPR meeting established an acceptable daily intake (ADI) for emamectin benzoate of 0–0.0005 mg/kg bw on the basis of an overall NOAEL of 0.25 mg/kg bw per day in the one-year and two-year rat studies, for increased body weight gain, triglyceride concentrations in serum and relative kidney weight at 1.0 mg/kg bw per day, and on the basis of an overall NOAEL of 0.25 mg/kg bw per day in 14- and 53-week toxicity studies in dogs, for histological changes in the brain, spinal cord and sciatic nerve and clinical signs of neurotoxicity at 0.5 mg/kg bw per day, using a safety factor of 500. An additional safety factor of 5 was applied to the default safety factor of 100, as a number of studies in mice, rats and dogs show steep dose–response curves and irreversible histopathological effects in neural tissue at the LOAEL. A NOAEL based predominantly on such histopathological changes is considered to be less sensitive than the observation of clinical signs. Moreover, in the one-year dog study, animals were killed in extremis at doses that were only three times higher than the NOAEL in this study. The meeting also established an acute reference dose (ARfD) of 0.03 mg/kg bw for emamectin benzoate, based on a NOAEL of 5 mg/kg bw for clinical signs of neurotoxicity (tremors and irritability) observed in an acute neurotoxicity study in rats at 10 mg/kg bw. A safety factor of 200 was applied, which includes a two-fold factor based on serious histopathological observations of degeneration of neurons in brain, spinal cord and sciatic nerve at 25 mg/kg bw. Observations of toxicity observed in neonatal rats in reproductive toxicity studies and a developmental neurotoxicity study were considered not relevant for setting an ARfD, as these effects are a direct consequence of low p-glycoprotein levels in the neonatal rat brain and incomplete development of the blood–brain barrier. In the developing human fetus, adult levels of p‑glycoprotein expression are attained by about 28 weeks of gestation, reflecting the integrity of the blood–brain barrier prior to birth.

JMPR (2014) reaffirmed the ADI; the acute RfD value (ARfD) was re-evaluated by the 2014 JMPR meeting which reduced the ARfD to 0.02 mg/kg bw expressed as emamectin benzoate.

EFSA (2011) provisionally refers to an ADI of 0.0025 mg/kg bw/day and an ARfD of 0.05 mg/kg bw for emamectin benzoate. EFSA (2012) quotes an ARfD value of 0.011 mg/kg as the benzoate. Based on the additional studies (EFSA 2018), the photodegradation metabolites included in the risk assessment residue definition were considered to be of the same or higher potency in comparison to the parent compound.

EC (2013) quotes an ADI of 0.0005 mg/kg/d for emamectin, and an ARfD of 0.01 mg/kg bw.

Emamectin benzoate did not cause oncogenic effects in either the rat or mouse studies. It also was negative in a number of genotoxicity tests. The USEPA classified emamectin benzoate as “not likely” to be a human carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Endosulfan

CAS No. 115-29-7. The IUPAC and CAS name for endosulfan is 1,4,5,6,7,7-hexachloro-8,9,10-trinorborn-5-en-2,3-ylenebismethylene sulfite, or 6,7,8,9,10,10-hexachloro-1,5,5a,6,9,9a-hexahydro-6,9-methano-2,4,3-benzodioxathiepine-3-oxide. It has also been called thiodan and benzoepin.

Endosulfan is a mixture of two isomers: α-endosulfan (CAS No. 959-98-8) and β‑endosulfan (CAS No. 33213-65-9), also called I-endosulfan and II-endosulfan, or the endo and exo isomers, usually in the ratio of about 70:30. The β form slowly and irreversibly converts to the α form. Endosulfan is considered as a single (homogenous) product in this datasheet. Both isomers are biologically active.

Endosulfan sulfate is a product of oxidation containing one extra O atom attached to the S atom. The CAS No. for endosulfan sulfate is 1031-07-8.

### Maximum Acceptable Value

WHO (2004/2011/2017) states that because endosulfan occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

WHO (2017) established a health based value of 0.02 mg/L.

In the 2005 DWSNZ, the provisional MAV for endosulfan in drinking-water had been 0.02 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Endosulfan sulfate and alpha-endosulfan and beta-endosulfan are “priority pollutants” under the US Clean Water Act.

Endosulfan and its related isomers were added to the Stockholm Convention list of Persistent Organic Pollutants (POPs); see <http://chm.pops.int/>. In 2007 endosulfan was recommended to be included in the Rotterdam Convention on Prior Informed Consent and in the list of chemicals banned under the Stockholm Convention on Persistent Organic Pollutants (POPs).

### Sources to water

Endosulfan is a chlorinated hydrocarbon insecticide of the cyclodiene subgroup. It is a derivative of [hexachlorocyclopentadiene](http://en.wikipedia.org/wiki/Hexachlorocyclopentadiene), and is chemically similar to [aldrin](http://en.wikipedia.org/wiki/Aldrin), [chlordane](http://en.wikipedia.org/wiki/Chlordane), and [heptachlor](http://en.wikipedia.org/wiki/Heptachlor). It acts as a non-systemic contact and stomach poison in a wide variety of insects and mites. It can also be used as a wood preservative. It is used primarily on food crops like tea, fruits, vegetables and on grains. In New Zealand the substance has been used to treat vegetable, ornamental and berry fruit crops. It had also been used for earthworm control at parks, sports grounds and sports clubs, although that use was not endorsed by suppliers of the product.

Endosulfan contamination does not appear to be widespread in the aquatic environment, but the chemical has been found in agricultural run-off and rivers in industrialised areas where it is manufactured or formulated, as well as in surface water and groundwater samples collected from hazardous waste sites in the USA.

Surface water samples in the USA generally contain less than 0.001 mg/L endosulfan.

Formulations containing endosulfan have been registered for use in New Zealand since 1963. The products containing endosulfan that are currently (up to 2008) registered for agricultural use in New Zealand are Flavylan 350EC, Thiodan, and Thionex Insecticide. Approval for the importation, manufacture and use of endosulfan and its formulations was revoked by ERMA, taking effect from 16 January 2009.

Because of its threats to human health and the environment, a global ban on the manufacture and use of endosulfan was negotiated under the [Stockholm Convention](http://en.wikipedia.org/wiki/Stockholm_Convention) in April 2011. The ban was to take effect in mid-2012, with certain uses exempted for five additional years. It is still used extensively in India, China, and few other countries. New Zealanders may remain exposed to endosulfan from imported tobacco products.

### Forms and fate in the environment

Endosulfan does not dissolve easily in water (solubility reported at 0.05–0.4 mg/L – solubility increases as pH drops). It adsorbs to soil particles readily. Transport of this pesticide is most likely occur if endosulfan is attached to soil particles in surface run-off. Large amounts of endosulfan can be found in surface water near areas of application. It has also been found in surface water at very low concentrations and has been detected in the air at minute levels. It has been found, but not quantified, in well water in California, however it is not expected to pose a threat to groundwater. Endosulfan has the potential for long-range transport.

In raw river water at room temperature and exposed to light, both isomers disappeared in four weeks. A breakdown product first appeared within the first week. Depending on the conditions in the water, endosulfan may break down within one day or it may take several months. The breakdown in water is faster (five weeks) under neutral conditions than at more acidic conditions (five months). The half-life is longer in anaerobic water. In water, endosulfan is mainly degraded to endosulfan diol. Under strongly alkaline conditions the half-life of the compound is one day.

The two isomers have different degradation times in soil. The half-life for the alpha isomer is 35 days and 150 days for the beta isomer under neutral conditions. These two isomers will persist longer under more acidic conditions. The compound is broken down in soil by fungi and by bacteria.

The breakdown product, endosulfan sulfate, has been observed in several field studies involving plants. The sulfate is even more persistent than the parent compound, accounting for 90 percent of the residue in 11 weeks. Sulfate formation increases as temperatures increase. However, sunlight may play a role in the reaction, perhaps in starting the process. On most fruits and vegetables, 50 percent of the parent residue is lost within three to seven days.

If released to soil, endosulfan is expected to have moderate to no mobility based upon Koc values of 350 to 19,953. Volatilisation from moist soil surfaces may be an important fate process based upon a Henry’s Law constant of 6.5 x 10-5 atm-cu m/mole, however, adsorption to soil may attenuate volatilisation. Endosulfan is not expected to volatilise from dry soil surfaces based upon its vapour pressure. Biodegradation may be an important environmental fate process with reported half-lifes of 32 and 150 days in aerobic and anaerobic soils, respectively. If released into water, endosulfan is expected to adsorb to suspended solids and sediment based upon the Koc values. Biodegradation in water is expected to be an important fate process with reported half-lives of two and eight days in aerobic and anaerobic waters, respectively. Volatilisation from water surfaces may be an important fate process based on its Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 33 hours and 16 days, respectively. However, volatilisation from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. Measured BCF values of 2,650 and 11,583 suggests bioconcentration in aquatic organisms is very high. Hydrolysis is expected to be an important environmental fate process with half-lifes of 9 to 533 hours in river water (EAWAG accessed February 2015).

If released to soil, endosulfan sulfate is expected to be immobile based upon an estimated Koc of 3.2 x 10+4. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 1.2 x 10-11 atm-cu m/mole. Endosulfan sulfate is expected to biodegrade slowly in soils based on its degradation in four soils, a Pliocene sand, an organic-rich orchard soil, an agricultural soil and soil from a volcanic area, with a half-life in each of 164, 157, 150, and 134 days, respectively. If released into water, endosulfan sulfate is expected to adsorb to sediment and suspended solids in water based upon the estimated Koc. Biodegradation of endosulfan sulfate in water is expected to be slow based on its degradation in soil. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 130 suggests the potential for bioconcentration in aquatic organisms is high. Based on a microcosm experiment in which 22 percent of initial concentration of endosulfan sulfate in water (pH not specified) degraded after 33 days suggests hydrolysis may be important. This degradation rate would correspond to a minimum hydrolysis half-life of 178 days (EAWAG accessed February 2015).

NPIC (1994) quotes for endosulfan a soil half-life of 50 days, water solubility of 0.32 mg/L and a sorption coefficient (soil Koc) of 12,400. This resulted in a pesticide movement to groundwater rating of extremely low. Its GUS score is -0.17, indicating that it should not leach to groundwater.

### Typical concentrations in drinking-water

Endosulfan has been found in groundwater in Tasman District, at 0.000031 mg/L (MAF 2006). A 2004 Environment Waikato study detected 0.004 to 0.005 mg/L of endosulfan in groundwater in the lower Waikato region.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Endosulfan I occurred at 0.031 µg/L, ie, 0.000031 mg/L.

Endosulfan was found in three bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008):

* 0.000008 mg/L endosulfan 1
* 0.000003 and 0.000019 mg/L endosulfan 2
* 0.000026 mg/L endosulfan sulphate.

The bores were in the Waikato region.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Endosulfan I was found in one sample, at 0.01 µg/L. Endosulfan II occurred at 0.022 µg/L. Endosulfan sulphate occurred at 0.075 µg/L.

One water utility in the US reported detecting endosulfan I in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

One water utility in the US reported detecting endosulfan II in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

One water utility in the US reported detecting endosulfan sulfate in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of endosulfan in water. Activated carbon and ozone treatment are also effective.

### Recommended analytical techniques

#### Referee method

None necessary, because no MAV now.

#### Some alternative methods

Extraction from water with methylene chloride followed by gas chromatography combined with electron capture detection. In considering residue levels, the sum of the α- and β- isomers plus the endosulfan sulfate metabolite, which is similar in toxicity to the parent compound, have to be considered. Detection limits are 0.000015 mg/L for α- endosulfan, 0.000024 mg/L for β-endosulfan and 0.000015 mg/L for endosulfan sulfate (ATSDR 2000).

### Health considerations

The main source of exposure of the general population is food, but generally residues have been found to be well below the FAO/WHO maximum residue limits. Another important route of exposure to endosulfan for the general population is the use of tobacco products.

Acute human exposure to organophosphate pesticides (including endosulfan) has been shown to result in the following symptoms: headache, giddiness, nervousness, blurred vision, weakness, nausea, cramps, diarrhoea, and discomfort in the chest. Signs include sweating, miosis, tearing, salivation and other excessive respiratory tract secretion, vomiting, cyanosis, papilledema, uncontrollable muscle twitches followed by muscular weakness, convulsions, coma, loss of reflexes, and loss of sphincter control. The last four signs are seen only in severe cases but do not preclude a favourable outcome if treatment is prompt and energetic. Cardiac arrhythmias, various degrees of heart block, and cardiac arrest may occur (Hayes and Laws). Endosulfan is most likely to affect kidneys, liver, blood chemistry and the parathyroid gland. Endosulfan primarily affects the nervous system. Toxic effects observed in animals from acute, subchronic, developmental neurotoxicity, and chronic/carcinogenic toxicity studies found that endosulfan causes neurotoxic effects, which are believed to result from over-stimulation of the central nervous system. Further, there is evidence (effects observed in a submitted chronic oral toxicity study in rats) that endosulfan acts as an endocrine disruptor (USEPA 2002).

The USEPA considers that for exposure resulting from applications of endosulfan, the most exposed population subgroup is children 1–6 years old. Endosulfan sulfate shows toxicity similar to that of endosulfan

In a summary of case reports of human poisoning incidents, the lowest reported dose that caused death was 35 mg/kg of body weight. Higher doses caused death within one hour. The clinical signs in these patients were dominated by tonic-clonic convulsions, consistent with the observations in experimental animals.

The oral RfD for endosulfan was calculated at 0.006 mg/kg/d (USEPA (1994). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.006 mg/kg/d, and an ARfD of 0.015 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for endosulfan is 0.15 mg/L.

The 1998 JMPR Meeting established an ADI of 0–0.006 mg/kg bw and an acute reference dose (ARfD) of 0.02 mg/kg bw. Residues are to be reported as the sum of alpha endosulfan, beta endosulfan and endosulfan sulfate.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.006 mg/kg body weight, with a NOEL of 0.57 mg/kg bw for decreased bodyweight gain in a 12-month dietary study in dogs, and a NOEL of 0.66 mg/kg bw/day for decreased bodyweight gain and damage to kidney tissue in long-term studies in rodents and a developmental study in rats. The ADI incorporates a safety factor of 100. The ARfD is 0.02 mg/kg bw.

As at August 2015 ATSDR (<http://www.atsdr.cdc.gov/mrls/pdfs/atsdr_mrls.pdf> ) quotes a minimal risk level (MRL) for endosulfan of:

* 0.007 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.005 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.005 mg/kg/day for chronic-duration oral exposure (>364 days).

JMPR concluded that endosulfan is not genotoxic, and no carcinogenic effects were noted in long-term studies using mice and rats. The kidney is the target organ for toxicity. Several recent studies have shown that endosulfan, alone or in combination with other pesticides, may bind to estrogen receptors and perturb the endocrine system.

Endosulfan is not classified as to its carcinogenicity to humans, and is not mutagenic in animal studies. Endosulfan exhibits weak oestrogenic activity, but no reproducible evidence of an effect in vivo. Several recent studies have shown that endosulfan, alone or in combination with other pesticides, may bind to estrogen receptors and perturb the endocrine system.

### Derivation of Maximum Acceptable Value

WHO (2004/2011/2017) states that endosulfan usually occurs at concentrations in drinking-water well below those at which toxic effects can be expected to occur, and it is therefore not considered necessary to derive a guideline value for endosulfan in drinking-water.

A health-based value of 20 μg/L can be calculated for endosulfan on the basis of an ADI of 0–0.006 mg/kg body weight, based on results from a two-year dietary study of toxicity in rats and supported by a 78-week study in mice, a one-year study in dogs and a developmental toxicity study in rats (WHO 2017).

In DWSNZ 2005, the MAV for endosulfan in drinking-water had been derived as follows:

0.006 mg/kg body weight per day x 70 kg x 0.1 = 0.021 mg/L (rounded to 0.02 mg/L)

2 L

where:

* allowable daily intake (ADI) = 0.006 mg/kg body weight based on results from a two-year dietary study of toxicity in rats, and supported by a 78-week study in mice, a one-year study in dogs, and a developmental toxicity study in rats
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult per day = 2 L.

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# Endothal

CAS No. 145-73-3 (the acid form); Aquathol K is 2164-07-0. The IUPAC and CAS name for endothal is 7-oxabicyclo[2.2.1]heptane-2,3-dicarboxylic acid. Endothall acid is described as 3,6-endoxohexahydrophthalic acid or 3,6-epoxy-cyclohexane-1,2-dicarboxylic acid. Sometimes spelt endothall.

### Maximum Acceptable Value

Endothal is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

There is a maximum contaminant level (MCL) in the US of 0.1 mg/L. The USEPA (2006/2009/2011) established a lifetime health advisory of 0.05 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2016) include a guideline value of 0.1 mg/L. While the health-based guideline is based on long-term effects, there is potential for effects on the gastrointestinal tract after short-term exposure at levels two to three times higher than the health-based guideline. Therefore, excursions above this level even for a short period are of concern.

EPA established an environmental exposure limit of 0.086 mg/L (86 µg/L) for potassium endothal in fresh water which is equivalent to 0.061 mg/L as endothal acid (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Endothal is a selective contact dicarboxylic acid herbicide that inhibits protein synthesis in plants. The potassium and amine salts are used as aquatic herbicides to control a variety of plants including plankton, pondweed, niad, coontail, milfoil, elodea, and algae in water bodies and rice fields. Endothall is also used to control annual grass and broadleaf weeds in sugar beets, spinach and turf. It reduces sucker branch growth in hops. Endothall is a desiccant to aid the harvest of alfalfa, potatoes, clover, and cotton. It has also been used as a biocide in cooling towers. The USEPA has classified endothall as Toxicity Class II – moderately toxic.

Endothal is often applied as a salt, eg, the dipotassium product (CAS No. 2164-07-0).

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Endothall is one of two herbicides (diquat is the other) registered for aquatic use in New Zealand. The a.i. is the dipotassium salt of endothall and it is marketed as two formulations; Aquathol® K (aqueous) and Aquathol® Super K (pellets). Endothall is contact herbicide that affects protein synthesis and auxin production (plant growth hormone). Endothall is used for submerged aquatic weed control (Auckland City 2013).

Endothal appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. A product used in New Zealand is called aquathol K. Aquathol Super K is 63 percent of dipotassium salt of endothall and 28 percent 2-propenamide polymer with potassium; acrylamide is a trace contaminant.

ERMA (2018) approvals HSR000946 and HSR000947 are modified to delete the following label statements from the 77A label control:

Warnings regarding the following restrictions on the use of treated water shall be stated on the labels of Aquathol K and Aquathol Super K:

* The following withholding periods shall apply to the taking of water for drinking, watering livestock, or preparing agrichemical sprays or irrigation, unless it can be shown that the water at the point of take has concentrations of dipotassium endothal below the TEL water and EEL water values established as applicable:
* 7 days following application with up to and including 0.5 mg/L dipotassium endothal
* 14 days following application with up to and including 4.25 mg/L dipotassium endothal
* 25 days following application with up to and including 5 mg/L dipotassium endothal.
* No taking of fish for consumption or use as feed within three days of application of the substance.

### Forms and fate in the environment

Endothal is highly mobile in soil, however rapid degradation limits the extent of leaching to groundwater. Endothal is rapidly degraded in water to carbon dioxide and other non-toxic substances. Its half-life is four to seven days for dipotassium endothall and about seven days for technical endothall in surface water. The degradation rate is somewhat dependant on the microbiological content of the water and sediments. It biodegrades more slowly in anaerobic conditions. Water solubility is about 10 percent. Water solubility of Aquathol is about 100 percent.

NPIC (1994) quotes for endothall salt a soil half-life of seven days, water solubility of 10 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

Twelve water utilities in the US reported detecting endothall in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.19 mg/L. This result is something of an outlier – the next highest was 0.014 mg/L.

### Removal methods

The weak soil adsorption and high solubility suggest that treatment processes that remove particulate matter should be ineffective at reducing the concentration of endothal in water. Endothal can be removed from drinking water using granular activated carbon.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

An example: USEPA 548.1 (<http://www.accustandard.com/asi/pdfs/epa_methods/548_1.pdf>)

### Health considerations

No adverse reproductive effects were observed (NOEL) at 5 mg/kg/day. Technical endothall was not teratogenic at the highest dose tested, 30 mg/kg/day. No statistically significant numbers or types of tumours were observed in rats fed as much as 125 mg/kg/day of disodium endothall for two years (EXTOXNET 1995).

The New York State (PMEP 2008) states:

“In order to allow for sufficient mixing of this product after application to bodies of water, swimming in the treated area is restricted until the day after application.”

Following endothall application, ERMA New Zealand imposed a three-day restriction on the taking of fish for consumption, and a 24-hour swimming restriction. For water treated at 5 ppm, there is a 25-day withholding period for water takes for domestic drinking or livestock supply unless it can be shown that the water at the point of take has concentrations below the tolerable exposure limit (TEL) water and environmental exposure limit (EEL) water, values established in the ERMA decision of 2004. The TEL water has been set at 0.28 mg/L dipotassium endothall (equivalent to 0.20 mg/L endothall acid) and the EEL water has been set at 0.086 mg/L dipotassium endothall (equivalent to 0.061 mg/L endothall acid). ERMA approval is required to use endothall in a waterbody (stated in NIWA 2008).

Endothall is not a neurotoxicant, nor does it induce developmental toxicity. Endothall is classified as “not likely to be carcinogenic to humans” and has no mutagenic potential. Endothall does not bioaccumulate (USEPA 2005).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 3.75 mg/kg bw from a long-term (one-year) study in dogs. This NOEL is based on liver necrosis and stomach hyperplasia and hyperkeratosis. The ADI incorporates a safety factor of 100.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.007 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.25 mg/L. The oral RfD had previously been 0.02 mg/kg/d based on increased absolute and relative weights of stomach small intestine in a two-year dog feeding study (USEPA 1991).

### Derivation of Maximum Acceptable Value

No MAV.

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# Endrin

CAS No. 72-20-8. The IUPAC name for endrin is (1R,4S,4aS,5S,6S,7R,8R,8aR)-1,2,3,4,10,10-hexachloro-1,4,4a,5,6,7,8,8a-octahydro-6,7-epoxy-1,4:5,8-dimethanonaphthalene, or 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a,5,6,7,8,8a-octahydro-exo-1,4-exo-5,8-dimethanonaphthalene. The CAS name is (1aR,2R,2aR,3R,6S,6aS,7S,7aS)-rel-3,4,5,6,9,9-hexachloro-1a,2,2a,3,6,6a,7,7a-octahydro-2,7:3,6-dimethanonaphth[2,3-b]oxirene.

The CAS No. for endrin aldehyde is 7421-93-4. Endrin ketone can also be found: CAS No. 53494-70-5.

### Maximum Acceptable Value

Based on health considerations, the concentration of endrin in drinking-water should not exceed 0.001 mg/L.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.002 mg/L. The USEPA (2006/2009/2011) also established a lifetime health advisory of 0.002 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

Endrin and endrin aldehyde are “priority pollutants” under the US Clean Water Act.

Endrin is one of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention; see <http://chm.pops.int/>.

### Sources to water

Endrin was a broad-spectrum contact and stomach poison used as a foliar organochlorine insecticide that acted against a wide range of agricultural pests. It was also used as a rodenticide. Small amounts of endrin can still be present in food, but the total intake from food has greatly decreased. Technical endrin was up to 92 percent pure. Impurities included aldrin, dieldrin, isodrin, endrin half-cage ketone, endrin aldehyde and heptachloro-norbornene.

Being a Persistent Organic Pollutant, it is not currently registered for use in New Zealand. It had previously been used in sheep dips.

### Forms and fate in the environment

Because endrin is not very soluble (about 0.2 mg/L, and the aldehyde about 0.05 mg/L), the most important route of water contamination is due to surface run-off from soil and crops. Run-off is affected by numerous, complex factors, such as intensity of precipitation, irrigation practices, soil permeability, topographic relief, organic content of the soil, and the degree of vegetative cover. Soils of low permeability and low organic content allow copious run-off after heavy precipitation.

Although endrin has strong absorptive properties in soils such as clay and sandy loam, limited residues were found. Far greater retention was found in soils with a high organic content, in which it was adsorbed quickly and was difficult to remove. The degree to which endrin was retained in the soil depended not only on the soil type but on numerous other factors such as volatilisation, leaching, wind erosion, surface run-off, and crop uptake Its half-life in soil can be as long as 14 years.

NPIC (1994) quotes for endrin a soil half-life of 4,300 days, water solubility of 0.23 mg/L and a sorption coefficient (soil Koc) of 10,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

In an area of the US that was treated with endrin, the mean residue levels in water samples was 0.0004 mg/L (IPCS).

Traces of endrin have been found in the drinking-water supplies of several countries (WHO 2004).

Twenty-five water utilities in the US reported detecting endrin in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0027 mg/L.

One water utility in the US reported detecting endrin aldehyde in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the concentration being 0.00002 mg/L.

### Removal methods

A concentration of endrin of 0.0002 mg/L should be achievable using GAC (WHO 2017). The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of endrin in water.

### Recommended analytical techniques

#### Some alternative methods

Endrin in water can be determined by extraction with hexane/ether followed by gas chromatography with electron capture detection. The detection limit is about 0.000002 mg/L (WHO 2004).

### Health considerations

Little is known about the properties of endrin aldehyde, an impurity and breakdown product of endrin, or endrin ketone, which is a product of endrin when it is exposed to light.

Unlike dieldrin, its stereoisomer, endrin is metabolised rapidly by animals, and very little is accumulated in fat in comparison with compounds of similar chemical structure. The primary site of action of endrin is the central nervous system.

The Tolerable Daily Intake (TDI) adopted in Australia is 0.0002 mg/kg body weight.

The reference dose or RfD (USEPA 1991/2006/2009/2011) is 0.0003 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.01 mg/L.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for endrin of:

* 0.002 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0003 mg/kg/day for chronic-duration oral exposure (>364 days).

Toxicological data are insufficient to indicate whether endrin is a carcinogenic hazard to humans. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

The MAV for endrin in drinking-water was derived as follows:

0.025 mg/kg body weight per day x 70 kg x 0.1 = 0.000875 mg/L (rounded to 0.001 mg/L)

2 L x 100

where:

* no-observable-adverse-effect level = 0.025 mg/kg body weight per day based on a two-year study in dogs
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult per day = 2 L
* uncertainty factor = 100 for intra- and interspecies variation.

Endrin is listed under the Stockholm Convention on Persistent Organic Pollutants. Hence, monitoring may occur in addition to that required by drinking-water guidelines.

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# Epoxiconazole

CAS No. 133855-98-8 (formerly 106325-08-0). The IUPAC name for epoxiconazole is (2RS,3SR)-1-[3-(2-chlorophenyl)-2,3-epoxy-2-(4-fluorophenyl)propyl]-1H-1,2,4-triazole. The CAS name is rel-1-[[(2R,3S)-3-(2-chlorophenyl)-2-(4-fluorophenyl)oxiranyl]methyl]-1H-1,2,4-triazole.

The structure would suggest that there is a possibility of diastero isomers, however epoxiconazole as defined by the ISO common name consists of only one of the possible pairs. Therefore epoxiconazole consists of one pair of enantiomers and it is racemic.

### Maximum Acceptable Value

Epoxiconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Epoxiconazole is a conazole (triazole) fungicide. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Epoxiconazole is fairly persistent in soil and water, and tends to adhere to soil particles so should not readily leach to groundwater. The half-life in soils is 20–70 days, and  
11–20 days in water. The DT90 is >1 year. Some sources quote >1,000 days. Epoxiconazole shares common metabolites with other triazole-derivative chemicals, including free triazole (1,2,4-triazole) and triazole-conjugated plant metabolites (such as triazole alanine and triazole acetic acid). These common metabolites have been the subject of separate risk assessments (USEPA 2005).

Water solubility is about 8 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The acceptable daily intake (ADI) for epoxiconazole is 0.008 mg/kg. The chronic reference dose (RfD) is 0.02 mg/kg/day, the ADI is 0.008 mg/kg/d, and the acute reference dose is 0.023 mg/kg/d (US and EC). But in Australia (APVMA 2002): an acceptable daily intake (ADI) of 0.01 mg/kg/day is recommended based on no observed effect levels (NOEL) of approximately 1 mg/kg/day in an 18-month study in mice and a 12‑month study in dogs, and applying a 100-fold safety factor. An acute reference dose (ARfD) of 0.2 mg/kg/day is recommended based on a NOEL of 15 and 20 mg/kg/day for embryotoxicity in rats and rabbits, and applying a safety factor of 100. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EFSA (2018) quotes an ADI of 0.008 mg/kg bw per day and an ARfD of 0.23 mg/kg bw. See datasheet for triazole metabolites for latest ADI and ARfD.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.02 mg/kg/d, and an ARfD of 0.05 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for epoxiconazole is 1.65 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

The USEPA (2006) considers epoxiconazole to be a likely human carcinogen by the oral route based on the occurrence of liver tumours in male and female mice. It is a suspected endocrine disruptor.

### Derivation of Maximum Acceptable Value

No MAV.

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# Esfenvalerate

CAS No. for esfenvalerate is 66230-04-4. The IUPAC name for esfenvalerate is (S)‑α‑cyano-3-phenoxybenzyl (S)-2-(4-chlorophenyl)-3-methylbutyrate. The CAS name is (S)-cyano(3-phenoxyphenyl)methyl (αS)-4-chloro-α-(1-methylethyl)benzeneacetate. Esfenvalerate is the purified SS-isomer of fenvalerate.

Some commercial products are no more than 75 percent esfenvalerate, and may contain xylene or ethylbenzene.

CAS No. for fenvalerate (called pydrin in the US) is 51630-58-1. Fenvalerate was the first synthetic pyrethroid having no cyclopropane ring in the molecule. Fenvalerate is a mixture of four stereoisomers (RR, RS, SR, SS) due to the two asymmetric carbon atoms in the molecule; they occur in roughly equal amounts. It has an α-cyanogroup on the 3-phenoxybenzyl alcohol and is a type II pyrethroid. The SS stereoisomer is the most biologically active and is sold as esfenvalerate (CAS No. 72650-28-3). Technical fenvalerate is usually 90–94 percent pure.

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.03 mg/L for esfenvalerate; minor excursions above this level would need to occur over a relatively long period to be a health concern, as the health-based guideline is based on medium-term effects.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.06 mg/L for fenvalerate; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Fenvalerate and esfenvalerate are broad-spectrum pyrethroid insecticides.

Esfenvalerate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

JMPR (2002) discussed the degradation of esfenvalerate in soils. Estimated half-lifes of esfenvalerate were in the range 36–59 days (other studies 80–90 days and up to 170 days in sandy loam) and of fenvalerate 35 and 48 days. The behaviour of esfenvalerate and fenvalerate was very similar.

NPIC (1994) quotes for esfenvalerate a soil half-life of 35 days, water solubility of 0.002 mg/L and a sorption coefficient (soil Koc) of 5,300. This resulted in a pesticide movement to groundwater rating of very low.

Degradation of fenvalerate in the environment is fairly rapid with half-lifes of 4 to 15 days in natural water, 8 to 14 days on plants, 1 to 18 days on soil, and 15 days to three months in soil. The stability of fenvalerate in sunlight allows its application against a wide range of pests. There is virtually no leaching of fenvalerate in the soil. Thus, it is unlikely that the compound will reach significant levels in the aquatic environment (IPCS HSG 1989). NPIC (1994) quotes for fenvalerate a soil half-life of 35 days, water solubility of 0.002 mg/L and a sorption coefficient (soil Koc) of 5300. This resulted in a pesticide movement to groundwater rating of very low.

In satisfactory field dissipation studies carried out at 11 sites across Europe (spray application to the soil surface on bare soil plots in summer and autumn) esfenvalerate exhibited very low to medium persistence. The potential for groundwater exposure was concluded to be low (EFSA 2014).

EFSA (2011) includes a list of esfenvalerate metabolites.

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

USEPA (2001) developed a chronic RfD of 0.02 mg/kg/d for esfenvalerate and 0.025 for fenvalerate. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0018 mg/kg/d, and an ARfD of 0.0018 mg/kg/d for esfenvalerate. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for esfenvalerate is 0.018 mg/L.

The Acceptable Daily Intakes (ADI) adopted in Australia are 0.008 mg/kg body weight, with a NOEL of 7.5 mg/kg bw for esfenvalerate, and 0.02 mg/kg body weight, with a NOEL of 1.7 mg/kg bw for fenvalerate.

The FAO/WHO JMPR 2012 meeting reaffirmed the ADI of 0–0.02 mg/kg bw for fenvalerate on the basis of a parental systemic toxicity NOAEL of 1.7 mg/kg bw per day observed in the three-generation reproduction study in rats, based on reduced mean body weights seen at 16.7 mg/kg bw per day and using a safety factor of 100. This ADI was supported by the NOAEL of 3.5 mg/kg bw per day observed in the long-term toxicity and carcinogenicity studies in mice, based on the slight decrease in erythrocyte counts, increased histiocytes and granulomatous changes in the liver and lymph nodes (mesenteric, visceral and peripheral) at 7.5 mg/kg bw per day.

The JMPR meeting established an acute reference dose (ARfD) of 0.2 mg/kg bw for fenvalerate on the basis of the NOAEL of 20 mg/kg bw observed in the single oral dose neurotoxicity study in rats, based on clinical signs of toxicity (muscular fibrillation, ataxia, salivation and/or hunched posture) seen at 90 mg/kg bw and using a safety factor of 100. This ARfD was supported by the developmental toxicity study in mice in which the NOAEL was 15 mg/kg bw per day, based on irregular respiration, hypersensitivity, tremors and salivation after administration of the compound (first  
30–60 minutes after dosing) seen at 50 mg/kg bw per day. In view of the closely related chemical composition of fenvalerate and esfenvalerate the meeting decided as an exception to apply its 2002 evaluation of esfenvalerate for decision making on fenvalerate without reiterating review of study data already reported.

The EC quote 0.02 and 0.05 mg/kg/d for the ADI and ARfD respectively for esfenvalerate.

EFSA (2014) changed both these values to 0.0175 mg/kg/d, based on the rat acute neurotoxicity study and applying an uncertainty factor of 100.

IARC has classified deltamethrin, fenvalerate and permethrin as Class 3 (not classifiable as to its carcinogenicity to humans).

USEPA (2015) found that there is no convincing evidence for a potential interaction with the estrogen or androgen pathways. For the thyroid pathway, the available Tier 1 EDSP assays and OSRI for esfenvalerate do not indicate a potential for thyroid interaction in mammals. However the weight-of-evidence cannot conclude whether esfenvalerate has the potential for thyroid interaction in non-mammalian species.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Ethanedinitrile

CAS No. 460-19-5. The IUPAC name for ethanedinitrile is oxalonitrile. It is also called EDN, carbon nitride, oxalyl cyanide, cyanogen, dicyan, oxalic acid dinitrile, dicyanogen, nitriloacetonitrile, N≡C−C≡N and various trade names.

### Maximum Acceptable Value

Ethanedinitrile does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Ethanedinitrile, C2N2, a new product developed by CSIRO, is used mainly as a fumigant to control pests in grains, timber, logs, and soil (particularly used for strawberries). It is sold as a compressed gas. Ethanedinitrile does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at January 2012 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register), but its use is under consideration (in 2018) as an alternative to methyl bromide (bromomethane, qv).

### Forms and fate in the environment

Ethanedinitrile degrades to release hydrogen cyanide, cyanates and other compounds ultimately degrading to compounds such as ammonia, carbon monoxide and carbon dioxide . Hydrogen cyanide is already an approved fumigant in New Zealand. Residues in soil and grain have been investigated and no cause for concern was identified when the substance is used for the proposed fumigant applications and recommended concentrations. Ethanedinitrile rapidly degrades on exposure to free moisture and is hydrolysed to oxalic acid and ammonia at high pH, and to formic acid and hydrogen cyanide at low pH. Breakdown in the presence of moisture is the most important degradation pathway in soil. The cyanide compounds are also degraded by micro-organisms in the soil. Ethanedinitrile is not expected to leach beyond 20 cm from the point of release because it rapidly hydrolyses to breakdown products. Its half-life period in soil is four to eight hours (EPA 2012).

MSDS sheets state that EDN is very toxic to aquatic organisms, and may cause long-term adverse effects in the aquatic environment.

Volatilisation is expected to be the predominant fate process for EDN in water. The main pathways for degradation of ethanedinitrile in water are likely to be hydrolysis to cyanide and cyanate followed by microbial conversion to ammonium and methanoate (formate). Water solubility: 450 mL of the gas dissolves in 1 litre of water (ie, 45 percent v/v); also reported at 10 g/L, ie, 1 percent w/v. Note that 1 mg/L = 470 ppm (ie, v/v).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Being in the form of a gas, the oral exposure route is not expected. It readily undergoes reduction to [cyanide](http://en.wikipedia.org/wiki/Cyanide).

In animals, rats and monkeys, no haematological, musculoskeletal, cardiovascular effects, no histopathological changes in eg, kidneys, liver, thyroid, spleen, heart, lungs, bone marrow, cerebellum, cerebrum or changes in T3 and T4 were found exposed to 25 ppm cyanogen (12.5 ppm cyanide) six hours/day, five days/week, for six months.

No respiratory effects were reported in rats exposed to 25 ppm cyanogen (12.5 ppm cyanide) six hours/day, five days/week, for six months and a decrease in total lung moisture content was the only finding in monkeys exposed to 11 ppm cyanogen (5.5 ppm cyanide), also for six months. Decreased body weight was reported in rats exposed to 25 ppm cyanogen (12.5 ppm cyanide) six hours/day, five days/week for six months. Only transitory behavioural changes were reported in monkeys exposed to 25 ppm cyanogen (12.5 ppm cyanide) for six months. No effects were found at 11 ppm cyanogen (5.5 ppm cyanide) exposure. NOAEL ≥ 25ppm C2N2 corresponding to daily doses ≥4.7 mg and 5.2 mg CN /kg bw in monkeys and rats, respectively, in a 180‑day inhalation study (EPA(2018).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Ethion

CAS No. 563-12-2. The IUPAC name for ethion is O,O,O′,O′-tetraethyl S,S′-methylene bis(phosphorodithioate). The CAS name is S,S′-methylene bis(O,O-diethyl phosphorodithioate). Sometimes called diethion.

### Maximum Acceptable Value

Ethion does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Ethion is a non-systemic aliphatic organothiophosphate acaricide and insecticide.

Ethion appears on EPA’s 27 June 2013 list of organophosphate and carbamate (OPC) pesticides which no longer are able to be manufactured in or imported into New Zealand. There did not appear to be any current usage of the product in New Zealand.

### Forms and fate in the environment

Ethion adsorbs strongly to soil particles and it is nearly insoluble in water (1 to 2 mg/L). It is therefore unlikely to leach or contaminate groundwater. In soil, ethion is subject to microbial degradation. It is resistant to hydrolysis, except in alkaline conditions: pH 9 or above (in EXTOXNET 1993).

If released to soil, ethion is expected to have no mobility based upon a Koc of 15,435. Volatilisation from moist soil surfaces is not expected to be an important fate process based on an estimated Henry’s Law constant of 3.8 x 10-7 atm-cu m/mole. Ethion will not volatilise from dry soil surfaces based upon its vapour pressure. The half-life of ethion in sterile sandy loam and organic soil was found to be greater than 24 weeks while the half-life in the nonsterile soils was seven to eight weeks. The half-life in red, black, and laterite soil was 9.0 to 15.5 days in the laboratory. If released into [water](https://pubchem.ncbi.nlm.nih.gov/compound/water), ethion is expected to adsorb to suspended solids and sediment based upon the Koc. Biodegradation in canal and marsh waters occurs with half-lifes ranging from 12 to 16 weeks. Volatilisation from [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 1600 suggests the potential for bioconcentration in aquatic organisms is very high. The hydrolysis half-lifes of ethion in distilled [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) ranged from 20.8 weeks to one day at pHs 4 to 10 at 30°C, and 99 to 8.4 weeks at pHs 4.5 to 8 at 25°C. NIH (accessed June 2016).

Water solubility is 0.6 mg/L; partition coefficient = Kow = 5.07; Koc about 4; Henry’s Law constant = 6.9 x 10-7 atm m3/mole (ATSDR 2000).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In a chronic toxicity study with rats fed 0, 0.1, 0.2 or 2 mg/kg/day for 18 months, decreased cholinesterase levels occurred in the high dose group. No other toxic effects were observed. The NOEL for this study was 0.2 mg/kg. A three-generation reproduction study with rats given dietary doses as high as 1.25 mg/kg/day did not show any ethion related reproductive effects. Once in the bloodstream, ethion may cross the placenta. No evidence of carcinogenicity was observed in mice fed dietary doses of up to 1.2 mg/kg/day for two years (from EXTOXNET 1993).

ATSDR (2000) reports a reference dose (RfD) of 0.0005 mg/kg/d, and oral minimal risk levels (MRLs):

An MRL of 0.002 mg/kg/day has been derived for intermediate-duration oral exposure (15–364 days) to ethion. This MRL is also applicable to acute-duration (14 days or less) oral exposure to ethion.

An MRL of 0.0004 mg/kg/day has been derived for chronic-duration (365 days or more) oral exposure to ethion.

FAO (1994) reports an ADI of 0.002 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted in Australia for ethion is 0.001 mg/kg body weight, with a NOEL of 0.1 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Ethofumesate

CAS No. 26225-79-6. The IUPAC name for ethofumesate is (RS)-2-ethoxy-2,3-dihydro-3,3-dimethylbenzofuran-5-yl methanesulfonate. The CAS name is 2-ethoxy-2,3-dihydro-3,3-dimethyl-5-benzofuranyl methanesulfonate. Ethofumesate is therefore a racemic mixture of two enantiomers.

### Maximum Acceptable Value

Ethofumesate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Ethofumesate is a [benzofuranyl alkylsulfonate selective contact herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#benzofuranyl_alkylsulfonate_herbicides) used mainly to control broadleaf weeds and grass, pre-and post-emergence. Ethofumesate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

JMPR (2007) reports that the manufacturer proposed that methanesulfonic acid ethyl ester (EMS), and methanesulfonic acid 2-methylpropyl ester (iBMS), should be designated as relevant impurities, with a limit of <0.1 mg/kg in each case. WHO/PCS confirmed that, as potent mutagens, EMS and iBMS compounds would qualify as relevant impurities at <1 g/kg. The manufacturer confirmed that, since commencing production in 1976, the manufacturing plant had employed process steps which ensured that both impurities remained essentially undetectable by analysis, using a method with a limit of quantification of 0.1 mg/kg.

### Forms and fate in the environment

If released into water, ethofumesate is expected to adsorb to suspended solids and sediment based upon the Koc data. Ethofumesate is stable to hydrolysis in pH 5, 7, and 9 aqueous buffer solutions, and has an environmental phototransformation half-life of approximately 14 days. It has a soil half-life of about 80 days (aerobic) and 700 days (anaerobic). In a river water-loamy sand sediment (pH 6.9) the half-life in the water was 35 days, in the sediment was 169 days, and in the total system was 105 days.

If released to soil, ethofumesate is expected to have moderate to high mobility based upon Koc values ranging from 55 to 500 measured in 10 different soils. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant (25°C) of 6.8 x 10-4 Pa.m3 mol-1. Ethofumesate is not expected to volatilise from dry soil surfaces based upon its vapour pressure. The biodegradation half-life of ethofumesate in soils under aerobic conditions was reported to range from 83 to 253 days. The major route of dissipation for ethofumesate in surface soil appears to be photodegradation (photolysis half-lifes were 28 to 31 hours in water and 165 hours in soil). However, ethofumesate below the soil surface appears more stable. It may dissipate by microbial metabolism with aerobic metabolism half-lifes between 83 and 253 days. Laboratory data indicate that ethofumesate is stable to hydrolysis and anaerobic soil metabolism (USEPA 2005).

Laboratory mobility data indicate that ethofumesate is very mobile in sand with a Kd of 0.73 and moderately mobile in most other soils. Groundwater monitoring data confirms that ethofumesate has the potential to impact groundwater resources. Water solubility is about 50 mg/L over a range of pH values.

NPIC (1994) quotes for ethofumesate a soil half-life of 30 days, water solubility of 50 mg/L and a sorption coefficient (soil Koc) of 340. This resulted in a pesticide movement to groundwater rating of moderate.

The partition coefficient of ethofumesate at 25°C and pH 6.44 is 486 (Pow) or 2.7 (log Pow) (EFSA 2016).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In a chronic feeding/oncogenicity study in rats, reduced body weight and body weight gain in females and liver cell histopathology in males was observed at 469 mg/kg/day and 1,003 mg/kg/day, respectively. The NOELs were 127 mg/kg/day in females and 332 mg/kg/day in males. The United States Environmental Protection Agency (USEPA), Office of Pesticide Programs (OPP), established a reference dose (RfD) for the general population of 1.3 mg/kg/day based on the NOEL of 127 mg/kg/day from this study and an uncertainty factor of 100. This RfD has not yet been adopted by the USEPA’s *Integrated Risk Information System (IRIS)*. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.3 mg/kg/d, and an ARfD of 0.3 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for ethofumesate is 9.90 mg/L.

Differences in metabolic degradation of enantiomers were observed in vitro. However, oxidation results in a loss of chirality so both enantiomers are rapidly and almost quantitatively degraded to the same metabolites. No unique human metabolite is expected (EFSA 2016).

The EC derived an ADI of 0.07 mg/kg body weight; an ARfD was considered to be unnecessary; reaffirmed by EFSA (2012). Subsequently (EFSA 2016), the majority of experts agreed to the new proposed ADI of 1 mg/kg bw per day, based on the re-assessment of the long-term NOAEL of 101 mg/kg bw per day for decreased body weight gain, increased liver weight, histopathological changes in liver observed in female rats treated at 1,169 mg/kg bw per day in the two-year study. An ARfD was not needed for ethofumesate.

The Acceptable Daily Intake (ADI) adopted in Australia for ethofumesate is 0.3 mg/kg body weight, with a NOEL of 30 mg/kg.

The USEPA has classified ethofumesate as not likely to be carcinogenic to humans.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Ethylene thiourea

CAS No. 96-45-7. Also called 2-imidazolidinethione, 1,3-ethylenethiourea, and sometimes abbreviated to ETU, and sometimes written as ethylenethiourea. Also called ethylenethiocarbamide, 4,5-dihydro-2-mercaptoimidazole and 2-thioimidazolidine.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because ethylene thiourea is unlikely to occur in drinking-water, a guideline value has not been derived.

The USEPA concluded on 22 September 2009 that ethylene thiourea is known or anticipated to occur in PWSs and may require regulation. Therefore they added ethylene thiourea to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009a).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.009 mg/L for ethylenethiourea (ETU); excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Ethylene thiourea is used as a vulcanising agent in the rubber industry. It is also used as a fungicide dust, for example on potatoes, and for spraying pear trees. Ethylene thiourea (or 2-imidazolidinethione) does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It appears as 2-imidazolidinethione.

It may not be used as much today as a pesticide, but is an important degradation product of the ethylene bisdithiocarbamate pesticides, eg, mancozeb, metam sodium, metiram and zineb (see individual datasheets).

### Forms and fate in the environment

Ethylene thiourea can be broken down by photolysis. JMPR (1993) lists hydantoin, ethyleneurea, 1-(2-imidazolin-2-yl)-2-imidazolidinethione and glycine as end-products, with glycine being predominant.

It is very soluble in water: 20,000 mg/L (2 percent).

### Typical concentrations in drinking-water

Ethylene thiourea was not found in samples from 264 groundwater stations in the USA.

### Removal methods

The solubility of ethylene thiourea suggests treatment with activated carbon would probably not be effective. Air stripping and ion exchange would not be effective either. Some newer advanced oxidation processes may be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

Gas chromatography with a nitrogen-phosphorus detector (USEPA Method 509).

### Health considerations

Ethylenethiourea may occur in cigarette smoke. The condensate of four of 12 brands of cigarettes contained 8 to 27 ng/cigarette of ethylenethiourea, owing to the use of ethylenebisdithiocarbamate on tobacco crops (IARC 2001).

The oral reference dose or RfD (USEPA 1996/2006) was 0.00008 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006) was 0.003 mg/L. The reference dose or RfD (USEPA 2009/2011) is 0.0002 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2009/2011) is 0.007 mg/L.

As at September 2008 the USEPA has classified ethylene thiourea as a probable human carcinogen (Group B). For a 70 kg person drinking two litres per day for a lifetime, a concentration of 0.0024 mg/L results in a 10-5 cancer risk level. The USEPA (2009/2011) quotes a health advisory of 0.06 mg/L for ethylene thiourea, representing a 10-4 cancer risk.

Ethylenethiourea appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

IARC (2001) stated that ethylenethiourea is not classifiable as to its carcinogenicity to humans (Group 3). In making its evaluation, the Working Group concluded that ethylenethiourea produces thyroid tumours in mice and rats by a non-genotoxic mechanism, which involves interference with the functioning of thyroid peroxidase resulting in a reduction in circulating thyroid hormone concentrations and increased secretion of thyroid-stimulating hormone. Consequently, ethylenethiourea would not be expected to produce thyroid cancer in humans exposed to concentrations that do not alter thyroid hormone homeostasis. An additional consideration of the Working Group, based on the lack of genotoxicity of ethylenethiourea, was that the liver tumours and benign pituitary tumours in mice were also produced by a non-genotoxic mechanism. Evidence from epidemiological studies and from toxicological studies in experimental animals provide compelling evidence that rodents are substantially more sensitive than humans to the development of thyroid tumours in response to thyroid hormone imbalance.

### Derivation of Maximum Acceptable Value

No MAV.

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# Etofenprox

CAS No. 80844-07-1. The IUPAC name for etofenprox is 2-(4-ethoxyphenyl)-2-methylpropyl 3-phenoxybenzyl ether. The CAS name is 1-[[2-(4-ethoxyphenyl)-2-methylpropoxy]methyl]-3-phenoxybenzene. Also called ethofenprox.

### Maximum Acceptable Value

Etofenprox does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Etofenprox is a non-ester pyrethroid, so called because it acts on the chloride channel of insect nervous systems, as pyrethrins and pyrethroids do, though the molecule lacks the otherwise common structural moiety of these classes of insecticides. It is used in agriculture, horticulture, viticulture, forestry, animal health and public health against many insect pests, for instance Lepidoptera, Hemiptera, Coleoptera, Diptera, Thysanoptera and Hymenoptera. In the public health sector, etofenprox is used for vector control either by direct application in infested areas or indirectly by impregnating fabrics, such as mosquito nets. It is also used as a spot treatment on cats.

WHO (2013) discusses the use of etofenprox in aircraft spraying. WHO recommends permethrin and d-phenothrin for this purpose, adding that etofenprox products are still under development.

Etofenprox appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Etofenprox is not ionised between pH 1 and 14 and its low water solubility (about 0.02 mg/L at pH 7) is essentially unaffected by pH. Hydrolysis does not occur to a significant extent between pH 4 and 9. Typical half-life in water is three hours and in soil six days.

JMPR (2011) reports: vapour pressure at 25°C 8.13 x 10-7 Pa; Henry’s Law constant = 0.0136 Pa.m3/mol; water (distilled) solubility 0.023 mg/L; n-octanol/water partition coefficient = logPow = 6.9 at 20°C; hydrolytically stable at pH 4, 7 and 9 under dark, sterile conditions; phototransformation: DT50 = 7.9 days in pond water at pH 7. Several water and sediment metabolites are tabulated. Water/sediment studies showed the DT50 for etofenprox was one to two days in pond water and 6.5 days for the entire system, and for the major degradate (4’-OH) a DT50 of 57 days was calculated for the whole system.

According to soil degradation studies DT90 values of etofenprox ranged between 43 and 580 days.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

An ADI of 0–0.03 mg/kg bw/day was allocated by the JMPR, with a NOAEL of 3.1 mg/kg bw per day, based on a long-term study in mice and 100-fold safety factor.

EFSA (2008/2017) and EC (2009) established an ADI of 0.03 mg/kg/d, and an ARfD of 1.0 mg/kg/d based on a rabbit developmental toxicity study in which an NOAEL of 100 mg/kg bw was identified, with the application of a UF of 100. These values were also reported in JMPR (2011).

The FAO/WHO 2011 meeting confirmed the ADI of 0–0.03 mg/kg bw on the basis of the NOAEL of 3.1 mg/kg bw per day from the 108-week carcinogenicity study in mice based on renal toxicity (an increased incidence of dilated and basophilic renal tubules) at 10.4 mg/kg bw per day and using a safety factor of 100. The ADI was supported by the NOAEL of 3.7 mg/kg bw per day from the two-year toxicity and carcinogenicity study in rats, based on an increase in foci or areas of eosinophilic hepatocytes in males and vacuolated hepatocytes in females and reduced body weight gain in males at 25.5 mg/kg bw per day. This ADI is adequately protective of renal cortical tumours occurring at higher doses in mice. The meeting also established an acute reference dose (ARfD) of 1 mg/kg bw on the basis of the overall NOAEL of 100 mg/kg bw per day from the two developmental toxicity studies in rabbits, based on the occurrence of reduced maternal body weight gain and feed consumption during the early dosing period (gestation day 6) and increased post-implantation loss, which could occur after a single exposure, and using a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for etofenprox is 0.03 mg/kg body weight, with a NOEL of 3.1 mg/kg bw. The ARfD is 1 mg/kg (<https://apvma.gov.au/>); the ARfD for etofenprox only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.

The chronic RfD was calculated to be 0.037 mg/kg/d; an acute RfD was not necessary. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.037 mg/kg/d. The Cancer Assessment Review Committee classified etofenprox as “Not likely to be carcinogenic to humans at doses that do not alter thyroid homeostasis” (USEPA 2007). The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for etofenprox is 0.26 mg/L (no acute one-day value available.)

Etofenprox is not genotoxic, and has not shown carcinogenic or specific reproductive toxic effects. Etofenprox has low acute toxicity (WHO 2013).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Etoxazole

CAS No. 153233-91-1. The IUPAC name for etoxazole is (RS)-5-tert-butyl-2-[2-(2,6-difluorophenyl)-4,5-dihydro-1,3-oxazol-4-yl]phenetole. The CAS name is 2-(2,6-difluorophenyl)-4-[4-(1,1-dimethylethyl)-2-ethoxyphenyl]-4,5-dihydrooxazole.

### Maximum Acceptable Value

Etoxazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Etoxazole is a diphenyloxazoline or oxazoline insecticide used as an acaricide/miticide/ovicide, often used in glasshouses and shadehouses. It is used on citrus fruit and grapes in Australia.

Etoxazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Available environmental fate data indicate that etoxazole degrades at moderate rates at pH 5 (approximately 10 days), and is relatively stable between pH 7 and 9. Etoxazole showed moderately rapid biodegradation in a variety of soils with a mean half-life of 20.5 days. 2,6-Difluorobenzoic acid (CAS No. 385-00-2) has been detected as a breakdown product, as have difluorophenyl and t-butylphenyl. Etoxazole is immobile in several soils tested. There appears to be little potential for etoxazole to be transported with water, although transport of residues adsorbed to the eroding soil is possible (USEPA 2002). See JMPR (2010) for further information on metabolites.

Under acidic conditions etoxazole is hydrolysed at a moderate rate with a half-life of 10 days. However, in neutral to lightly alkali conditions, etoxazole resists hydrolysis and is almost stable with a 165 day half-life. Etoxazole reaction to sunlight (photolysis) is similar in water and soil. Its half-life in water ranges from 16–17 days and 22–25 days in soil. The aerobic soil metabolism study indicated that etoxazole is relatively unstable with a half-life of 19–24 days. With anaerobic water conditions, the estimated half-life was 133–142 days (California Government 2004).

As DT90 values of etoxazole are expected to be lower than 31 days and no relevant soil metabolites were identified, investigation of residues in rotational crops is not required and relevant residues in these crops are not expected (EFSA 2012).

The potential for groundwater exposure above the parametric drinking water limit of 0.1 μg/L consequent to the uses assessed, was assessed as low for etoxazole and all its identified soil metabolites (EFSA 2017).

Water solubility about 0.06 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See JMPR (2010) and EFSA (2017).

### Health considerations

Etoxazole had low acute toxicity in rats, causing no mortality at the limit dose after oral exposure, median lethal dose or LD50 >5,000 mg/kg bw (JMPR 2010).

EC (2004) quotes an ADI of 0.04 mg/kg bw/d, based on a two-year study on rats, and using a safety factor of 100. An ARfD was considered unnecessary (restated by EFSA 2012/2017).

The 2010 JMPR meeting established an acceptable daily intake (ADI) of 0–0.05 mg/kg bw on the basis of an overall NOAEL of 5.33 mg/kg bw per day in the 90-day and one-year studies in dogs for liver effects (eg, increases in serum levels of alkaline phosphatase and triglycerides, absolute and relative liver weights and incidence of centrilobular hepatocyte hypertrophy). A safety factor of 100 was applied. The meeting concluded that it was not necessary to establish an acute reference dose (ARfD) for etoxazole in view of its low acute toxicity, the absence of relevant developmental toxicity in rats and rabbits that could have occurred as a consequence of an acute exposure, and the absence of any other toxicological effect that would be elicited by a single dose (FAO/WHO 2010).

Preliminary results suggest that there is no evidence of carcinogenicity in the rat or mouse as a result of oral administration of etoxazole. Studies to date show no signs of mutagenicity (USEPA 2002; EC 2004; JMPR 2010).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.04 mg/kg body weight, with a NOEL of 4 mg/kg bw. The ARfD is 25 mg/kg bw. In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.046 mg/kg/d for etoxazole. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for etoxazole is 0.32 mg/L (no acute one-day value available.)

Based on available genotoxicity studies, the substance is unlikely to be genotoxic in vivo. The majority of experts agreed that substance is not carcinogenic and considered testicular findings in rats not treatment related. No carcinogenic potential was observed in mice (EFSA 2017).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Etridiazole

CAS No. 2593-15-9. The IUPAC name for etridiazole is ethyl 3-trichloromethyl-1,2,4-thiadiazol-5-yl ether. The CAS name is 5-ethoxy-3-(trichloromethyl)-1,2,4-thiadiazole. A trade name is Terrazole.

### Maximum Acceptable Value

Etridiazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Etridiazole is a thiazole (or thiadiazol) fungicide used as a soil treatment against seedling and root diseases on field crops, vegetables, grass and ornamentals.

Etridiazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Etridiazole is a mobile compound with moderate persistence and high volatility. Under aerobic soil metabolism conditions, etridiazole breaks down slowly.

Because etridiazole is stable to hydrolysis and aqueous photolysis, it may persist for considerable periods of time in the aquatic environment. Water solubility is about 120 mg/L.

Available data indicate that the degradate 3-dichloromethyl-5-ethoxy-1,2,4-thiadiazole (3-DCMT) is highly toxic to aquatic organisms. Dichloroetridiazole is a relevant end product too. Major plant metabolites are 5-hydroxyethoxyetridiazole acid and 3‑hydroxymethyletridiazole.

NPIC (1994) quotes for etridiazole a soil half-life of 103 days, water solubility of 50 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

Acute and chronic risks from groundwater are not of concern in the US where etridiazole is not used on food crops (USEPA 2000).

### Removal methods

The weak soil adsorption and fairly high solubility suggest that treatment processes that remove particulate matter should be ineffective at reducing the concentration of etridiazole in water. Trials with activated carbon may provide positive information.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

An acute reference dose (aRfD) of 0.15 mg/kg/day was determined for the subpopulation group, females 13–50 years, based on the NOAEL of 15 mg/kg/day in the developmental toxicity study in rabbits and an uncertainty factor of 100 (10x for inter-species extrapolation and l0x for intra-species variation). A chronic reference dose (RfD) of 0.016 mg/kg/day was established based on the NOAEL of 4.8 mg/kg/day from the two-year carcinogenicity study in rats and the application of an uncertainty factor of 300 (l0x for intraspecies extrapolation, 10x for interspecies variation and 3x applied under FIFRA for the lack of an acceptable chronic study) (USEPA 2000b).

The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for Terrazole (etridiazole) is 4.95 mg/L.

Acute and chronic non-cancer aggregate risks are not of concern. The chronic non-cancer NOAEL of 4.8 mg/kg/day was established based on increased absolute and relative liver weights, renal tubule cell karyomegaly, hepatocytomegaly and spongiosis hepatis observed in a carcinogenicity study in rats at the LOAEL of 30.43 mg/kg/day.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 2.9 mg/kg bw from a long-term (one-year dietary) study. The NOEL is based on decreased bodyweight gain and increased serum ALP activity in dogs. The ADI incorporates a safety factor of 100.

EFSA (2017) derived an acceptable daily intake (ADI) of 0.015 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.15 mg/kg bw.

As at September 2008 the USEPA has classified etridiazole (under the trade name of terrazole) in Group B: a probable human carcinogen, based on multiple tumour types in the liver, bile duct, mammary gland, thyroid and testes in rats. Sources considered for aggregate exposure were food, drinking-water, and exposure to treated golf courses. The cancer aggregate risk from exposure to food and treated golf courses is 1.1 x 10-6, which slightly exceeds a level the USEPA considers negligible, without including exposure from drinking-water. Further, estimated cancer risk from drinking-water alone exceeds a level the USEPA considers negligible. Thus, aggregate cancer risk is of concern.

### Derivation of Maximum Acceptable Value

No MAV.

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USEPA. 2000b. Etridiazole. *Revised Human Health Risk Assessment* [150 pp]. <http://www3.epa.gov/pesticides/chem_search/hhbp/R003495.pdf>

# Famphur

CAS No. 52-85-7. The IUPAC name for famphur is O-4-dimethylsulfamoylphenyl O,O‑dimethyl phosphorothioate or 4-dimethoxyphosphinothioyloxy-N,N-dimethylbenzenesulfonamide. The CAS name is O-[4-[(dimethylamino)sulfonyl]phenyl] O,O-dimethyl phosphorothioate. Sometimes called famophos or famphos.

### Maximum Acceptable Value

Famphur does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Famphur is a systemic phenyl organothiophosphate insecticide, often used as a veterinary chemical to control parasites in livestock.

Famphur appears on EPA’s 27 June 2013 list of organophosphate and carbamate (OPC) pesticides which no longer are able to be manufactured in or imported into New Zealand. There did not appear to be any current usage of the product in New Zealand.

### Forms and fate in the environment

If released to [water](https://pubchem.ncbi.nlm.nih.gov/compound/water), famphur is expected to undergo slow hydrolysis; an experimentally determined half-life of 115 days has been determined under neutral conditions. Hydrolysis under basic conditions will occur at a more rapid rate, with a calculated half-life value of 60 days at pH 10. A calculated Koc of 419, based on the estimated log Kow of 2.29, suggests that famphur would be expected to adsorb to sediment and suspended organic matter. A calculated bioconcentration factor of 31.8, also based on the log Kow, suggests that bioconcentration in fish and aquatic organisms is not expected to be a significant fate process. If released to soil it will show moderate mobility and undergo slow hydrolysis (NIH accessed June 2016).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Only famphur and its oxygen analogue, famoxon, were of toxicological significance; the other metabolites were not important (Eisler 1994).

The Acceptable Daily Intake (ADI) adopted in Australia for famphur is 0.00002 mg/kg body weight, with a NOEL of 0.0375 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fenamidone

CAS No. 161326-34-7. The IUPAC name for fenamidone is (S)-1-anilino-4-methyl-2-methylthio-4-phenylimidazolin-5-one, or (S)-5-methyl-2-methylthio-5-phenyl-3-phenylamino-3,5-dihydroimidazol-4-one. The CAS name is (5S)-3,5-dihydro-5-methyl-2-(methylthio)-5-phenyl-3-(phenylamino)-4H-imidazol-4-one. The S-isomer has been shown to be the biologically active enantiomer.

### Maximum Acceptable Value

Fenamidone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Fenamidone is an imidazole (or imidazolinone) broad spectrum fungicide and nematicide, commonly used on grapes and vegetables against foliar diseases.

Fenamidone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Fenamidone is broken down primarily by microbial degradation. Its field dissipation rate ranged from a half-life of 8.7 days on a sandy loam soil in Washington to 81.5 days on a sandy loam soil in California. The geometric mean half-life of these and other field dissipation studies in Florida and North Dakota was 24 days. Three major degradation products resulted from microbial breakdown of fenamidone. Some were more persistent, but all were significantly less toxic than the parent compound.

Fenamidone is removed from water by photolysis, sedimentation, and microbial degradation. In two studies, the rate of photolysis in water ranged from half-lifes of 5 to 5.8 days. In aerobic, sandy-clay-loam sediment-water system, fenamidone partitioned slowly from water to sediment. The half-lifes were 21 days for water and 108 days for the entire system; the half-life in sediment was not calculated. In an aerobic sandy-loam sediment system, the half-lifes of fenamidone were 12, 85, and 67 days in water, sediment, and the entire system, respectively. In an anaerobic sediment-water system, fenamidone partitioned rapidly to sediments with a half-life of about a day for the water column. It degraded from the sediments much more slowly than in aerobic sediments, however, with a half-life of 1,386 days (NY State 2006).

Fenamidone was readily degraded under both irradiated and non-irradiated soil conditions (primarily degraded by the action of aerobic soil micro‑organisms) and it is concluded that photolytic processes do not contribute significantly to the degradation of fenamidone applied to the soil surface. The aerobic half-lifes in a range of soils and conditions are reported in the range of 4 to 10 days. Field dissipation studies were undertaken at four sites in Europe using clay loam, silt loam and sandy loam soils. In all cases dissipation of fenamidone was rapid with a mean half life of five days; metabolites are more persistent. Fenamidone was found to be stable to hydrolysis in the pH range 5 to 7. Metabolites are discussed (JMPR 2014).

JMPR (2014) states: Henry’s Law constant = 0.5 x 10–5 Pa m3/mol (20°C). Water solubility 7.8 mg/L (20°C, pH 4–10). Partition coefficient = Log Pow = 2.8 (20°C). Hydrolysis half-life 222 days (pH 5), 411 days (pH 7), 27.6 days (pH 9). Photolysis half-life = DT50 = 25.7 hours, corresponding to five days Florida summer sunlight.

The only significant metabolite is the 2-oxo-metabolite, formed by hydrolysis of the thio-methyl side chain (EFSA 2012).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Fenamidone shows no overall genotoxic potential of relevance to human risk assessment, no reproductive toxicity (except some growth retardation in offsprings at high doses), no teratogenic potential, and no carcinogenicity potential in rodents (EC 2003). The ADI was estimated to be 0.03 mg/kg based on a two-year rat study, with an acute reference dose (ARfD) considered to be unnecessary; reaffirmed by EFSA (2012). EFSA (2014) notes that the JMPR in 2013 has proposed an ARfD of 1 mg/kg bw – confirmed in JMPR (2014).

The acute reference dose (aRfD) of 0.13 mg/kg/day is based on a NOAEL of 125 mg/kg/day from the neurotoxicity study in rat and a 10X database uncertainty factor (UF) recently applied by the Agency for lack of a developmental neurotoxicity study. The chronic reference dose (cRfD) of 0.002 mg/kg/day from the two-year rat chronic study and the UF of 10X (USEPA 2004). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0283 mg/kg/d, and an ARfD of 1.25 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenamidone is 12.5 mg/L.

The liver is the target organ in chronic studies in the rat, mouse and dog. The thyroid is also a target organ in the rat. The USEPA (2009) has classified fenamidone as “not likely to be a human carcinogen” by all relevant routes of exposure. The NOAELs of 10.4, 5.4 and 2.83 mg/kg/day used for short-term, intermediate-term and long-term risk assessments, respectively, are considerably (9- to 45-fold) lower than the offspring NOAEL of 92.3 mg/kg/day in the developmental neurotoxicity study.

Fenamidone is not considered mutagenic and is not considered a reproductive toxicant at non-maternally toxic dose levels and shows no evidence of endocrine effects (USEPA 2004).

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenamiphos

CAS No. 22224-92-6. The IUPAC name for fenamiphos is (RS)-(ethyl 4-methylthio-m-tolyl isopropylphosphoramidate). The CAS name is ethyl 3-methyl-4-(methylthio)phenyl (1-methylethyl)phosphoramidate. Sometimes spelt phenamiphos.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because fenamiphos is unlikely to occur in drinking-water, a guideline value has not been derived.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0005 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The USEPA concluded on 22 September 2009 that fenamiphos is known or anticipated to occur in PWSs and may require regulation. Therefore they added fenamiphos to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009a).

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.0007 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

### Sources to water

Fenamiphos is a long-lasting systemic organophosphate nematicide and insecticide. It is used on a variety of plants including citrus and other fruit vines, and grains. The compound is absorbed by roots and is then translocated throughout the plant, blocking the enzyme acetylcholinesterase in the target pest.

In the USA, all uses of fenamiphos in areas with extremely vulnerable soils and shallow water tables were phased out by 31 May 2005 (USEPA 2008).

Fenamiphos is also found in other formulations, eg, with carbofuran. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 10.8 tonnes of fenamiphos were used in New Zealand in 2004, at an application rate of 8,000 grams of active ingredient per hectare. After 1 July 2023 fenamiphos will no longer able to be manufactured in or imported into New Zealand.

### Forms and fate in the environment

Fenamiphos is of moderate persistence in the soil environment, with a reported soil half-life of about 50 days. Fenamiphos disappears quickly from water in acidic and alkaline water, but it is stable in neutral water when held in the dark. The compound, when in the presence of artificial light, disappears very rapidly. In a neutral solution, half of the initial amount of the compound degraded within four hours.

It is very soluble in water: 700 mg/L.

NPIC (1994) quotes for fenamiphos a soil half-life of 50 days, water solubility of 400 mg/L and a sorption coefficient (soil Koc) of 100. This resulted in a pesticide movement to groundwater rating of high.

Fenamiphos and metabolites M01 and M02 exhibited very high to medium mobility in soil. M12 and M13 exhibited very high soil mobility, and M14 exhibited high soil mobility. It was concluded that the adsorption of fenamiphos and its metabolites was not pH dependent. In laboratory incubations in dark aerobic natural sediment water systems, fenamiphos exhibited low to high persistence. The potential for groundwater exposure from the representative uses by fenamiphos above the parametric drinking water limit of 0.1 μg/L was concluded to be low for fenamiphos and metabolite M12 (EFSA 2019).

### Typical concentrations in drinking-water

In calculating risks to populations drinking groundwater, the USEPA (2002) assessment found that the expected concentrations of fenamiphos in drinking water will vary depending on the type of soil and depth to groundwater. When soils are extremely vulnerable and the groundwater is shallow, fenamiphos is expected to rapidly leach into groundwater. As the soils become less vulnerable, the expected concentrations drop. Extremely vulnerable soils are defined as, “hydrologic soil group A soils that are excessively drained and predominantly sand or loamy sand, such as soils in the suborder psamments”. However, neither fenamiphos nor its breakdown products have been found in over 1,200 wells tested in six states in the USA.

### Removal methods

Granular activated carbon is effective in removing many trace organic substances from water, including fenamiphos.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

ICPS (1994) lists three methods. EFSA (2019) states the components of the residue definition (fenamiphos, M01 and M02) in groundwater can be monitored by liquid chromatography with tandem mass spectrometry (LC–MS/MS) with LOQs of 0.1 μg/L.

### Health considerations

The toxicological profile of fenamiphos in mammalian species is typical of organophosphate substances with cholinergic effects as main toxicological endpoints.

Fenamiphos is readily absorbed through the digestive tract and lungs. One study placed the amount absorbed near 95 percent of the ingested dose. The compound is rapidly broken down within the organism, and the by-products are excreted in the urine. The majority of a dose was recovered in urine within 15 hours after treatment.

The 1997 JMPR allocated an ADI of 0–0.0008 mg/kg bw and concluded that the available data did not permit the establishment of an ARfD different from the ADI. The 2002 JMPR allocated a new ARfD of 0.003 mg/kg bw. Residues are reported as the sum of fenamiphos, its sulfoxide and sulfone, expressed as fenamiphos.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand is 0.0001 mg/kg body weight, with a NOEL of 0.014 mg/kg bw from a two-year dietary study in dogs. The NOEL is based on inhibition of plasma cholinesterase activity. The ADI incorporates a safety factor of 100 and it was established in 2005. This ADI is supported by a NOEL of 0.011 mg/kg bw/day based on plasma cholinesterase inhibition in a 6-month dietary dog study. The ARfD is 0.003 mg/kg bw based on a NOEL of 0.25 mg/kg bw/day from an acute oral toxicity study in dogs. The ARfD incorporates a safety factor of 100.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.0001 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.0035 mg/L. The oral RfD had previously been 0.00025 mg/kg/d (USEPA (1990).

EC (2006) established an ADI of 0.0008 mg/kg/d and an ARfD of 0.0025 mg/kg/d.

The dog was considered the most sensitive species and the no observed adverse effect level (NOAEL) of 0.083 mg/kg body weight (bw) per day (one‐year dog study), based on erythrocyte ChE inhibition, was used to set the acceptable daily intake (ADI) of 0.00083 mg/kg bw per day using an uncertainty factor of 100. An ARfD was set at 0.0025 mg/kg based on the acute oral neurotoxicity study in dogs with a NOAEL of 0.25 mg/kg bw, which was based on erythrocyte ChE inhibition, clinical signs and application of an UF of 100.

As at September 2008 the USEPA has classified fenamiphos in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenarimol

CAS No. 60168-88-9. The IUPAC chemical name for fenarimol is (RS)-2,4′-dichloro-α-(pyrimidin-5-yl)benzhydryl alcohol. The CAS name is α-(2-chlorophenyl)-α-(4-chlorophenyl)-5-pyrimidinemethanol.

### Maximum Acceptable Value

Fenarimol does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.04 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Fenarimol is a systemic pyrimidine fungicide commonly used on a wide range of fruit, vegetables and wheat, mainly to control black spot and powdery mildew.

Fenarimol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). The main imputities are the 2,2`-, 2,3`- and 4,4`-dichloro isomers of fenarimol but should represent <3 percent of the product.

### Form and fate in the environment

In aerobic and anaerobic soils, the half-life of fenarimol has been reported at >1,000 days (JMPR quotes 21–130 days in field studies), although in sunlight, the aerobic half-life may be nearer 100 days. The half-life in a 2 mg/L water solution in summer sun was 12 hours. Small amounts of chlorobenzoic acids appear in the photolytic breakdown products. Fenarimol is not likely to volatilise.

Water solubility about 15 mg/L; fenarimol has more potential to accumulate in sediment than to leach to groundwater.

NPIC (1994) quotes for fenarimol a soil half-life of 360 days, water solubility of 14 mg/L and a sorption coefficient (soil Koc) of 600. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

No data available.

### Removal methods

Water treatment processes that remove particulate matter are likely to reduce the concentration of fenarimol in water.

### Analytical methods

#### Referee method

A referee method cannot be selected for because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

Fenarimol has moderate acute toxicity. The developmental and reproductive toxicity studies showed no evidence of increased sensitivity or susceptibility of young rats or rabbits following pre- or postnatal exposure to fenarimol. EC (2007) states that fenarimol is not carcinogenic.

Fenarimol appears on some lists of possible endocrine disruptors. In the rat multi-generation reproduction studies there was an inhibition of aromatase. Aromatase, also known as estrogen synthetase, is the key enzyme for the conversion of androgens to estrogens and is therefore a potentially critical enzyme in maintaining hormone balance in human physiology.

PMEP (1985) states that fenarimol produces reproductive, teratogenic, and oncogenic effects in laboratory animals. The chemical inhibits testosterone aromatase activity, which results in irreversible infertility in male rats. The inhibition of testosterone aromatase is not involved in the fertility of guinea pigs and humans. NHMRC, NRMMC (2011) states that fenarimol is not considered to be genotoxic, based on in vitro and in vivo short-term studies.

The Acceptable Daily Intake (ADI) adopted by EC (2007) is 0.01 mg/kg body weight based on a two-year rat study, and the acute reference dose (ARfD) is 0.02 mg/kg/d. These values were reaffirmed by EFSA (2011).

The Acceptable Daily Intake (ADI) adopted in Australia for fenarimol is 0.01 (pre-1990 it was 0.025) mg/kg body weight, with a NOEL of 1 mg/kg from a reproduction study and a long-term (two-year) dietary study in rats. The NOEL is based on liver toxicity in the form of fatty changes in the liver, hepatic nodules, and increased blood glucose in the long-term studies, and increased gestation time in the reproduction studies. The ADI incorporates a safety factor of 100.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.006 mg/kg/d for fenarimol. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenamirol is 0.042 mg/L (no acute one-day value available.)

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenbuconazole

CAS No. 114369-43-6. The IUPAC chemical name of fenbuconazole is (RS)-4-(4-chlorophenyl)-2-phenyl-2-(1H-1,2,4-triazol-1-ylmethyl)butyronitrile. The CAS name is α-[2-(4-chlorophenyl)ethyl]-α-phenyl-1H-1,2,4-triazole-1-propanenitrile. Dow markets this as Enable, Impala and Indar. Has appeared misspelt as febuconazole.

### Maximum Acceptable Value

Fenbuconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Fenbuconazole is a conazole (or triazole) fungicide. It works systemically to prevent the growth of fungi by interrupting their normal growth cycle. Fenbuconazole is used to control powdery mildew, leaf spots and blotches, rusts, smuts, root/stem rots, and fruit scab. It is primarily used as a preventive fungicide. It is used on a variety of crops, including cereals, vines, pome and stone fruits (DOW 2011).

Fenbuconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Form and fate in the environment

The half-life of fenbuconazole in soil depends on the soil type and ranges from 30 to 590 days. Fenbuconazole binds tightly to soil and is practically insoluble in water, so is unlikely to leach into groundwater. The adsorption coefficient (Koc) is about 4.43. Some of the degradation products are mobile in soil and could reach groundwater (EFSA 2010). The USEPA expects fenbuconazole not to exceed 0.00003 mg/L in groundwater.

In aerobic natural sediment water systems (laboratory incubations) fenbuconazole dissipated relatively rapidly from the water phase via partitioning to the sediment.

Water solubility is about 2.5 mg/L over a fairly wide pH range.

EFSA (2010) reports Henry’s Law constant as 3 x 10-5 Pa m3 mol-1, and a partition coefficient of log POW = 3.23 at 25°C.

### Typical concentrations in drinking-water

No data available.

### Removal methods

Water treatment processes that remove particulate matter should reduce the concentration of fenbuconazole.

### Analytical methods

#### Referee method

No MAV.

#### Some alternative methods

Fenbuconazole is a racemic mixture of enantiomers; analytical methods are not stereo-selective, so results should be considered as “sum of enantiomers”.

### Health considerations

Fenbuconazole is of low acute toxicity after oral or dermal exposure, or by inhalation. The metabolites 1,2,4-triazole, triazole alanine and triazole acetic acid are toxicologically relevant metabolites (EFSA 2010). See datasheet for triazole metabolites for latest ADI and ARfD.

IPCS (1997) allocated an ADI for humans of 0–0.03 mg/kg bw on the basis of the NOAEL of 3 mg/kg bw per day in the two-year study in rats and a safety factor of 100.

EFSA (2010) report an Acceptable Daily Intake (ADI) of 0.006 mg/kg bw/day, derived from the one-year dog study (safety factor 100). The Acute Reference Dose (ARfD) of 0.3 mg/kg bw is derived from the maternal effects seen in the rat developmental study, supported by the findings in the rabbit developmental study, and using a safety factor of 100. These values are also adopted by the EU (2010).

Fenbuconazole is not genotoxic in vitro or in vivo; IPCS (1997). In the long-term studies with rats and mice, the main target organ was the liver, with thyroid tumours in rats. The increased incidence of thyroid tumours in rats (rodent specific) and hepatocellular carcinomas in mice (common in mice at prolonged high doses of xenobiotics) is unlikely to pose a carcinogenic risk to humans. The relevant long-term NOAELs are 3 mg/kg bw/day for rats, and 1.3 mg/kg bw/day for mice.

JMPR (2013) and FAO/WHO (2013) report an ADI of 0–0.03 mg/kg bw and an ARfD of 0.2 mg/kg bw.

The USEPA developed a reference dose (chronic RfD) of 0.03 mg/kg/day, based on the chronic toxicity study in the rat, which had a NOAEL of 3.03 and 4.02 mg/kg/day in males and females, respectively. PMEP (2002) and USEPA (2013). The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenbuconazole is 9.9 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

The USEPA classified fenbuconazole as a Group C (possible human) carcinogen, based on the tumours in rodents and the structural correlation with other triazole pesticides which also are carcinogenic (PMEP 2002, USEPA 2013).

The Acceptable Daily Intake (ADI) adopted in Australia for fenbuconazole is 0.006 mg/kg body weight, with a NOEL of 0.6 mg/kg bw. The ARfD is 0.2 mg/kg bw. In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenbutatin oxide

CAS No. 13356-08-6. The IUPAC chemical name of fenbutatin oxide is bis[tris(2-methyl-2-phenylpropyl)tin] oxide. The CAS name is hexakis(2-methyl-2-phenylpropyl)distannoxane.

### Maximum Acceptable Value

Fenbutatin oxide does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Fenbutatin oxide is a non-systemic organotin acaricide, generally used to protect fruit.

Fenbutatin oxide does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](https://eatsafe.nzfsa.govt.nz/web/public/acvm-register%20and%20select%20entire%20register)). However, it does appear in ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008.

Fenbutatin oxide should not contain more than 20 g/kg of bis[hydroxybis(2-methyl-2-phenylpropyl)tin]oxide.

### Form and fate in the environment

Fenbutatin-oxide photodegraded in sterile water at pH 7 with a half-life of 55 days under continuous irradiation. This half-life would translate to a half-life of over 100 days if the chemical were exposed to 12 hours of irradiation alternated with 12 hours of darkness.

The half-life of fenbutatin-oxide in soil is much more than a year, it is not mobile, and microbial degradation in soil is very slow.

Water solubility about 0.013 mg/L.

NPIC (1994) quotes for fenbutatin oxide a soil half-life of 90 days, water solubility of 0.013 mg/L and a sorption coefficient (soil Koc) of 2300. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

No data available.

### Removal methods

No information available.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

The USEPA (1994) classified fenbutatin-oxide as a Group E carcinogen (signifies evidence of non-carcinogenicity in humans) and established a reference dose (cRfD) of 0.05 mg/kg/day. The reference dose is based on a NOEL of 5.2 mg/kg/day for reduced body weight and food consumption in both sexes of pups of the first and second generations at 17.4 and 20.3 mg/kg/day in a two-generation study in rats. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.017 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenbutatin-oxide is 0.12 mg/L (no acute one-day value available.)

<http://ec.europa.eu/sanco_pesticides/public/index.cfm> quotes an ADI and ARfD of 0.05 mg/kg/d for fenbutatin-oxide, referring to an EFSA source. These values were confirmed in EFSA (2017).

The Acceptable Daily Intake (ADI) adopted in Australia for fenbutatin-oxide is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for fenbutatin-oxide since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenhexamid

CAS No. 126833-17-8. The IUPAC chemical name of fenhexamid is 2′,3′-dichloro-4′-hydroxy-1-methylcyclohexanecarboxanilide. The CAS name is N-(2,3-dichloro-4-hydroxyphenyl)-1-methylcyclohexanecarboxamide. Sometimes spelt fenhexamide.

### Maximum Acceptable Value

Fenhexamid does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for fenhexamid in fresh water (set by an approval under Part 5 of the HSNO Act) of 0.013 mg/L (13 µg/L).

EPA established an environmental exposure limit of 0.013 mg/L (13 µg/L) for fenhexamid in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Fenhexamid is a anilide (or hydroxyanilide) fungicide. Fenhexamid is a protectant fungicide used on horticultural crops and vegetables. It inhibits spore germ tube development and hyphal growth.

Fenhexamid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Two impurities were found to be relevant, 4-amino-2,3-dichlorophenol (DCHA) and toluene, although no concern is raised at the level specified (EFSA 2014).

### Form and fate in the environment

Fenhexamid is not persistent in the environment under aerobic conditions and is unlikely to reach surface water or groundwater; however, if fenhexamid reached an anaerobic environment, it would be considered moderately persistent (USEPA 1999). Batch equilibrium studies indicate fenhexamid will have low mobility in most soils. Thus, transport of fenhexamid in the environment will most likely occur in association with movement of soil particles. Soil studies demonstrated that the degradation rate of fenhexamid is rapid; The DT50 is up to 1 day and the maximum DT90 based on laboratory studies was 10 days (from EFSA 2013/2014).

Water solubility is about 15 to 25 mg/L at pH 5 to 7, and about 400 mg/L at pH 9. In laboratory aerobic aquatic systems (half-life about 14 to 24 days) over 70 percent of the fenhexamid had partitioned to the sediment and was unidentified by 100 days where up to about 6 percent of total residues were identified as fenhexamid (USEPA 1999).

See JMPR (2005) for discussion on metabolites.

### Typical concentrations in drinking-water

No data available.

### Removal methods

No information available.

### Analytical methods

Fenhexamid can be monitored in drinking water by HPLC-MS/MS with a LOQ of 0.1 μg/L and in surface water by HPLC-ELCD with a LOQ of 0.05 μg/L respectively (EFSA 2014).

### Health considerations

USEPA (1999) states that there is no evidence of carcinogenicity, and that fenhexamid is not mutagenic. An acute Reference Dose (RfD) was not identified because there were no adverse effects attributable to a single (acute) exposure. A chronic RfD of 0.17 mg/kg/day was selected (NOAEL = 17 mg/kg/day) for use in assessing chronic dietary risk. This RfD is based on the one-year chronic oral toxicity study in dogs, in which decreased red blood cell (RBC) counts, haemoglobin and hematocrit and increased Heinz bodies in RBC were seen at the LOAEL of 124/133 mg/kg/day in males/females; also, in females, increased absolute and relative adrenal weights correlated with histopathological observations of increases in the incidence and severity of intracytoplasmic vacuoles in the adrenal cortex. The chronic population-adjusted dose (cPAD) = 0.057 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.17 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenhexamid is 1.19 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.2 mg/kg body weight, with a NOEL of 17.4 mg/kg bw. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

EC (2000) quotes an acute ADI of 0.2 mg/kg/d. EFSA (2013 and 2014) also quote an ADI value of 0.2 mg/kg bw per day. The relevant long term NOAEL is 28 mg/kg bw per day from the two-year rat study. The relevant short term NOAEL is 19.2 mg/kg bw per day from the one-year study in dogs. No ARfD was deemed necessary.

JMPR (2005) established an ADI of 0 to 0.2 mg/kg bw based on a NOAEL of 17.4 mg/kg bw per day for increased adrenal weight and the presence of intracytoplasmic vacuoles in the adrenal cortex of females and haematopoietic effects (increase in the number of Heinz Bodies, decrease erythrocyte count, haemoglobin concentration and erythrocyte volume fraction) seen at higher doses in both sexes in a 52-week study in dogs fed with fenhexamid, and a 100-fold safety factor. An ARfD is unnecessary. In view of the lack of genotoxicity and the absence of carcinogenicity in rats and mice, the meeting concluded that fenhexamid is unlikely to pose a carcinogenic risk to humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenitrothion

CAS No. 122-14-5. The IUPAC chemical name of fenitrothion is O,O-dimethyl-O-(4-nitro-m-tolyl) phosphorothioate. The CAS name is O,O-dimethyl-O-(3-methyl-4-nitrophenyl) phosphorothioate. Also called O,O-dimethyl-O-(4-nitro-m-tolyl)-thiophosphate.

### Maximum Acceptable Value

WHO (2004/2011/2017) states that because fenitrothion occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

WHO (2017) established a health-based value of 0.008 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Fenitrothion is a broad-spectrum non-systemic organophosphate (phosphorothionate) insecticide and selective acaricide. In New Zealand, fenitrothion is applied to pasture, cereals, lucerne, brassicas and fruit trees to control porina and army caterpillars, brassica seedling pests, lucerne fleas, sitona weevils and tasmanian grass grubs. It is also used to kill borers in wood, and can be used as a fly, mosquito, and cockroach residual contact spray for farms and public health programmes.

Formulations containing fenitrothion have been registered for use in New Zealand since at least 1969. Caterkil 1000 is the only product containing fenitrothion that is currently registered for agricultural use in New Zealand. There is also a timber treatment product in use in New Zealand: Borer Fluid FN. Fenitrothion is also used as a preservative for two veterinary medicine products.

In the 1981 spruce budworm spray programme in Canada, the concentrations of fenitrothion residues detected in water were low (maximum 0.0013 mg/L).

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Since July 2016 fenitrothion was no longer able to be manufactured in or imported into New Zealand.

Fenitrothion should not contain more than 20 g/kg of S-methyl fenitrothion, 2 percent of O-methyl-O,O-(3-methyl-4-nitrophenyl)phosphate, or 3 g/kg tetramethyl pyrophosphorothioate (TMPP) – see JMPR for details for different formulations. See IPCS HSG (1991) for impurities.

### Form and fate in the environment

Fenitrothion is stable in water only in the absence of sunlight or microbial contamination. In soil, biodegradation is the primary route of degradation, although photolysis may also play a role. Preliminary data indicates fenitrothion degrades fairly rapidly in soil with a half-life of less than one week in non-sterile muck, sandy loam soils.

Fenitrothion is not readily hydrolysed at slightly acidic and neutral pH (half life of several months at pH 4 and 7, somewhat faster hydrolysis at pH 9, respectively) but photolysis is comparatively rapid. It is of short persistence in animals, plants, soil and water and therefore bioaccumulation is unlikely to occur despite an octanol/water partition coefficient of 3.3.

Water solubility is about 14–20 mg/L. Fenitrothion residues detected in water were low (maximum 0.0013 mg/L) during a forest spray programme. Following the spraying of forests, water samples did not contain detectable amounts of fenitrothion; post-spray samples contained <0.00001 mg/L. The half-life in natural water is generally less than 24 hours.

Levels of fenitrothion residues in fruits, vegetables and cereal grains decline rapidly after treatment, with a half-life of 1–2 days.

JMPR (2010) states that fenitrothion is not persistent in soil, nor is leaching significant. Therefore there is negligible risk to succeeding crops or of groundwater contamination. Volatilisation is a significant dissipative process in the environment although, once in the vapour phase, fenitrothion is short-lived. Transport to surface water via spray drift poses a risk to aquatic species, although the duration of exposure is brief because fenitrothion dissipates in microbially active natural water systems with a half-life of less than one week. The compound will also tend to migrate to sediment.

NPIC (1994) quotes for fenitrothion a soil half-life of four days, water solubility of  
20–30 mg/L and a sorption coefficient (soil Koc) of 2,000. This resulted in a pesticide movement to groundwater rating of very low.

### Typical concentrations in drinking-water

No data available.

WHO (2017) states that fenitrothion residues detected in water were low (maximum 1.30 μg/L) during the spruce budworm spray programme. Following the spraying of forests to control spruce budworm, water samples did not contain detectable amounts of fenitrothion; post-spray samples contained less than 0.01 μg/L.

### Removal methods

No information available. However, it is likely that some of the newer advanced oxidation technologies may be effective.

### Analytical methods

#### Referee method

A referee method cannot be selected for because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

WHO (2004) states the common procedure for determining residues in foods and environmental media consists of extraction, partition, chromatographic separation (clean-up) and qualitative and quantitative analysis using gas chromatography with a flame photometric or a nitrogen-specific detector or using high-pressure liquid chromatography. The detection limit is 0.001 mg/L.

### Health considerations

Intake of fenitrothion appears to be primarily (95 percent) from food.

When volunteers were given single oral doses ranging from 2.5 to 20 mg/person, the maximal concentration of p-nitro-m-cresol in the urine was reached within 12 hours, and nearly the entire amount discharged was eliminated during the first 24 hours.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw following a one-year dietary study in dogs. This NOEL is based on plasma cholinesterase inhibition. The ADI incorporates a safety factor of 100 and was established in 1997. The previous ADI had been 0.003 mg/kg bw/day based on a NOEL of 0.3 mg/kg bw/day from a 92-week rat study. The ARfD is 0.03 mg/kg bw based on a NOEL of 0.33 mg/kg bw/day from a single dose study in humans for plasma and red blood cell cholinesterase inhibition. The ARfD incorporates a safety factor of 10 (for intraspecies variation).

JMPR (2010) quotes an ADI of 0–0.005 mg/kg/d; the ARfD is 0.04 mg/kg bw for fenitrothion.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.00125 mg/kg/d, and an ARfD of 0.0025 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenitrothion is 0.025 mg/L.

On the basis of testing in an adequate range of studies in vitro and in vivo, JMPR concluded that fenitrothion is unlikely to be genotoxic. It also concluded that fenitrothion is unlikely to pose a carcinogenic risk to humans (WHO 2017).

As at September 2008 the USEPA has classified fenitrothion in Group E: evidence of non-carcinogenicity for humans. In long-term studies of toxicity, inhibition of cholinesterase activity was the main toxicological finding in all species.

### Derivation of Maximum Acceptable Value

WHO (2017) states that as fenitrothion usually occurs in drinking-water at concentrations well below those at which toxic effects may be expected to occur, it is not considered necessary to derive a guideline value for fenitrothion in drinking water.

However, a MAV for fenitrothion in drinking-water could be derived as follows (WHO 2011/2017 calls this a health-based value):

0.5 mg/kg body weight per day x 70 kg x 0.05 = 0.00875 mg/L (rounded to 0.01 mg/L)

2 L x 100

where:

* allowable daily intake (ADI) = 0.5 mg/kg body weight per day for inhibition of brain and erythrocyte cholinesterase activity in a two-year study of toxicity in rats, and supported by a NOAEL of 0.57 mg/kg of body weight per day for inhibition of brain and erythrocyte cholinesterase activity in a three-month study of ocular toxicity in rats, and a NOAEL of 0.65 mg/kg of body weight per day for reduced food consumption and body weight gain in a study of reproductive toxicity in rats
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.05
* average quantity of water consumed by an adult per day = 2 L
* uncertainty factor = 100.

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# Fenoprop

CAS No. 93-72-1. The IUPAC name for fenoprop is (RS)-2-(2,4,5-trichlorophenoxy)propionic acid. The CAS name is 2-(2,4,5-trichlorophenoxy)propanoic acid. Also called silvex (in the US) or 2,4,5-TP or 2,4,5-TCPPA.

### Maximum Acceptable Value

Based on health considerations, the concentration of fenoprop in drinking-water should not exceed 0.01 mg/L.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.05 mg/L. The USEPA (2006/2009/2011) also established a lifetime health advisory of 0.05 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity. Despite the above, it appears that the USEPA cancelled all registered uses of Silvex in 1993 (PMEP).

### Sources to water

Fenoprop may enter source waters as a result of its use as a selective chlorophenoxy systemic hormone-type herbicide. It is absorbed by the roots and leaves and is used to control woody plants on non-crop areas and pastures and broadleaved weeds in a variety of crops. It can be applied as a variety of salts and esters. Fenoprop is a plant growth regulator (a synthetic hormone in the auxin family).

Concentrations of fenoprop in 1339 surface water samples from western Canada were less than 4 ng/L (0.000004 mg/L).

It is not currently registered (as at 2005/2009) in New Zealand but has been in the past. This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Fenoprop is non-volatile. Reported half-lifes of fenoprop are in the range of a week or two to three to four months. In soil fenoprop is degraded to 2,4,5-trichlorophenol which is very resistant to further breakdown; see datasheet in organic chemicals section.

Water solubility ranges from 140 to 170 mg/L. Fenoprop was essentially cleared from three Louisiana ponds within five weeks of treatment (WHO 2011).

NPIC (1994) quotes for fenoprop a soil half-life of 21 days, water solubility of 140 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 157 zones, did not find any detectable concentrations of fenoprop (limit of detection = 0.0001 mg/L) (ESR 2001).

Chlorophenoxy herbicides are not frequently found in drinking-water; when detected, concentrations are usually no greater than a few micrograms per litre (WHO 2004/2017).

Most groundwaters surveyed in the USA contained less than 0.0001 mg/L fenoprop per litre. Twenty water utilities in the US reported detecting 2,4,5-TP (Silvex) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.028 mg/L.

### Removal methods

No specific information on methods of removing fenoprop from water is available. However, slow sand filtration can partially remove members of the chlorophenoxy acid pesticide family of which fenoprop is a member. Ozone has shown varying degrees of effectiveness in oxidising the chlorophenoxy acids. WHO (2011/2017) states that 0.001 mg/L should be achievable using GAC.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 515.).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6640B).

### Health considerations

In general, chlorophenoxy herbicides are absorbed rapidly from the gastrointestinal tract and are distributed evenly throughout the body. Accumulation in human tissues is not expected, and a steady-state level in the human body will be achieved within  
3–5 days of exposure. Elimination occurs primarily in the urine, mostly in the unchanged form. Biological half-lifes of chlorophenoxy herbicides in mammals range from 10 to 33 hours. Metabolic conversions occur only at high doses. The salt and ester forms are hydrolysed rapidly and follow the same pharmacokinetic pathways as the free acid forms.

No adverse effects were reported following ingestion of a single dose of 1 mg fenoprop/kg body weight by eight human volunteers.

The results from short and long-term exposure studies in animals report depressed body weight gain and liver and kidney damage at elevated doses. Effects observed in long-term studies with beagle dogs given fenoprop in the diet include mild degeneration and necrosis of hepatocytes and fibroblastic proliferation in one study and severe liver pathology in another study. In rats, increased kidney weight was observed in two long-term dietary studies (WHO 2017).

The oral reference dose or RfD (USEPA 1988/2006/2009/2011) is 0.008 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.3 mg/L.

Fenoprop has not exhibited mutagenic activity in a bacterial assay test.

Chlorophenoxy herbicides as a group, including 2,4-D and MCPA, have been classified by the International Agency for Research on Cancer in Group 2B (possibly carcinogenic to humans). However, based on the available data from studies on exposed populations and on animals, it is not possible to assess the carcinogenic potential of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects (WHO 2017).

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV for fenoprop in drinking-water. The no-observable-adverse-effect level used in the derivation is from a study in which beagle dogs were administered fenoprop in the diet for two-years.

The MAV for fenoprop in drinking-water was derived as follows:

0.9 mg/kg body weight/day x 70 kg x 0.1 = 0.01 mg/L

2 L/day x 300

where:

* no observable adverse effect level = 0.9 mg/kg body weight per day for adverse effects on the liver in a study in which beagle dogs were administered fenoprop in the diet for two years
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 300 (100 for inter and intra-species variation and 3 for limitations of the data base).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for 2-(2,4,5-trichlorophenoxy)propanoic acid is 0.05 mg/L.

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# Fenoxaprop-p-ethyl

CAS No. 66441-23-4. The IUPAC name for fenoxaprop-ethyl is ethyl (RS)-2-[4-(6-chloro-1,3-benzoxazol-2-yloxy)phenoxy]propionate or ethyl (RS)-2-[4-(6-chlorobenzoxazol-2-yloxy)phenoxy]propionate. Fenoxaprop-ethyl is also called ethyl 2‑[4-[(6-chloro-2-benzoxazolyl)oxy]phenoxy]propanoate.

The (R)-isomer of fenoxaprop-ethyl has the ISO common name [fenoxaprop-p-ethyl](http://www.alanwood.net/pesticides/derivatives/fenoxaprop-p-ethyl.html) (CAS No. 71283-80-2). The (R)-isomer is biologically active. The S-enantiomer (fenoxaprop-M-ethyl), does not carry herbicidal activity and is regarded as a non relevant impurity. The total amount of fenoxaprop-ethyl in the commercial product is about 960 g/kg, with an R to S enantiomeric ratio of typically 98 to 2.

The (R)-isomer of fenoxaprop has the ISO common name fenoxaprop-P (CAS No. 113159-40-0).

Fenoxaprop-ethyl and fenoxaprop-p-ethyl are derivatives of [fenoxaprop](http://www.alanwood.net/pesticides/fenoxaprop.html) (CAS No. 95617-09-7).

Fenoxaprop is also known as fenoxoprop. Fenoxaprop-p-ethyl is also known as fenoxaprop ethyl and fenoxaprop-P.

### Maximum Acceptable Value

Fenoxaprop-p-ethyl does not have a MAV in the DWSNZ; fenoxaprop-p-ethyl is not mentioned in the WHO Guidelines.

### Sources to water

Fenoxaprop-p-ethyl is a fairly new [aryloxyphenoxypropionic herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#aryloxyphenoxypropionic_herbicides) (replacing fenoxaprop-ethyl), commonly used post-emergence to control grass weeds in cereals, inhibiting acetyl coenzyme A carboxylase activity. Fenoxaprop-p-ethyl is often sold mixed with other pesticides. Its use is increasing due to some weeds acquiring resistance to isoproturon.

Fenoxaprop-p-ethyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is structurally similar to fluazifop. Fenoxaprop appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Fenoxaprop formulations usually contain the ‘safener’ mefenpyr-diethyl (qv).

### Forms and fate in the environment

Fenoxaprop-p-ethyl is not expected to volatilise significantly due to its low vapour pressure of 1.4 x 10-8 torr. Fenoxaprop-p-ethyl is slightly-to-barely mobile (Kd of 12.6 to 443); however, its primary degradation product, fenoxaprop-p acid is mobile, so potentially presents a groundwater concern in some soils. Solubility in water is about 0.7 mg/L.

NPIC (1994) quotes for fenoxaprop-ethyl a soil half-life of nine days, water solubility of 0.8 mg/L and a sorption coefficient (soil Koc) of 9,490. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See Ozhan et al.

### Health considerations

For fenoxaprop-ethyl the chronic RfD = 0.0025 mg/kg/day. The hazard component of chronic risk for fenoxaprop-ethyl was the NOAEL of 0.25 mg/kg/day based on decreased total blood lipids/cholesterol at the LOAEL of 1.5 mg/kg/day in a rat reproductive toxicity study. Furthermore, the highest dose of 9 mg/kg/day also produced increased absolute and relative brain and kidney weights with increased incidence of nephrocalcinosis reported in a previous study. The reproductive LOAEL of 1.5 mg/kg/day was based on reduced pup body weights. The interspecies x intraspecies (10 x 10) Uncertainty Factor was 100, and the FQPA Safety Factor was 1. The FQPA Safety Factor was reduced to 1 since developmental toxicity studies showed no increased sensitivity; foetal malformations in the rat developmental study were only at maternally toxic doses; and a multi-generation reproduction rat study showed no increased sensitivity to pups as compared to adults (USEPA 2007). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0025 mg/kg/d, and an ARfD of 0.32 mg/kg/d for fenoxaprop-ethyl. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenoxaprop-ethyl is 10.6 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for fenoxaprop-ethyl is 0.004 mg/kg body weight, with a NOEL of 0.4 mg/kg bw.

A decision on the carcinogenicity of fenoxaprop-p-ethyl is awaited, although there is negligible cancer risk from chronic exposures to fenoxaprop-ethyl in drinking water and food. As at September 2008 the USEPA has classified fenoxaprop-p-ethyl as likely to be carcinogenic to humans. Fenoxaprop-ethyl appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Potential fenoxaprop-ethyl residues in drinking water were found not to be greater than the level of concern for acute aggregate (women <13 years) or for chronic aggregate risk.

For fenoxaprop-ethyl, for acute drinking-water exposure for both adults and children, the level of concern was 960 mg/L. For chronic and cancer exposure in drinking-water the levels of concern were 0.08 mg/L and 0.00011 mg/L, respectively. For adults, the estimate was based on a body weight of 70 kg and consumption of two litres of water per day; for children, a body weight of 10 kg and a consumption of one litre of water per day. The USEPA estimates for contamination of drinking-water from the registered uses of fenoxaprop-ethyl is less than 0.001 mg/L for acute exposure and less than 0.0001 mg/L for chronic exposure. These levels are not greater than levels of USEPA concern.

EC (2007) established an ADI for fenoxaprop-P of 0.01 mg/kg/d, and an ARfD of 0.1 mg/kg/d.

Fenoxaprop-P-ethyl has not been evaluated by the FAO/WHO JMPR and WHO/IPCS (JMPR 2010).

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenoxycarb

CAS No. 72490-01-8 (formerly 79127-80-3). The IUPAC name for fenoxycarb is ethyl 2‑(4-phenoxyphenoxy)ethylcarbamate. The CAS name is ethyl [2‑(4‑phenoxyphenoxy)ethyl]carbamate.

### Maximum Acceptable Value

Fenoxycarb does not have a MAV in the DWSNZ; fenoxycarb is not mentioned in the WHO Guidelines.

### Sources to water

Fenoxycarb is a non-neurotoxic juvenile hormone mimic (carbamate) insecticide. Fenoxycarb blocks the ability of an insect to change into an adult from the juvenile stage (metamorphosis). It also interferes with the moulting of larvae. It is used as a fire ant bait and for flea, mosquito and cockroach control. Fenoxycarb can also be used to control butterflies and moths, scale insects, and sucking insects on olives, vines, cotton and fruit. It is also used to control these pests on stored products (EXTOXNET 1993).

Fenoxycarb does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Despite that, ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (as amended), as at 22 May 2008 lists a “flammable aerosol containing 1.07 g/kg fenoxycarb and 10 g/kg permethrin”; see: <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides.

### Forms and fate in the environment

Fenoxycarb is readily broken down in soil by the chemical action of water (hydrolysis). Residues in soil were no longer detectable three days after application. The compound also has a low potential for leaching from the soil and has a moderate to strong soil binding tendency. These characteristics of fenoxycarb in soil indicate that it is unlikely to contaminate groundwater.

The compound is stable to hydrolysis in acidic water. It breaks downs very rapidly in the presence of sunlight (photodegrades) in water. Half of the initial amount of the compound is broken down by this means within five hours. It readily attaches on to organic matter which may limit its persistence in water. Residues in the water could be detected for only two days following an aerial treatment of ponds for the control of mosquitoes. Urethane is a potential metabolite.

Water solubility is about 6 mg/L.

NPIC (1994) quotes for fenoxycarb a soil half-life of one day, water solubility of 6 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Rats fed very low doses of fenoxycarb for a year had no compound-related effects at or below the 10 mg/kg/day dose. Dogs fed the compound at doses of 15.9 mg/kg/day or below for 1.5 months experienced no adverse effects. Similar results were noted for the compound in mice (1.4 mg/kg) and in rats (0.8 mg/kg/day) over a longer period. It has a low toxicity for [bees](http://en.wikipedia.org/wiki/Bees), [birds](http://en.wikipedia.org/wiki/Birds), and [humans](http://en.wikipedia.org/wiki/Humans), but is toxic to [fish](http://en.wikipedia.org/wiki/Fish).

In 1995 the USEPA OPP peer review committee determined fenoxycarb “to be a likely carcinogen”, ie, Group 2B – a probable human carcinogen. It is also a suspected endocrine disruptor.

The Acceptable Daily Intake (ADI) adopted in Australia for fenoxycarb is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> an ARfD of 0.20 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenoxycarb is 2.0 mg/L.

<http://ec.europa.eu/sanco_pesticides/public/index.cfm> quotes an ADI of 0.053 mg/kg/d and an ARfD of 2 mg/kg/d referring to an EFSA source. These values were also derived in EFSA (2015).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fenpiclonil

CAS No. 74738-17-3. The IUPAC and CAS name for fenpiclonil is 4‑(2,3‑dichlorophenyl)-1H-pyrrole-3-carbonitrile.

### Maximum Acceptable Value

Fenpiclonil does not have a MAV in the DWSNZ; fenpiclonil is not mentioned in the WHO Guidelines.

### Sources to water

Fenpiclonil is a broad spectrum pyrrole (or phenylpyrrole) fungicide commonly used for seed treatment and on vegetables and cereals, and is also a wood preservative. The antifungal antibiotic activity of pyrrolnitrin was first discovered following isolation from Pseudomonas pyrrocinia. Pyrrolnitrin was subsequently synthesised. Although it showed excellent activity in vitro and in the greenhouse against the fungal plant pathogens Botrytis cinerea and Pyricularia oryzae, its performance in the field was disappointing, because the natural product rapidly decomposed when exposed to sunlight. It soon became apparent that replacement of the chloro substituent in the three-position of the pyrrole by a cyano group led to an enhancement in stability. Thus the half-life of fenpiclonil in simulated sunlight is 48 hours compared with half an hour for pyrrolenitrin. Finally, the biological activity was optimised by appropriate substitution on the phenyl ring. Two commercial products emerged from these efforts, fenpiclonil and fludioxonil (qv). Fludioxonil has tended to replace fenpiclonil (ECSOC).

Fenpiclonil does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)), but it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides). Some commercial products are sold mixed with imazalil.

Fenpiclonil is on the list of active ingredients to be removed in July 2003 in Europe under Directive 91/414/EEC.

### Forms and fate in the environment

Fenpiclonil is persistent in soils, with a half-life of about eight months. The hydrolysis half-life is about 23 days. Its aqueous photolysis rate is high, with a half-life of <1 day in some conditions. Fenpiclonil is non-volatile. The octanol-water partition coefficient at pH 7 and 20oC (ie, LogP) is 3.86. It has a potential to bind to particles. Fenpiclonil and its metabolites have a low potential for leaching to groundwater. Water solubility is about 5 mg/L.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of fenpiclonil in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Fenpiclonil has low acute toxicity via oral routes.

The Acceptable Daily Intake (ADI) adopted in Australia for fenpiclonil is 0.01 mg/kg body weight, with a NOEL of 1.2 mg/kg bw.

An ADI of 0.23 mg/kg bw is quoted in DEFRA and IUPAC. No ARfD was allocated.

### Derivation of Maximum Acceptable Value

No MAV.

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# Fenpropidin

CAS No. 67306-00-7. The IUPAC name for fenpropidin is 1-[(RS)-3-(4-tert-butylphenyl)-2-methylpropyl]piperidine. The CAS name is 1-[3-[4-(1,1-dimethylethyl)phenyl]-2-methylpropyl]piperidine.

### Maximum Acceptable Value

Fenpropidin does not have a MAV in the DWSNZ; fenpropidin is not mentioned in the WHO Guidelines.

### Sources to water

Fenpropidin is a piperidine fungicide, used control powdery mildews, rusts and Rynchosprium secalis in cereal crops. Fenpropidin is proposed (as at 2007) for use in New Zealand as a fungicide for wheat and barley.

Fenpropidin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Water solubility is about 530 mg/L (SITEM). Fenpropidin is described as moderately persistent, with a water/sediment half-life of about a month – it would appear to preferentially attach to sediment, hence is not likely to leach to groundwater. Aerobic soil half-lifes are about 60 to 90 days.

EFSA (2011a) includes a list of metabolites.

### Removal methods

Treatment processes that remove particulate matter from water should reduce the concentration of fenpropidin.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The toxicological profile of fenpropidin was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI of 0.02 mg/kg bw/d and an ARfD of 0.02 mg/kg bw/d (EC 2008; EFSA 2011).

An acute lethality study shows that fenpropidin is not acutely toxic by the oral route of exposure. Clinical signs of neurotoxicity and neuropathology are the other major toxic effects observed following oral exposure in the rat and dog, and the dog is the most sensitive species for the neurotoxic effects. The most sensitive acute RfD (which = aPAD) was for infants and children and = 0.07 mg/kg/day (USEPA 2014).

In the chronic toxicity/carcinogenicity study in rats, benign pancreatic cell adenomas were seen in high-dose male rats. Tumours were not increased in the mouse carcinogenicity study in either sex or in the female rat. Mutagenicity is not of concern. The cRfD and cPAD endpoint for all populations was 0.023 mg/kg/d, and this will adequately account for all chronic toxicity, including carcinogenicity, that could result from exposure to fenpropidin.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fenpropimorph

CAS No. 67564-91-4. The IUPAC name for fenpropimorph is cis-4-[(RS)-3-(4-tert-butylphenyl)-2-methylpropyl]-2,6-dimethylmorpholine. The CAS name is (2R,6S)-rel-4-[3-[4-(1,1-dimethylethyl)phenyl]-2-methylpropyl]-2,6-dimethylmorpholine.

### Maximum Acceptable Value

Fenpropimorph does not have a MAV in the DWSNZ; fenpropimorph is not mentioned in the WHO Guidelines.

### Sources to water

Fenpropimorph is a morpholine fungicide, whose major use is to control powdery mildew and rust in cereals. It is often mixed with other pesticides. Fenpropimorph provides protectant and eradicant activity by inhibiting ergosterol biosynthesis.

Fenpropimorph appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Fenpropimorph is resistant to hydrolysis and photolysis. Under field conditions degradation in soil proceeds by oxidation and opening of the morpholine ring to give BF 421-2 (the acid), BF 421-7, BF 421-8 (the hydroxyethylamine) and BF 421-10 (dimethylmorpholine).

In aerobic water/soil systems the degradation is similar except that the morpholine ring is not opened. In addition to these compounds, BF 421-13 (the alkyl ketone) and BF 421-15 (the morpholine-3-one derivative) can be formed by photolysis of fenpropimorph in soil. The half-life in various soils has been reported to range from about 10 to 90 days.

EFSA (2015 – see <http://www.efsa.europa.eu/en/efsajournal/pub/4050.htm>) reports that soil studies demonstrated the degradation rate of fenpropimorph is slow; the field DT90 was expected to range between 285–11,705 days.

Fenpropimorph is unlikely to leach to groundwater. Water solubility is about 3 to 7 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See FAO (1995).

### Health considerations

The chronic RfD = 0.032 mg/kg/day based on NOAEL = 3.2 mg/kg/day and uncertainty factor of 100 (USEPA 2006). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.032 mg/kg/d, and an ARfD of 0.15 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenpropimorph is 4.95 mg/L.

Fenpropimorph was first evaluated by the 1994 JMPR, which established an ADI of  
0–0.003 mg/kg bw on the basis of a NOAEL of 0.3 mg/kg bw per day, in a two-year study of toxicity and carcinogenicity in rats. At the 2001 JMPR, an ARfD of 1 mg/kg bw was established on the basis of a NOAEL of 100 mg/kg bw per day in an acute neurotoxicity study in rats. JMPR (2004) states that ARfD was revised to 0.2 mg/kg/d on the basis of an overall NOAEL of 15 mg/kg bw per day for embryo- and fetotoxicity and teratogenicity in two studies of prenatal developmental toxicity in rabbits and using a safety factor of 100. JMPR (2016) adjusted the ADI to 0.004 mg/kg bw, and established an ARfD of 0.1 mg/kg bw for women of child-bearing age, and an ARfD of 0.4 mg/kg bw for the general population. Reaffirmed in 2017.

EC (2008) established an ADI of 0.003 mg/kg/d and an ARfD of 0.03 mg/kg/d. Reaffirmed in EFSA (2013/2015).

The USEPA classified fenpropimorph as “not likely to be carcinogenic to humans”; no increased incidences in tumours in a chronic/carcinogenicity rat study or a carcinogenicity mouse study.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2008. *Review Report for the Active Substance Fenpropimorph*. European Commission, Health & Consumer Protection Directorate-General. *SANCO*/134/08 – rev. 0 [7 pp]. See: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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# Fenpyrazamine

CAS No. 473798-59-3. The IUPAC name for fenpyrazamine is S-allyl 5-amino-2,3-dihydro-2-isopropyl-3-oxo-4-(o-tolyl)pyrazole-1-carbothioate. The CAS name is S‑2‑propen-1-yl 5-amino-2,3-dihydro-2-(1-methylethyl)-4-(2-methylphenyl)-3-oxo-1H-pyrazole-1-carbothioate.

### Maximum Acceptable Value

Fenpyrazamine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Fenpyrazamine is a non-systemic [pyrazole](http://www.alanwood.net/pesticides/class_herbicides.html#aryloxyphenoxypropionic_herbicides) fungicide used for the control of grey mould (Botrytis cinerea) in grapes. Fenpyrazamine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2016 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Fenpyrazamine has adsorption coefficients (Koc) between 123 and 766, which indicates a moderate mobility in certain soil types. In addition, fenpyrazamine is considered moderately persistent to persistent with longer degradation half-lifes in acidic soils. Accordingly, the product label carries advisories that warn of potential groundwater contamination in areas where soils are permeable and potential surface water contamination in areas with poorly draining soils prone to run-off (PMEP 2014).

The water solubility of fenpyrazamine is 20.4 mg/L. The partition coefficient is Pow = 3307, or log Pow = 3.52; Henry’s Law Constant = 1.62 x 10-4 Pa.m3/mole at 20°C. The hydrolysis half-life at pH 7 is >1 year. The photolysis half-life in sterile water at pH 7 and 25°C is 1.7 days. Fenpyrazamine in soil was found to be stable to photolysis in laboratory conditions with DT50 values varying from 74–80 days. Fenpyrazamine is not readily biodegradable, with minimal degradation observed over 28 days. However, in soil biotic degradation is a major pathway and fenpyrazamine generally degraded fairly readily, with DT50 values of 24–68 days. Under anaerobic conditions fenpyrazamine degraded more slowly, with a DT50 of 129 days. Under aerobic conditions in water/sediment systems, fenpyrazamine is slightly degradable, with DT50 values of between 18 and 68 days, and in anaerobic conditions in water/sediment the DT50 is about 19 days. Fenpyrazamine is generally regarded as having medium mobility with a mean Koc of 310 mL/g (APVMA 2016).

EFSA (2017) reports 90 percent dissipation (DT90 values) of fenpyrazamine in field studies up to 134 days.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Fenpyrazamine caused some toxicity in chronic feeding studies in laboratory animals. In a chronic feeding study in dogs, fenpyrazamine caused alterations in hematology and clinical chemistry parameters (increased mean corpuscular volume, platelet counts and alkaline phosphatase and decreased mean corpuscular hemoglobin concentration) at 100 mg/kg/day; the NOEL was 25 mg/kg/day. In a chronic feeding/oncogenicity study in rats, fenpyrazamine caused decreased body weight, hepatocyte fatty change and vacuolated foci at 107 mg/kg/day in males and 130 mg/kg/day in females; the NOELs were 51.9 mg/kg/day and 63.6 mg/kg/day, respectively. In a chronic feeding study in mice, alterations in hematology (increased mean corpuscular volume and mean corpuscular hemoglobin and decreased red blood cell count, hemoglobin and hematocrit) were observed at 349 mg/kg/day in males and 552 mg/kg/day in females; the respective NOELs were 176 mg/kg/day and 283 mg/kg/day (PMEP 2014).

The Acceptable Daily Intake (ADI) adopted in Australia for fenpyrazamine is 0.13 mg/kg body weight, based on application of a 100-fold safety factor to the NOEL of 300 ppm (12.72/15.64 mg/kg bw/d for M/F) for both sexes in a chronic dietary study in rats. The ARfD was established at 0.2 mg/kg bw, based on a 100-fold safety factor and the NOEL of 400 ppm (20.3/28.5 mg/kg bw/d for M/F) for both sexes in a two-generation reproductive toxicity study in rats. APVMA (2016). In February 2017 APVMA adjusted the ARfD to 0.8 mg/kg based on an acute neurotoxicity rat study – a NOAEL of 80 mg/kg bw was based on a reduction in motor activity and number of rearings at the next higher dose.

EFSA (2016/2017) adopted an acceptable daily intake (ADI) of 0.13 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.3 mg/kg bw.

The JMPR (2017) Meeting established an ADI of 0–0.3 mg/kg bw, and an ARfD of 0.8 mg/kg bw. Fenpyrazamine is unlikely to pose a carcinogenic risk to humans, there was no evidence of genotoxicity, teratogenicity, and fenpyrazamine is not teratogenic, neurotoxic or immunotoxic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fenpyroximate

CAS No. 134098-61-6. Also allocated CAS No. 111812-58-9. The IUPAC name for fenpyroximate is tert-butyl (E)-α-(1,3-dimethyl-5-phenoxypyrazol-4-ylmethyleneaminooxy)-p-toluate. The CAS name is 1,1-dimethylethyl 4-[[[(E)-[(1,3-dimethyl-5-phenoxy-1H-pyrazol-4-yl)methylene]amino]oxy]methyl]benzoate. The technical material contains 960 g/kg of the E-isomer, much of the remainder being the Z-isomer.

### Maximum Acceptable Value

Fenpyroximate does not have a MAV in the DWSNZ; fenpyroximate is not mentioned in the WHO Guidelines.

### Sources to water

Fenpyroximate is a [pyrazole](http://www.alanwood.net/pesticides/class_herbicides.html#aryloxyphenoxypropionic_herbicides) acaricide or miticide, commonly used on pome fruits in New Zealand. Fenpyroximate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register) as an ectoparasiticide, endoparasiticide and insecticide. Approved in the US for the control of the Varroa mite in beehives.

### Forms and fate in the environment

Fenpyroximate was degraded with a half-life of 34 to 50 days in diluvial soil and 26 to 36 days in volcanic ash soil. Eleven degradation products were identified. A laboratory column leaching study was carried out with three different sandy soils, fenpyroximate was then added at the highest recommended field application rate of 150 g ai/ha; the concentration of fenpyroximate in the leachate of the sand was 0.21 mg/L (0.27 percent of the applied amount), and below the detection limit of 0.1 mg/L in the other leachates.

Based on laboratory fate properties and proposed application methods, fenpyroximate (combined residues) is expected to persist long enough to become available for transport in run-off events to surface and groundwater environments. However, strong sorption to soil (Kd of 75 to 1365 mL/g) is expected to reduce concentrations of parent fenpyroximate in water; transport via run-off is likely to include the parent and M-1 isomer sorbed to sediment.

The longest calculated field DT50 and DT90 values of fenpyroximate were 16.7 and 48 days, respectively. For metabolite M-3 the highest laboratory DT50 and DT90 values were 68 and 225 days, respectively (EFSA 2013).

Fenpyroximate is stable to sterile hydrolysis and degrades slowly due to anaerobic aquatic metabolism and aerobic aquatic metabolism with combined residue half-lifes ranging from 125 to 170 days and 20 to 33 days, respectively. Aqueous photolysis is expected to be negligible because the parent and M-1 in water will tend to sorb to soil particles and not be available for degradation. Also, shading of surface water and turbidity will reduce photodegradation. Water solubility is about 0.02 to 0.03 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of fenpyroximate in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Fenpyroximate was evaluated by the 1995 JMPR, when an ADI of 0–0.01 mg/kg bw was established on the basis of a NOAEL of 1 mg/kg bw per day in a 104-week study in rats and a safety factor of 100. This was reaffirmed in 2017. The lowest levels causing no effect were 1 mg/kg bw per day (104-week study in rats of carcinogenicity), and 2.5 mg/kg bw per day (maternal toxicity in study of developmental toxicity in rabbits (IPCS 1995).

The JMPR meeting established an ARfD of 0.01 mg/kg bw on the basis of the a minimal LOAEL of 2 mg/kg bw per day for the induction of diarrhoea at the beginning of a 13‑week study of toxicity in dogs. It was unclear whether the diarrhoea was the result of a direct irritant or pharmacological effect of fenpyroximate. A safety factor of 200 was used since no NOAEL was identified. This ARfD is probably conservative and could be refined using the results of an appropriately designed study (JMPR 2004). In JMPR (2013) the ARfD is quoted as 0.02 mg/kg bw (since 2007). In JMPR (2017) is quoted as 0.02 mg/kg bw again.

USEPA (2004) quotes an acute RfD of 0.05 mg/kg/day, and a chronic RfD of 0.01 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.05 mg/kg/d. Fenpyroximate is classified as not likely to be carcinogenic to humans. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenpyroximate is 1.65 mg/L.

The EC (2009) confirmed the JMPR ADI of 0.01 mg/kg/d and derived an ARfD of 0.02 mg/kg bw. These values were reaffirmed by EFSA (2013 and 2016). With particular regard to residues, the EC review established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health.

EFSA (2013) considers fenpyroximate is unlikely to be genotoxic, carcinogenic, neurotoxic or toxic for reproduction.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fenthion

CAS No. 55-38-9. The IUPAC name for fenthion is O,O-dimethyl O-4-methylthio-m-tolyl phosphorothioate. The CAS name is O,O-dimethyl O-[3-methyl-4-(methylthio)phenyl] phosphorothioate. May be sold as the ester – fenthion-ethyl.

### Maximum Acceptable Value

Fenthion does not have a MAV in the DWSNZ; fenthion is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Fenthion is a phenyl organothiophosphate contact and stomach insecticide used for pre- and post-harvest treatment of various fruits and vegetables. Its mode of action is via [cholinesterase inhibition](http://en.wikipedia.org/wiki/Cholinesterase_inhibition). It is particularly effective against fruit flies, leaf hoppers, cereal bugs, stem borers, mosquitoes, animal parasites, mites, aphids, and codling moths; it is commonly used on cherries, peaches, citrus fruit and olives. Fenthion is also used as a paint, paste or gel on cattle, swine, and dogs to control lice, fleas, ticks, flies, and other external parasites. It is also described as an avicide (WHO 1976).

Fenthion appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Its use is restricted or banned in some countries due to its effect on birds.

### Forms and fate in the environment

In soil, fenthion degradation ranges from four to six weeks and occurs through photodegradation as well as anaerobic or non-photolytic organisms. Soil particles strongly adsorb fenthion that makes it less susceptible to percolate with water through the soil.

In one study of its persistence in water, 50 percent of applied fenthion remained in river water two weeks later, while 10 percent remained after four weeks. Residue levels of 0.016 mg/L of fenthion were found in the water from which dead birds were retrieved, in an area that had been sprayed two days earlier with recommended mosquito control levels of the insecticide.

Fenthion is slowly hydrolysed in water at pH 5 and somewhat more rapidly at pH 7 and 9 but it is subject to rapid photolysis and is readily degraded biologically. It has no acidic or basic properties (WHO 2006).

Unstable in the presence of sunlight and air, completely degrading within one to three days, with the oxidation products rapidly decomposing themselves to non-insecticidal compounds. Relatively stable in acidic conditions, and moderately stable in alkaline conditions. From NSW Government (2013).

Water solubility is about 5 mg/L. The partition coefficient is log Pow = 4.84 at 20°C.

NPIC (1994) quotes for fenthion a soil half-life of 34 days, water solubility of 4.2 mg/L and a sorption coefficient (soil Koc) of 1500. This resulted in a pesticide movement to groundwater rating of low.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of fenthion in water. Activated carbon is likely to enhance the removal.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In animals, fenthion is quickly absorbed into the bloodstream through the digestive tract, lungs, and skin, and then broken down. Its breakdown products are eliminated through the urine and the faeces in a three-day period. An estimated acceptable daily intake (ADI) of 0.01 mg/kg/day for humans has been reported in INCHEM (1997), based on a NOAEL of 1 mg/kg bw in rats and applying a safety factor of 100. The 1997 JMPR established an acute RfD of 0.01 mg/kg bw, and this was also reported in JMPR (2000).

The Acceptable Daily Intake (ADI) adopted in Australia for fenthion is 0.002 mg/kg body weight, with a NOEL of 0.02 mg/kg bw from a 28-day human study showing cholinesterase inhibition. The ADI incorporates a safety factor of 10. The ARfD is 0.007 mg/kg bw based on a NOEL of 0.07 mg/kg bw/day from a 28-day oral study in human volunteers. The ARfD incorporates a safety factor of 10. This NOEL is further supported by a NOEL of 0.07 mg/kg bw from an acute neurotoxicity study in rats.

There was no evidence of weight loss or decreased food consumption in dogs that were given 50 mg/kg of fenthion in their diets for one year.

USEPA (2002) states that for chronic risk, the most highly exposed subgroup is children 1–6 years, and in 2000, the technical registrant (Bayer) requested a phased voluntary cancellation of all five of their livestock products. Fenthion is one of the more potent cholinesterase inhibitors, having an acute No Observed Adverse Effect Level (NOAEL) of 0.07 mg/kg/day in a two-year oral monkey study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.00007 mg/kg/d, and an ARfD of 0.0007 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fenthion is 0.007 mg/L.

The National Cancer Institute (USA) performed carcinogenicity tests on fenthion that indicated that this insecticide may be a carcinogen in male mice. However, no carcinogenic effects were observed in other two-year feeding studies of rats and mice.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fipronil

CAS No. 120068-37-3. The IUPAC name for fipronil is 5-amino-1-(2,6-dichloro-α,α,α-trifluoro-p-tolyl)-4-trifluoromethylsulfinylpyrazole-3-carbonitrile. The CAS name is 5‑amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfinyl]-1H-pyrazole-3-carbonitrile. Has sometimes been called fluocyanobenpyrazole.

### Maximum Acceptable Value

Fipronil does not have a MAV in the DWSNZ; fipronil is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0007 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.000078 mg/L (0.078 µg/L) for fipronil in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Fipronil is a broad spectrum [phenylpyrazole](http://www.alanwood.net/pesticides/class_herbicides.html#aryloxyphenoxypropionic_herbicides) acaricide or insecticide, commonly used to control ants, cockroaches, and German wasps (Etheridge 2001). It is also used as a seed dressing. It is an ingredient in Frontline, a topical [flea](http://en.wikipedia.org/wiki/Flea) and [tick](http://en.wikipedia.org/wiki/Tick) control used on dogs and cats. JMPR (1997) states that fipronil has been proposed for indoor and outdoor use in the control of the mosquito that carries the malaria parasite.

Fairly widespread contamination of eggs and chicken by fipronil has been found in Europe resulting from its illegal use on laying hens and their farms (EFSA 2018).

Fipronil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register) as an ectoparasiticide, endoparasiticide and insecticide. It is used to eradicate Argentinian ants in New Zealand.

### Forms and fate in the environment

Fipronil has a relatively low vapour pressure (2.8 x 10-9 mm Hg at 25°C) and a low Henry’s Law constant, so fipronil does not readily volatilise.

The half-life of fipronil applied by soil incorporation ranged from 3 to 7.3 months. Residues remain mainly in the upper 12 inches of soil. Fipronil has low soil mobility. It binds to the soil and has little potential for groundwater contamination. In studies where fipronil was exposed to light, fipronil had a half-life of 3.6 hours in water and 34 days in loamy soil. Octanol-Water Partition Coefficient (Kow): 1 x 104. Henry’s constant: 3.7 x 10-5 atm·m3/mol. Soil Sorption Coefficient (Koc): 825 ±214 when tested on eight soil types.

Fipronil degrades slowly in water and sediment that lack oxygen with a half-life ranging from 116–130 days. Fipronil is stable to breakdown by water at mildly acid to neutral pH. It degrades with a half-life of 28 days in higher pH solutions. Water solubility is about 2 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of fipronil in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2012).

### Health considerations

Fipronil is a possible human carcinogen (USEPA Group C, as at September 2008), and is a suspected endocrine disruptor. JMPR (2010) states that no genotoxic or carcinogenic potential is demonstrated.

The RfD for fipronil is 0.0002 mg/kg/day using a NOEL of 0.019 mg/kg/day established from a combined chronic toxicity/carcinogenicity study in rats and an uncertainty factor of 100 (USEPA 1998). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0002 mg/kg/d, and an ARfD of 0.025 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fipronil is 0.25 mg/L.

JMPR (1997) developed an ADI of 0–0.0002 mg/kg body weight for fipronil on the basis of the NOAEL of 0.019 mg/kg bw per day in the two-year study of toxicity and carcinogenicity in rats and incorporating a safety factor of 100. The meeting also considered that a separate ADI should be established for fipronil-desulfinyl (a photodegradation product of fipronil) on the basis that it could be a significant residue and that its toxicity is greater than that of the parent molecule fipronil. A temporary ADI of 0–0.00003 mg/kg bw for fipronil-desulfinyl was established on the basis of the NOAEL of 0.029 mg/kg bw per day in the 90-day study in rats and a safety factor of 1,000 in view of the lack of a long-term study by oral administration in rats and a study of neurotoxicity in rats given repeated oral doses. The meeting also allocated an acute reference dose (RfD) of 0.003 mg/kg bw for both fipronil and fipronildesulfinyl on the basis of the NOAEL of 0.3 mg/kg bw per day in a study of neurotoxicity in rats given repeated doses of fipronil, and a safety factor of 100.

JMPR (2010) states that fipronil had been evaluated for the first time by the JMPR in 1997, and again in 2000–2001, establishing an ADI of 0.0002 mg/kg body weight and an acute RfD of 0.003 mg/kg body weight.

The EC (2010) adopted the above ADI, and concluded that the International Estimated Daily Intake (IEDI, STMR values from maize, sunflower and animal products) for a 60 kg adult is 3 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994), and <20 percent for infants and toddlers, based on the French Dietary model. Additional intake from water and products of animal origin are not expected to give rise to intake problems. EC also adopted an ARfD of 0.009 mg/kg/d (EFSA 2012).

The acute RfD established by the 1997 JMPR was 0.003 mg/kg bw for both fipronil and fipronil-desulfinyl, on the basis of the NOAEL of 0.3 mg/kg bw per day in a study of neurotoxicity in rats given repeated doses of fipronil, and a safety factor of 100. JMPR (2007) confirmed this as a group acute RfD for fipronil and fipronil-desulfinyl, alone or in combination.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0002 mg/kg body weight, with a NOEL of 0.02 mg/kg bw from a two-year rat dietary study for effects on the nervous system, thyroids and kidneys. The ADI includes a safety factor of 100. The ARfD is 0.02 mg/kg bw based on a NOEL of 2.5 mg/kg bw for effects on the nervous system in an acute dietary study in rats. This incorporates a safety factor of 100. The previous (pre-2006) ARfD had been 0.003 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# Flamprop-isopropyl

CAS No. 52756-22-6. The IUPAC name for flamprop-isopropyl is isopropyl N-benzoyl-N-(3-chloro-4-fluorophenyl)-DL-alaninate. The CAS name is 1-methylethyl N-benzoyl-N-(3-chloro-4-fluorophenyl)-DL-alaninate.

The parent compound is [flamprop](http://www.alanwood.net/pesticides/flamprop.html) (CAS No. 58667-63-3): N-benzoyl-N-(3-chloro-4-fluorophenyl)-DL-alanine. The d-isomer of flamprop is referred to as flamprop-M.

Flamprop-isopropyl is sometimes referred to as l-flamprop-isopropyl (CAS No. 57973-67-8), which has superior herbicidal properties to the d-isomer. The d-isomer is usually referred to as flamprop-M-isopropyl (CAS No. 63782-90-1).

Flamprop-methyl (CAS No. 52756-25-9) and its d-isomer, flamprop-M-methyl (CAS No. 63729-98-6), is sold in some countries, eg, in Australia.

### Maximum Acceptable Value

Flamprop-isopropyl does not have a MAV in the DWSNZ; it is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.004 mg/L for flamprop-methyl; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Flamprop-isopropyl is a post-emergent arylalanine herbicide, commonly used to control wild oats growing amongst cereals.

Flamprop-M-isopropyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)); a trade name is Crusader. It is not registered for use in the US, and its use in Canada ceased from 2008. Flamprop-isopropyl is approved for the use on malting barley in the UK (<http://www.fluoridealert.org/pesticides/beer.uk.pesticides.2002.htm>).

### Forms and fate in the environment

The half-life of flamprop-isopropyl in soil is 4 to 20 weeks depending on soil type and conditions. Minor leaching of flamprop-M-isopropyl and flamprop (free acid) was measured but not in unacceptable levels. Apart from two samples, all concentrations were below 0.1 µg/L (PLAP 2003). Solubility in water is about 10–20 mg/L.

### Removal methods

The fairly strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of flamprop-isopropyl in water. Activated carbon processes should enhance the removal.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Flamprop-isopropyl residues were not found in the NZFSA 2003–2004 survey of foods ([www.nzfsa.govt.nz/science/research-projects/total-diet-survey/reports/full-final-report/nzfsa-total-diet.pdf](http://www.nzfsa.govt.nz/science/research-projects/total-diet-survey/reports/full-final-report/nzfsa-total-diet.pdf)).

In two-year dietary studies in rats and dogs, liver hypertrophy and increased liver weight were seen at 12.5 mg/kg bw/day in rats, and at 2.5 mg/kg bw/day in dogs. The lowest overall NOEL in these studies was 0.125 mg/kg bw/day in rats. Based on a two-year study in rats, there is no evidence of carcinogenicity for flamprop-methyl. Flamprop-methyl is not considered to be genotoxic, based on in vitro and in vivo short-term studies. A three-generation reproduction study in rats and a developmental study in rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity. A health-based guideline value of 0.004 mg/L for flamprop-methyl was proposed (NHMRC 2011).

The Acceptable Daily Intake (ADI) adopted in Australia for flamprop-methyl is 0.001 mg/kg body weight, with a NOEL of 0.125 mg/kg bw from a long-term study. The NOEL is based on liver hypertrophy and increased liver weight in a two-year dietary study. The ADI incorporates a safety factor of 100.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

NHMRC, NRMMC. 2011. *Australian Drinking Water Guidelines Paper 6 National Water Quality Management Strategy*. Canberra: National Health and Medical Research Council, National Resource Management Ministerial Council, Commonwealth of Australia [1244 pp]. <http://www.nhmrc.gov.au/guidelines/publications/eh52>

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# Flazasulfuron

CAS No. 104040-78-0. The IUPAC name for flazasulfuron is 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-trifluoromethyl-2-pyridylsulfonyl)urea. The CAS name is N-[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]-3-(trifluoromethyl)-2-pyridinesulfonamide. Sometimes called SL-160.

### Maximum Acceptable Value

Flazasulfuron does not have a MAV in the DWSNZ; flazasulfuron is not mentioned in the WHO Guidelines.

### Sources to water

Flazasulfuron is selective, systemic, [pyrimidinylsulfonylurea herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#pyrimidinylsulfonylurea_herbicides) applied pre- and post-emergence, commonly used to control a broad spectrum of annual and perennial grasses, sedges and broadleaf weeds in non-cropped areas growing on turf, including golf courses. The plant has to absorb the flazasulfuron and metabolise it into active compounds. It is being used increasingly in place of diuron and dichlobenil, sometimes mixed with glyphosate.

Flazasulfuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Flazasulfuron is expected to be relatively persistent in soil and water (half-life about one month). Flazasulfuron’s persistence is likely to increase with increasing pH of the media. Chemical and enzyme-mediated hydrolysis is a major route of transformation of flazasulfuron in water, soil, and water-sediment systems. Both the rate (half-life) and mechanism of hydrolysis (ie, how products are formed) are pH dependent. There are four major hydrolytic and five metabolic products. Flazasulfuron does not sorb strongly to soils and has the potential to leach to groundwater and/or reach surface water during run-off events.

EC (2003) and IUPAC state there are three major metabolites in soils (DTPP, DTPU and TPSA), and DTPP, DTPU and HTPP are important in water; these metabolites are persistent. DTPU is the major metabolite in water at pH 4–7, and DPTT is the major metabolite at pH 9. EFSA (2016) states that metabolite TPSA (SSRE-001) may be found at levels above 0.75 μg/L in groundwater.

In laboratory incubations in dark aerobic natural sediment water systems, flazasulfuron exhibited moderate persistence, forming the major metabolites DTPU (maximum 28 percent AR in water and 16 percent in sediment, exhibiting moderate persistence), HTPP (maximum 6 percent AR in water and 29 percent in sediment, exhibiting moderate to very high persistence) and TPSA (maximum 4 percent AR in water and 2.4 percent in sediment, that exhibited medium to high persistence) (EFSA 2016).

Water solubility is about 27 mg/L at pH 5, 2,000 mg/L at pH 7; flazasulfuron is unstable at pH 9.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2016).

### Health considerations

Based on lack of carcinogenic effects in the rat and mouse carcinogenicity studies and lack of a mutagenicity concern, flazasulfuron can be classified as “No evidence of carcinogenicity to humans” (USEPA 2007). Flazasulfuron (and its metabolites found in water) have no genotoxic potential (EC 2003).

In chronic dietary (food and water) trials, the dog appears to be the most sensitive, with a NOAEL of 2 mg/kg/d bw and a LOAEL of 10 mg/kg/day based on changes in liver (increase in: inflammatory cell infiltration, hepatocellular necrosis, hepatocellular swelling, and bile duct proliferation). A chronic RfD was developed (USEPA 2007) equal to 0.013 mg/kg/d, using an uncertainty factor of 100. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.013 mg/kg/d, and an ARfD of 0.50 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for flazasulfuron is 5.0 mg/L.

The EC (2003) quote an ADI of 0.013 mg/kg bw, based on a two-year rat study using a safety factor of 100; and ARfD was considered not necessary; reaffirmed by EFSA (2012). EFSA (2016) adopted an ARfD of 1 mg/kg/d based on developmental toxicity in rats with a NOAEL of 100 mg/kg bw per day for maternal toxicity in rats observed in the first days of dosing, an UF of 100 was applied.

The Acceptable Daily Intake (ADI) adopted in Australia for flazasulfuron is 0.013 mg/kg body weight, with a NOEL of mg/kg bw. An ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Flocoumafen

CAS No. 90035-08-8. The IUPAC name for flocoumafen is 4-hydroxy-3-[(1RS,3RS;1RS,3SR)-1,2,3,4-tetrahydro-3-[4-(4-trifluoromethylbenzyloxy)phenyl]-1-naphthyl]coumarin. The CAS name is 4-hydroxy-3-[1,2,3,4-tetrahydro-3-[4-[[4-(trifluoromethyl)phenyl]methoxy]phenyl]-1-naphthalenyl]-2H-1-benzopyran-2-one.

The commercial product is mixture of cis- and trans-isomers in the ratio range of 60:40 to 40:60 respectively.

### Maximum Acceptable Value

Flocoumafen does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Flocoumafen is a second generation coumarin rodenticide (anticoagulant), used in baits mainly against rats. It has a very high toxicity and (in the UK) is restricted to indoor use and in sewers. This restriction is mainly due to the increased risk to non-target species. Studies have shown that rodents’ resistant to first generation anticoagulants, can be adequately controlled with flocoumafen.

Flocoumafen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Flocoumafen has a high persistence in soil, with a reported half-life exceeding six months. It also resists hydrolysis.

Studies of the degradation of flocoumafen in rat carcasses, rat faeces, loose grain and wax block baits placed on small soil plots found overall losses of flocoumafen ranged from 85 percent to 95 percent over the 12-month study. The majority of the rodenticide present in samples collected after four months was found in the upper 15 cm of the soil. Only very small quantities were found in the lower soil layers.

Solubility in water is about 1 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

No toxicological or pathological changes were observed in rats fed diets containing 0.01 or 0.05 mg/kg of diet.

Flocoumafen did not induce reverse gene mutation in Salmonella typhimurium strains TA98, TA100, TA1535, TA1537, TA1538 nor in Escherichia coli WP2uvrA pkm 101 either with or without metabolic activation. Flocoumafen was tested at concentrations ranging from 0.031 to 2 mg/plate (IPCS 1995).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.000001 mg/kg body weight, with a NOEL of 0.0014 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# Flonicamid

CAS No. 158062-67-0. The IUPAC name for flonicamid is N-cyanomethyl-4-(trifluoromethyl)nicotinamide. The CAS name is N-(cyanomethyl)-4-(trifluoromethyl)-3-pyridinecarboxamide.

### Maximum Acceptable Value

Flonicamid does not have a MAV in the DWSNZ; flonicamid is not mentioned in the WHO Guidelines.

### Sources to water

Flonicamid is a pyridinecarboxamide or nicotinoid insecticide used on vegetable crops against pests such as aphids. Flonicamid exhibits systemic and translaminar activity and inhibits feeding.

Flonicamid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2016 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Toluene as an impurity is considered as relevant due to its toxicological properties.

### Forms and fate in the environment

The potential for groundwater exposure from intended uses above the parametric drinking water limit of 0.1 μg/L by parent flonicamid and its 5 identified soil metabolites 4-trifluoromethylnicotinic acid (TFNA), TFNA-OH, TFNA-AM, N‑(4‑trifluoromethylnicotinoyl)glycine (TFNG) and TFNG-AM, was concluded to be low, in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios (EFSA 2010).

If released to soil, flonicamid is expected to have very high mobility based upon an estimated Koc of 25. Volatilisation from moist soil surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant of 4.1 x 10-13 atm-cu m/mole. Biodegradation data were not available. If released into water, flonicamid is not expected to adsorb to suspended solids or sediment based on the estimated Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic organisms is low. Chemical hydrolysis is not expected to be an important environmental fate process since amides do not hydrolyse under environmental conditions (pH 5 to pH 9). NIH.

The DT90 value for flonicamid and its metabolites in the soil are all expected to be far below the trigger value of 100 days, actually 1.5 to 8.7 days (EFSA 2018).

Hydrolysis of flonicamid was not observed at pH 5 or 7 at 25°C and only slowly at 50° at pH 7 where the flonicamid half-life was 578 days. At pH 9 and 25°C, the half-life for flonicamid hydrolysis was 204 days. When flonicamid in aqueous solution at pH 7 was continuously exposed to simulated sunlight for 15 days, limited degradation occurred with a calculated half-life for flonicamid under continuous radiation of 267 days. Under aerobic aquatic conditions, flonicamid was extensively degraded in both the river and pond water/sediment systems with significant mineralisation taking place in the river water phase after 145 days. Half-lifes of flonicamid in river and pond water were 37.3 and 30.3 days while in the whole river water/sediment and whole pond water/sediment systems, the DT50 values were, respectively, 43.6 and 35.7 days. Whole river and pond water/sediment systems DT90 values were, respectively, 144.8 and 118.7 days (APVMA 2014).

Water solubility is 5,200 mg/L at 20°C. Octanol/water partition coefficient (POW): 1.9 (LogPow = 0.3) at 29.8°C.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

EFSA (2010) adopted an ADI and ARfD of 0.025 mg/kg/d, reaffirmed by EFSA (2018).

The ADI for flonicamid was established at 0.025 mg/kg bw, based on a NOEL of 2.5 mg/kg bw/day in a rabbit developmental study for developmental toxicity and using a default 100-fold safety factor to account for potential interspecies and intra-species variation. The ARfD for flonicamid was established at 0.025 mg/kg bw, based on a NOEL of 2.5 mg/kg bw in a rabbit developmental study for developmental toxicity and using a default 100-fold safety factor to account for potential interspecies and intra-species variation (APVMA 2014). In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

Flonicamid was not mutagenic in bacteria or mammalian cells in vitro with and without metabolic activation. Flonicamid was not genotoxic in an in vitro mammalian chromosome aberration assay with and without metabolic activation. In vivo, flonicamid was not genotoxic in a micronucleus assay in mice, and did not induce DNA damage in the rat liver in a UDS assay. The test material was not carcinogenic to male or female rats (APVMA 2014).

JMPR (2016, reaffirmed in 2017) established an ADI of 0–0.07 mg.kg bw; no ARfD was considered necessary.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2014. *Public Release Summary on the Evaluation of the New Active Flonicamid in the product Mainman 500 WG Insecticide*. APVMA Product Number P66373 [59 pp]. <http://apvma.gov.au/sites/default/files/publication/13721-prs-flonicamid.pdf>

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EFSA. 2018. *Modification of the Existing Maximum Residue Levels for Flonicamid in Various Root Crops* [26 pp]. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5414>

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# Florasulam

CAS No. 145701-23-1. The IUPAC name for florasulam is 2′,6′,8-trifluoro-5-methoxy[1,2,4]triazolo[1,5-c] pyrimidine-2-sulfonanilide. The CAS name is N‑(2,6‑difluorophenyl)-8-fluoro-5-methoxy[1,2,4]triazolo[1,5-c] pyrimidine-2-sulfonamide.

### Maximum Acceptable Value

Florasulam does not have a MAV in the DWSNZ; florasulam is not mentioned in the WHO Guidelines.

### Sources to water

Florasulam, a [sulfonanilide or](http://www.alanwood.net/pesticides/class_herbicides.html#sulfonanilide_herbicides) triazolopyrimidine herbicide, is usually used as a wettable granule herbicide containing 200 g/kg halauxifen-methyl (qv) and 200 g/kg florasulam for the control of broadleaf weeds in cereals.

Florasulam does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2015 but is in the process of application (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register for latest information).

### Forms and fate in the environment

In soil laboratory incubations under aerobic conditions in the dark, florasulam exhibited very low to low persistence, forming the major metabolite 5-OH florasulam (maximum 71.6 percent AR) which exhibited low to moderate persistence, metabolite DFP-ASTCA (maximum 17.8 percent AR) which exhibited low to moderate persistence, metabolite ASTCA (maximum 40.0 percent AR) which exhibited high to very high persistence, and metabolite TSA (maximum 15.9 percent AR) which exhibited low to high persistence.

Florasulam and its metabolites 5-OH florasulam and TSA exhibited very high to high mobility in soil; metabolite DFP-ASTCA exhibited very high to medium soil mobility and ASTCA exhibited high to medium soil mobility. There was no evidence of a correlation of adsorption with soil pH for either florasulam or its metabolites.

Florasulam is hydrolytically stable at ambient temperature (20 to 25°C) in acidic and neutral environment. In alkaline environment it will be hydrolytically degraded to 5-OH florasulam. In natural water exposed to sunlight the degradation was demonstrated to be extensive and relatively rapid, with several major degradation products formed: 5‑OH florasulam (maximum 16.6 percent AR), ASTCA (maximum 53.8 percent AR), TPSA (21.9 percent AR), ASTP (21.9 percent AR) and 5-OH ASTP (28.9 percent AR). In laboratory incubations in dark aerobic natural sediment water systems, florasulam exhibited low to moderate persistence, forming the major metabolite 5-OH florasulam (maximum 83.1 percent AR in the water and maximum 35.1 percent AR in sediment).

For the active substance and the metabolites 5-OH florasulam and DFP-ASTCA the potential for groundwater exposure from the representative uses by florasulam above the parametric drinking water limit of 0.1 μg/L was concluded to be low.

Water solubility is 84 mg/L at pH 5; 6360 mg/L at pH 7; 9420 mg/L at pH 9.

The water/octanol partitioning coefficient for florasulam is -1.22 at pH 7.

### Typical concentrations in drinking-water

Based on the available data and on the toxicological profile of florasulam, the metabolites ASTCA, TSA and 5-OH-florasulam are not considered toxicologically relevant groundwater metabolites.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2015).

### Health considerations

The toxicokinetic data for florasulam showed a high bioavailability after oral administration, a large distribution without bioaccumulation and a rapid excretion, mainly via urine. The acute toxicity of florasulam was shown to be low, either orally, dermally or by inhalation, with no irritating or sensitising properties. In short term studies, adverse effects were observed in the blood (anaemia), in the liver and in the kidney.

The acceptable daily intake (ADI) is 0.05 mg/kg bw per day on the basis of the one-year dog study, and applying an uncertainty factor of 100. On the basis of the toxicological profile of florasulam, the derivation of an ARfD was not considered necessary (EFSA 2005).

The Acceptable Daily Intake (ADI) adopted in Australia for florasulam is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw. An ARfD was considered unnecessary.

The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for florasulam is 0.35 mg/L (no acute one-day value available.)

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EFSA. 2012. Conclusion on the peer review of the pesticide risk assessment of the active substance florasulam. *EFSA Journal* 13(1): 3984 [138 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/3984.pdf>

# Fluazifop-p-butyl

CAS No. 79241-46-6. The IUPAC name for fluazifop-p-butyl is butyl (R)-2-{4-[5-(trifluoromethyl)-2-pyridyloxy]phenoxy}propionate. Fluazifop-p-butyl is also called butyl (2R)-2-[4-[[5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoate.

Fluazifop-p-butyl is a derivative of [fluazifop-P](http://www.alanwood.net/pesticides/fluazifop-p.html) (CAS No. 83066-88-0). The unresolved isomeric mixture of this substance has the ISO common name [fluazifop-butyl](http://www.alanwood.net/pesticides/derivatives/fluazifop-butyl.html). Fluazifop-p-butyl is the n-butyl ester of the acid fluazifop-p. Fluazifop-p is the R‑enantiomer (“dextro” or “plus”) of the acid, while fluazifop typically contains equal proportions of both the R- and S-enantiomers. Fluazifop-p (the R-enantiomer) is the herbicidally active portion of the mixture and usually comprises about 97 percent of the commercial product. The core substance, fluazifop, has CAS No. 69806-50-4.

### Maximum Acceptable Value

Fluazifop-p-butyl does not have a MAV in the DWSNZ; fluazifop-p-butyl is not mentioned in the WHO Guidelines.

### Sources to water

Fluazifop-p-butyl is an [aryloxyphenoxypropionic herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#aryloxyphenoxypropionic_herbicides) (sometimes called FOPs), commonly used post-emergence on broad-leaved crops to control grass weeds, inhibiting acetyl coenzyme A carboxylase activity. Fluazifop-p-butyl is often sold mixed with other pesticides, often fenoxaprop-p-ethyl.

Fluazifop-p-butyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Fluazifop is structurally similar to fenoxaprop. Fluazifop appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

The impurity 2-chloro-5-(trifluoromethyl)pyridine (R150881) was considered to be a relevant impurity in fluazifop-P-butyl technical material based on its hazards, with a maximum limit of 1.5 g/kg (EFSA 2012).

### Forms and fate in the environment

Fluazifop-p-butyl is of low persistence in moist soil environments, with a reported half-life in these conditions of less than one week, breaking down rapidly to the acid (fluazifop-p), which has fairly low persistence. Fluazifop-p is then hydrolysed to 5‑trifluoromethylpyrid-2-one, and 2-(4-hydroxyphenoxy)propionic acid, both of which are further degraded, ultimately to CO2.

Fluazifop-p-butyl is rapidly hydrolysed in water under most conditions to the fluazifop acid. It is relatively stable to breakdown by UV or sunlight, and non-volatile. Solubility in water is about 1 mg/L. Fluazifop-p-butyl is not a common contaminant of groundwater because it is rapidly broken down in water and has low mobility in soils.

NPIC (1994) quotes for fluazifop-p-butyl a soil half-life of 15 days, water solubility of 2 mg/L and a sorption coefficient (soil Koc) of 5,700. This resulted in a pesticide movement to groundwater rating of very low.

### Typical concentrations in drinking-water

Fluazifop-p-butyl has been found in a community water supply in the US at 0.00006 to 0.00017 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Fluazifop-p-butyl is a slightly to practically nontoxic compound in USEPA toxicity Class IV, and WHO Class III. Rats fed small amounts of fluazifop-p-butyl for 90 days developed no compound-induced effects at doses at or below 10 mg/kg/day. Numerous tests have shown the compound to be non-mutagenic. Fluazifop-butyl appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. However, in accordance with the USEPA’s Guidelines for Carcinogen Risk Assessment, fluazifop-P-butyl is classified as “not likely to be carcinogenic to humans”. No mutagenic potential was observed in adequate in vivo and in vitro studies with fluazifop-P-butyl.

The chronic dietary endpoint for all populations is based on decreased spleen, testes, and epididymal weights in males and decreased uterine and pituitary weights in females observed in a two-generation reproduction study in rats at the LOAEL of 5.8 mg/kg/day in males and 7.1 mg/kg/day in females. The NOAEL in this study was 0.74 mg/kg/day (USEPA 2005). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0074 mg/kg/d, and an ARfD of 0.50 mg/kg/d for fluazifop and fluazifop-p-butyl. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluazifop and fluazifop-P-butyl is 16.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for fluazifop-butyl is 0.003 mg/kg body weight, with a NOEL of 0.3 mg/kg bw.

EFSA (2012 and 2015) states the acceptable daily intake (ADI) is 0.01 mg/kg bw per day (expressed as fluazifop acid), based on the overall long-term NOAEL of 1 mg/kg bw per day and applying a safety factor of 100. The acute reference dose (ARfD) is 0.017 mg/kg bw (expressed as fluazifop acid) based on the NOAEL of 2 mg/kg bw per day for developmental effects observed in the developmental rat study, and applying a safety factor of 100.

The chronic dietary (food and water) assessment concluded that for all commodities, the chronic dietary risk estimates are below the USEPA’s level of concern for the US population.

JMPR (2016) established an ADI of 0–0.004 mg/kg bw (as fluazifop acid), based on an overall NOAEL of 0.44 mg/kg bw per day (for decreased body weight and organ weight changes) in two- and three-generation reproductive toxicity studies in rats performed with fluazifop-butyl, using a safety factor of 100. The meeting established an ARfD for fluazifop-P-butyl, expressed as fluazifop acid, of 0.4 mg/kg bw, based on systemic toxicity effects (body weight loss, clinical signs of toxicity, lower body temperature and decreased locomotor activity) in an acute neurotoxicity study in rats occurring at the lowest dose of 500 mg/kg bw, using a safety factor of 100 (for intraspecies and interspecies variability) and an additional safety factor of 10 for use of a LOAEL instead of a NOAEL and correcting for molecular weight. The ADI and ARfD can be applied to fluazifop acid (metabolite II), metabolite III (despyridinyl acid), metabolite X (CF3‑pyridone) and metabolite XL (hydroxy fluazifop acid).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EFSA. 2012. Conclusion on the peer review of the pesticide risk assessment of the active substance fluazifop-P (evaluated variant fluazifop-P-butyl). *EFSA Journal* 10(11): 2945 [77 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm> and for 2015 [74 pp]: <http://www.efsa.europa.eu/en/efsajournal/pub/4228>

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USEPA. 2005. *Overview of the Fluazifop-P-butyl Risk Assessments* [8 pp]. See: <http://www.fluoridealert.org/pesticides/fluazifop-p-butyl.page.htm>

USEPA. 2005. *Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Fluazifop-P-butyl*. EPA 738‑R‑05‑005 [14 pp]. <http://www.epa.gov/pesticides/reregistration/status.htm>

# Fluazinam

CAS No. 79622-59-6. The IUPAC name for fluazinam is 3-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-2,6-dinitro-p-toluidine. The CAS name is 3‑chloro-N-[3-chloro-2,6-dinitro-4-(trifluoromethyl)phenyl]-5-(trifluoromethyl)-2-pyridinamine.

### Maximum Acceptable Value

Fluazinam does not have a MAV in the DWSNZ; fluazinam is not mentioned in the WHO Guidelines.

### Sources to water

Fluazinam is a pyridine (pyridinamine) fungicide (for Oomycetes) commonly used to control potato blight.

Fluazinam appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Fluazinam was found in potatoes above the applicable MRL in the 2013/14 FRSP programme. MPI Technical Paper No: 2016/11. <http://www.mpi.govt.nz/news-and-resources/publications>

### Forms and fate in the environment

Fluazinam appears to degrade at moderate to low rates in aerobic soils, but it is more rapidly transformed into other compounds of similar backbone structure in high pH solutions or in aerobic or anaerobic aquatic media. The transformation products of fluazinam appear to be relatively persistent under most conditions. Fluazinam shows low mobility in soils. A major metabolite is 5-((3-chloro-5-(trifluoromethyl)-2-pyridyl)amino)-α,α,α-trifluoro-4,6-dinitro-o-cresol, which appears to be more toxic than the parent. Trifluoroacetic acid is important as well.

Fluazinam may be photolysed relatively rapidly in water, resulting in a tricyclic compound. The hydrolysis of fluazinam is pH dependent. It was relatively stable at pH 5, and hydrolysed with half-lifes of 42 days and six days at pHs of 7 and 9, respectively.

Solubility in water is up to 0.1 mg/L for pH 5–7, and about 350 mg/L at pH 11.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

When used correctly, it was calculated that the acute and chronic risks due to exposure to residues in food and water were below the USEPA’s level of concern for all population subgroups, including infants and children. PMEP (2001) quotes an acute dietary RfD of 0.07 mg/kg/d for females 13–50 years of age, and a chronic RfD of 0.011 mg/kg/d for all populations. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.011 mg/kg/d, and an ARfD of 0.07 mg/kg/d for fluazinam. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluazinam is 2.3 mg/L.

In subchronic and chronic oral, dermal and inhalation studies in rats, dogs and mice, the liver was a major target organ and signs of liver toxicity were regularly observed in many studies. These signs included changes in clinical chemistries indicative of liver toxicity, increased absolute and/or relative liver weights, increased incidences of macroscopic liver lesions and increased incidences of a variety of microscopic liver lesions.

A neurotoxic lesion described as vacuolation of the white matter of the brain and sometimes cervical spinal cord which was initially observed in long-term (1–2 years) chronic studies in mice and dogs. Fluazinam, per se, was not responsible for the induction of this lesion. Evaluation of the effects of impurities present in technical grade fluazinam revealed that one single impurity, Impurity-5, was solely responsible for the induction of this lesion. (White matter vacuolation in the central nervous system (CNS) was reversible. The myelin sheaths appeared to recover completely during a recovery period of up to 56 days.)

At the current maximum concentration of Impurity-5 in technical grade fluazinam of 0.1 percent, the NOAEL for CNS effects of 0.02 mg/kg/day for Impurity-5 is equivalent to a NOAEL for CNS effects of 20 mg/kg/day for technical grade fluazinam, which is comparable to the NOAEL for chronic effects for technical grade fluazinam of 1.1 mg/kg/day used to establish the chronic RfD for fluazinam. Therefore, based on a consideration of all the available data and information relating to this treatment-related neurotoxic lesion, it was concluded that the chronic dietary RfD of 0.011 mg/kg/day for “all populations”, including infants and children, is protective of the CNS effects caused by the presence of Impurity-5 in technical-grade fluazinam (USEPA 2001).

The EC (2008) derived an ADI of 0.01 mg/kg bw/day and an ARfD 0.07 mg/kg bw/day; reaffirmed by EFSA (2012/2014/2015). The EC has stated that the manufacturing impurity: 5-chloro-N-(3-chloro-5-trifluoromethyl-2-pyridyl)-α,α,α-trifluoro-4,6-dinitro-o-toluidine, is of toxicological concern and must not exceed maximum levels of 2 g/kg (0.2 percent) in the technical material.

EFSA (2014) includes data for the metabolite trifluoroacetic acid: ADI and ARfD are 0.05 mg/kg/d bw. EFSA (2017) reports an ADI of 0.01 mg/kg/d and ARfD are 0.07 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.004 mg/kg body weight, with a NOEL of 0.4 mg/kg bw.

As at September 2008 the USEPA considers that fluazinam shows “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential”. In a carcinogenicity study in rats, an increased incidence of thyroid gland follicular cell tumours was observed in males. In this study, there were statistically significant positive trends for thyroid gland follicular cell adenocarcinomas and combined follicular cell adenomas/adenocarcinomas. There was also a statistically significant increase by pair-wise comparison of the high dose group (40 mg/kg/day) with the control group for combined follicular cell adenomas/adenocarcinomas. Fluazinam was not genotoxic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Fludioxonil

CAS No. 131341-86-1. The IUPAC and CAS name for fludioxonil is 4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1H-pyrrole-3-carbonitrile. Also called (or misspelt?) fluidoxonil and fludioxonyl.

### Maximum Acceptable Value

Fludioxonil does not have a MAV in the DWSNZ, and it is not mentioned in the WHO Guidelines.

### Sources to water

Fludioxonil is a pyrrole (or phenylpyrrole) fungicide, commonly used on grapes, vegetables and fruit. Fludioxonil is related to the antifungal antibiotic pyrrolnitrin extracted from Pseudomonas pyrrocinia. It is structurally similar to fenpiclonil (qv).

Fludioxonil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Fludioxonil was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in strawberries.

### Forms and fate in the environment

The average aerobic soil half-life is about 3 months, and about a year in anaerobic soil. The metabolic pattern includes a large number of metabolites but the parent fludioxonil remained by far the major constituent of the residues.

Solubility in water is about 2 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See JMPR (2002).

### Health considerations

For subchronic and chronic toxicity, the primary effects in the mouse and rat were similar and included decreased body weight and food consumption associated with clinical pathological and histopathological effects in the liver and kidney. In the subchronic dog study, diarrhoea was the most sensitive indicator of toxicity. In contrast, decreased weight gain in females was the most sensitive indicator of toxicity in the chronic toxicity study in dogs. Liver toxicity was observed in both dog studies at higher doses. The available data did not indicate a need for acute or subchronic neurotoxicity studies. Fludioxonil was not teratogenic in rabbits. In a rat developmental toxicity study, it caused an increase in foetal incidence and litter incidence of dilated renal pelvis at the limit dose (1,000 mg/kg/day). There was no quantitative or qualitative evidence of increased susceptibility following in utero exposure to rats and rabbits or following pre-/post-natal exposure to rats. The USEPA determined that fludioxonil was not classifiable as to human carcinogenicity but nonetheless poses a negligible cancer risk. This conclusion was based on the fact that cancer studies with fludioxonil only showed marginal evidence of cancer in one sex of the species. There was no evidence of carcinogenicity in mice when tested up to the limited dose 7,000 ppm. There was no evidence of carcinogenicity in male rats, but there was a statistically significant increase, both trend and pairwise, of combined hepatocellular tumours in female rats. The pairwise increase for combined tumours was significant at p = 0.03, which is not a strong indication of a positive effect. Further, statistical significance was only found when liver adenomas were combined with liver carcinomas. Finally, the increase in these tumours was within, but at the high end, of the historical controls. Fludioxonil was not mutagenic in the tests for gene mutations. However, based on the induction of polyploidy in the in vitro Chinese hamster ovary cell cytogenetic assay and the suggestive evidence of micronuclei induction in rat hepatocytes in vivo, additional mutagenicity testing was performed in three studies specifically designed to address the concerns regarding aneuploidy. The results of these assays were negative for aneuploidy activity (USEPA 2008).

USEPA (2004) quotes an acute RfD = 1.0 mg/kg/day, and a chronic RfD = 0.03 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.03 mg/kg/d, and an ARfD of 1.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fludioxonil is 33 mg/L.

The 2004 JMPR meeting established an ADI of 0.0–0.4 mg/kg bw, the establishment of an ARfD was considered unnecessary. Reaffirmed in JMPR (2012/2013) and FAO/WHO (2013).

The Acceptable Daily Intake (ADI) adopted in Australia for fludioxonil is 0.03 mg/kg body weight, with a NOEL of 3.1 mg/kg bw. An ARfD was considered to be unnecessary (<https://apvma.gov.au/>).

EC (2007) quotes an ADI of 0.37 mg/kg bw, and stated that an ARfD was not considered necessary due to the low acute toxicity of fludioxonil. EFSA (2011 and 2016) reaffirmed these values. IUPAC (2009) also quotes an ADI of 0.37 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2007. *Final Review Report for the Active Substance Fludioxonil*. European Commission, Health & Consumers Directorate-General. *SANCO*/2818/07 – rev. 2 [9 pp]. Available at: [www.furs.si/law/EU/ffs/eng/annexI/direktive/RR/fludioxonil.pdf](http://www.furs.si/law/EU/ffs/eng/annexI/direktive/RR/fludioxonil.pdf)

EFSA. 2011. Modification of the existing MRLs for fludioxonil in various leafy crops. *EFSA Journal* 9(12): 2487 [27 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/2487.pdf>

EFSA. 2012. Reasoned opinion on the modification of the existing MRLs for fludioxonil in celery, celery leaves and radishes. *EFSA Journal* 10(12): 3014 [26 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm> see also EFSA 2016: <http://www.efsa.europa.eu/en/efsajournal/pub/4372>

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USEPA. 2004. Fludioxonil: pesticide tolerances. *Federal Register* 69(188): 58084–91. Rules and Regulations, 29 September, Accessed via <http://pmep.cce.cornell.edu/profiles/index.html>

USEPA. 2008. Fludioxonil: pesticide tolerances. *Federal Register* 73(176): 52597–603. Rules and Regulations, 10 September. See: <http://www.epa.gov/EPA-PEST/2008/September/Day-10/p20547.htm>

# Flufenacet

CAS No. 142459-58-3. The IUPAC name for flufenacet is 4′-fluoro-N-isopropyl-2-[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yloxy]acetanilide. The CAS name is N-(4-fluorophenyl)-N-(1-methylethyl)-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]acetamide. Has sometimes been called fluthiamide and thiaflumide.

### Maximum Acceptable Value

Flufenacet does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Flufenacet is a selective anilide or thiadiazole soil [herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#triazolopyrimidine_herbicides), commonly used to control annual grasses in cereal and potato crops.

Flufenacet appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

EC (2003) established a maximum application rate of 0.6 kg/ha.

### Forms and fate in the environment

Flufenacet is stable to hydrolysis. In the laboratory and on soil surfaces flufenacet did not photolyse during 10.5 continuous days of irradiation. The calculated half-lifes were 248 days for the irradiated samples and 167 days for the dark control samples. Flufenacet is moderately stable in the aerobic soil environment tested. Flufenacet was relatively stable in the anaerobic soil environment tested. Flufenacet was stable in a pond water/soil system incubated under anaerobic conditions for approximately 90 days. Flufenacet is very mobile to mobile in sand, loamy sand, clay loam, silt loam, and sandy loam soils. Flufenacet degradates are very mobile to mobile in sand, sandy loam, silty loam, and clay loam soils. In column leaching study aged flufenacet was shown to be moderately to very mobile in sand, sandy loam, silt loam and clay loam soils. In field dissipation studies in North Carolina and Wisconsin, there was no evidence that parent flufenacet leached below 5 inches. The last detection of parent compound was at 135 and 369 days after application. In the North Carolina study, at day 5, the thiadone degradate was recovered at 0.06 and 0.02 mg/L in the 6- to 12- and the 12- to 18-inch depths, respectively. No flufenacet residues (parent or degradates) were detected in groundwater in an Iowa study. In Nebraska studies flufenacet degradates were detected in groundwater at a maximum concentration of 0.90 ppb (0.66 ppb sulfonic acid, 0.18 ppb thiadone, 0.06 ppb oxalate) (USEPA 1998).

EC (2003) reports half-lifes of two to three months in water and water/sediment tests, with fluorophenyl and thiadiazole being important metabolites.

4-Fluoro-N-methylethyl benzenamine is an important metabolite and is included with the parent in most tolerance regulations (USEPA 1998).

Solubility in water is about 56 mg/L.

### Removal methods

GAC is likely to be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

A rat metabolism study showed that flufenacet was rapidly absorbed and metabolised by both sexes. Urine was the major route of excretion at all dose levels and smaller amounts were excreted via the faeces.

The Reference Dose (RfD) for flufenacet is 0.004 mg/kg/day. This value is based on the systemic LOEL of 1.2 mg/kg/day in the rat chronic feeding / carcinogenicity study with a 300-fold safety factor to account for interspecies extrapolation (10 x), for intraspecies variability (10 x), and because of the lack of a NOEL in the rat chronic feeding / carcinogenicity study (3 x) (USEPA 1998). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0017 mg/kg/d, and an ARfD of 0.0017 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for flufenacet is 0.017 mg/L.

EC (2003) report an ADI of 0.005 mg/kg bw/d, and an acute reference dose (ARfD) of 0.017 mg/kg bw/d (EFSA 2012).

Flufenacet was shown to be negative in assays for gene mutation in bacteria and mammalian cells.

Flufenacet is classified as a “Not Likely” carcinogen based on the lack of carcinogenicity in rats and mice (USEPA 1998).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2003. *Review Report for the Active Substance Flufenacet*. 7469/VI/98-Final [30 pp]. <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for flufenacet according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 10(4): 2689. <http://www.efsa.europa.eu/en/efsajournal/doc/2689.pdf>

USEPA. 1998. *Pesticide Factsheet: Flufenacet* [31 pp]. See: <http://www.epa.gov/opprd001/factsheets/flufenacet.pdf> or <http://www.epa.gov/opprd001/factsheets/>

# Flumethrin

CAS No. for flumethrin is 69770-45-2. The IUPAC name is (RS)-α-cyano-4-fluoro-3-phenoxybenzyl (1RS,3RS;1RS,3SR)-(EZ)-3-(β,4-dichlorostyryl)-2,2-dimethylcyclopropanecarboxylate or (RS)-α-cyano-4-fluoro-3-phenoxybenzyl (1RS)‑cis-trans-(EZ)-3-(β,4-dichlorostyryl)-2,2-dimethylcyclopropanecarboxylate. The CAS name is cyano(4-fluoro-3-phenoxyphenyl)methyl 3-[2-chloro-2-(4-chlorophenyl)ethenyl]-2,2-dimethylcyclopropanecarboxylate. Flumethrin is a Type II synthetic pyrethroid ester acaricide.

Flumethrin is a complex mixture of [stereoisomers](http://en.wikipedia.org/wiki/Stereoisomer). The molecule contains three [asymmetric carbon](http://en.wikipedia.org/wiki/Asymmetric_carbon) atoms, there is [cis-trans isomerism](http://en.wikipedia.org/wiki/Cis-trans_isomerism) at the cyclopropane ring, and cis-trans isomerism at the carbon-carbon double bond of the alkene. So there are 16 different isomers. Commercial flumethrin typically contains 92 percent of the trans isomers on the cyclopropane ring and the cis-configuration at the olefinic carbon-carbon double bond and 8 percent of the isomer with cis geometry on the cyclopropane ring and the cis-configuration at the olefinic carbon-carbon double bond.

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

### Sources to water

Flumethrin is a [pyrethroid](http://en.wikipedia.org/wiki/Pyrethroid) [insecticide](http://en.wikipedia.org/wiki/Insecticide), commercially developed in 1982. It is used externally (pour-on) in veterinary medicine against parasitic insects and ticks on cattle, sheep, goats, horses, and dogs. It is commonly used in products to protect pets against fleas such as flea and tick collars. It is also used for control of mites (including varroa in New Zealand) in beehives.

Flumethrin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Unlike the closely related chemical fluvalinate, residues are not a major problem for flumethrin, probably because the amount of active ingredient in miticide strips is significantly lower for Bayvarol (3.6 mg of flumethrin) than for Apistan (880 mg of fluvalinate) (MPI 2001).

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Flumethrin was absorbed rapidly, but not completely, after oral administration in all species investigated. The concentrations in the tissues of rats two days after dosing were 3- to 50-fold lower than those in the blood. Elimination was mainly in the faeces. The main metabolite was flumethrin acid, which was distinctly less toxic than the parent substance in acute and four-week dietary studies in rats and did not induce reverse mutations in bacteria. An ADI of 0–0.004 mg/kg bw was allocated, on the basis of the NOAEL of 0.36 mg/kg bw per day in the two-generation study of reproductive toxicity in rats, using a 100-fold safety factor (FAO 1996).

The Acceptable Daily Intake (ADI) adopted in Australia for flumethrin is 0.003 mg/kg body weight, with a NOEL of 0.31 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

FAO. 1996. 4.15 *Flumethrin* (195). <http://www.fao.org/docrep/w3727e/w3727e0l.htm>

MPI. 2001. *A Review of Treatment Options for Control of Varroa Mite in New Zealand*. [http://www.biosecurity.govt.nz/pests-diseases/animals/varroa/paper/varroa-treatment-options.htm#7](http://www.biosecurity.govt.nz/pests-diseases/animals/varroa/paper/varroa-treatment-options.htm%237)

UKPIS. 1998 update. Flumethrin. *UKPID Monograph*. National Poisons Information Service. IPCS. <http://www.inchem.org/pages/ukpids.html> or [www.inchem.org/documents/ukpids/ukpids/ukpid66.htm](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\INetCache\Content.Word\www.inchem.org\documents\ukpids\ukpids\ukpid66.htm)

# Flumetsulam

CAS No. 98967-40-9. The IUPAC name for flumetsulam is 2′,6′-difluoro-5-methyl[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonanilide. The CAS name is N‑(2,6‑difluorophenyl)-5-methyl[1,2,4]triazolo[1,5-a]pyrimidine-2-sulfonamide.

### Maximum Acceptable Value

Flumetsulam does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Flumetsulam is a post-emergent sulfonanilide or [triazolopyrimidine herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#triazolopyrimidine_herbicides), commonly used for broadleaf control, eg, buttercup in pasture.

Flumetsulam appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The average soil half-life and water half-life for flumetsulam is about 45 days.

In 1998, 210 water samples were collected during post-application run-off events at 75 surface-water and 25 groundwater sites in the US Midwest (USGS 2004) to gain an understanding of the occurrence of 16 sulfonylurea, sulfonamide, and imidazolinone herbicides, being the newer products for which data is relatively sparse. Imazethapyr was detected most frequently (69 percent of samples) followed by flumetsulam (62 percent) and nicosulfuron (51 percent).

Solubility in water is about 5,500 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Flumetsulam is classified as a Group E pesticide, ie, evidence of non-carcinogenicity to humans (USEPA 2006).

The Acceptable Daily Intake (ADI) adopted in Australia for flumetsulam is 1 mg/kg body weight, with a NOEL of 100 mg/kg bw.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 1.0 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for flumetsulam is 7.0 mg/L (no acute one-day value available.)

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

USEPA. 2006. *Flumetsulam: Pesticide tolerance*. Final Rule. See: <http://www.epa.gov/EPA-PEST/2006/October/Day-04/p16271.htm>

USGS. 2004. *Sulfonylurea, Sulfonamide, Imidazolinone, and Other Pesticides*. <http://co.water.usgs.gov/midconherb/html/sulfonylurea.html>

# Flumioxazin

CAS No. 103361-09-7. The IUPAC name for flumioxazin is N-(7-fluoro-3,4-dihydro-3-oxo-4-prop-2-ynyl-2H-1,4-benzoxazin-6-yl)cyclohex-1-ene-1,2-dicarboximide. The CAS name is 2-[7-fluoro-3,4-dihydro-3-oxo-4-(2-propynyl)-2H-1,4-benzoxazin-6-yl]-4,5,6,7-tetrahydro-1H-isoindole-1,3(2H)-dione.

### Maximum Acceptable Value

Flumioxazin does not have a MAV in the DWSNZ and is not mentioned in the WHO Guidelines.

### Sources to water

Flumioxazin is a broad spectrum dicarboximide or N-phenylphthalimide or diphenylether herbicide used for season-long weed control in grapes, kiwifruit, pipfruit and stonefruit. It is structurally related to carfentrazone-ethyl.

Flumioxazin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at Nov 2018 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

If released to soil, flumioxazin is expected to have a low potential to leach based on column leaching studies and a fast degradation rate. An estimated Koc value of 13,000 indicates that flumioxazin is expected to adsorb to suspended solids and sediment. Volatilisation from moist soil surfaces is negligible. Flumioxazin degrades rapidly in soil water via hydrolysis with half-lifes of 3.4 to 5.1 days at pH 5.0, 21.4–24.6 hours at pH 7.0, and 14.6–22.0 minutes at pH 9.0; therefore, aqueous chemical hydrolysis in moist soils will be an important fate process. Microbial degradation in soil is also an important fate process; the half-life for aerobic soil metabolism is 11.9 to 17.5 days, with an average of 14.7 days. The photolysis half-life on soil is 3.2 to 8.4 days (average 5.8 days). The rapid soil dissipation rate indicates flumioxazin is not persistent in soil. If released into water, chemical hydrolysis will be a major degradation process. Flumioxazin has an anaerobic aquatic metabolism half-life of 0.2 days. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 18 suggests the potential for bioconcentration in aquatic organisms is low. Photodegradation in shallow water can occur (surface half-life of about one day at pH 5) (Pub Chem).

Characterisation of the residues showed that the major metabolites were the amide 482-HA (due to imido ring opening of flumioxazin), THPA (hydrolysis of 482-HA) and 1-OH-HPA-1 (hydroxylation of THPA) (APVMA 2003).

Flumioxazin exhibited moderate persistence in soil (20°C laboratory DT90 up to 115 days) and it degraded into a number of metabolites, of which THPA and its corresponding cyclic anhydride were major transformation products, predominantly formed by photolysis that exhibited very low to low soil persistence (20°C laboratory DT90 up to 13 days) (EFSA 2018).

Solubility in water is about 1.8 mg/L at 25°C. The octanol/water partition coefficient, log Kow, is 2.55 at 20°C.

### Typical concentrations in drinking-water

Available data indicate that flumioxazin is relatively unstable and its potential to leach to groundwater is low. However, the potential for the degradation products APF and THPA to leach to groundwater is high. The mobility of the major degradation product, 482-HA, detected in the hydrolysis and the unidentified residues detected in the aqueous photolysis and anaerobic aquatic metabolism studies are unknown. These residues may persist in the environment and may leach to groundwater (USEPA 2001). However, flumioxazin leaches significantly in sandy soils; APVMA (2003). Although the potential for flumioxazin to leach to groundwater is low, its two degradates (APF and THPA) may contaminate groundwater due to their high persistence and mobility (USEPA 2003).

Groundwater estimated environmental concentrations (µg/L) for flumioxazin and its major degradates in various pH (USEPA (2003):

|  |  |  |  |
| --- | --- | --- | --- |
| **Compound** | **pH5** | **pH7** | **pH9** |
| flumioxazin | negligible | negligible | negligible |
| 482-HA | negligible | 45.3 | 466 |
| APF | 2.8 | 2.7 | negligible |
| THPA | 210 | 182 | negligible |

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of flumioxazin from surface waters.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In repeated dose studies in mice, rats and dogs, flumioxazin caused liver toxicity characterised by alterations in liver function and enzyme activities. Oral and dermal exposure induced anaemia and other haematological disturbances in rats. Flumioxazin was negative in studies designed to detect its potential to damage genetic material (DNA), and it did not induce cancers in life-time exposure studies in animals. In developmental studies, an increased incidence of foetal death, impaired foetal development and growth retardation was observed in rats, following oral or dermal exposure at levels which were not toxic to the dams. This has necessitated a label warning statement to alert women of child-bearing age to avoid mixing, loading or spraying any product containing flumioxazin (APVMA 2003).

The acute RfD and acute PAD is 0.03 mg/kg/d; the chronic RfD and chronic PAD is 0.02 mg/kg/d, where PAD is the Population Adjusted Dose (USEPA 2012).

The ADI for flumioxazin was established at 0.003 mg/kg bw/day based on a NOEL of 3 mg/kg bw/day in an oral developmental study in rats and using a 1,000-fold safety factor in view of the nature and irreversibility of the effect. The highest acute dose of flumioxazin at which no evidence of toxicity was detected was 3 mg/kg bw in a rat oral developmental study. The ARfD was established at 0.03 mg/kg bw on the basis of this NOEL and using a 100-fold safety factor (APVMA 2003).

The JMPR meeting established an acceptable daily intake (ADI) of 0–0.02 mg/kg bw on the basis of a NOAEL of 1.8 mg/kg bw per day for anaemia in a long-term study in rats, with application of a safety factor of 100. The meeting established an acute reference dose (ARfD) of 0.03 mg/kg bw on the basis of a NOAEL of 3 mg/kg bw per day for malformations in a developmental toxicity study in rats, with application of a safety factor of 100. This ARfD applies to women of childbearing age only. The meeting concluded that it is not necessary to establish an ARfD for the remainder of the population in view of the low acute oral toxicity of flumioxazin and the absence of other toxicological effects that would be likely to be elicited by a single dose (JMPR 2015).

EFSA (2018) established an ADI of 0.018 mg/kg/d, and an ARfD of 0.1 mg/kg/d.

Flumioxazin is classified as a “not likely” human carcinogen. There is increased susceptibility of rats (but not rabbits) to in utero and postnatal exposure to flumioxazin, and the FQPA 10X Safety Factor has been retained. The data available at this time indicate that flumioxazin is highly phytotoxic; however, it is unlikely that flumioxazin will pose a risk of acute or chronic toxicity to non-target animals (USEPA 2001).

Flumioxazin was negative in a bacterial mutation assay and a mammalian cell mutation assay in both the presence and absence of metabolic activation and did not induce unscheduled DNA synthesis in rat hepatocytes in an in vivo assay. Flumioxazin was not carcinogenic in mice or rats (JMPR 2015).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2003. *Evaluation of the New Active Flumioxazin in the Product Pledge 500 WG Herbicide*. Australian Pesticides and Veterinary Medicines Authority [59 pp]. <https://apvma.gov.au/sites/default/files/publication/13776-prs-flumioxazin.pdf>

ERMA. 2018. *Approval to Import or Manufacture a Pesticide: Chateau Herbicide*. <https://www.epa.govt.nz/database-search/hsno-application-register/view/APP203429>

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USEPA. 2001. *Pesticide Factsheet: Flumioxazin*. <http://enfo.agt.bme.hu/drupal/sites/default/files/flumioxazin.pdf>

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USEPA. 2012. Flumioxazin: pesticide tolerances. *Federal Register* 77 FR : 58493–9. <https://www.federalregister.gov/documents/2012/09/21/2012-23352/flumioxazin-pesticide-tolerances>

# Fluopicolide

CAS No. 239110-15-7. The IUPAC name for fluopicolide is 2,6-dichloro-N-[3-chloro-5-(trifluoromethyl)-2-pyridylmethyl]benzamide. The CAS name is 2,6-dichloro-N-[[3-chloro-5-(trifluoromethyl)-2-pyridinyl]methyl]benzamide.

### Maximum Acceptable Value

Fluopicolide does not have a MAV in the DWSNZ; fluopicolide is not mentioned in the WHO Guidelines.

### Sources to water

Fluopicolide is a benzamide (benzamido-pyridine, pyridine or acylpicolide) mesosystemic fungicide used for the control of fungal diseases such as downy mildew and blight mainly on grapes. It has a mode of action unlike the known modes of action of other registered fungicides.

Fluopicolide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The impurity toluene must not exceed 3 g/kg in the technical material (EC 2010).

### Forms and fate in the environment

When fluopicolide is released into the environment some of it can be found in soil and surface water. In the terrestrial environment, fluopicolide is expected to be persistent and residues may carryover into the following growing season. Fluopicolide is shown to bind weakly to soils, however, there is evidence that adsorption to soil may increase over time as the product is used. The major transformation product, 2,6‑dichlorobenzamide (BAM), is expected to be mobile in soils. Both fluopicolide and BAM are expected to leach through soil and have the potential to reach groundwater, particularly in areas where soils are permeable and/or the depth to the water table is shallow. In aquatic environments, fluopicolide is expected to be persistent and to partition from the water phase to the sediment; the major transformation product BAM has been shown to partition mainly into the water phase; it is also a metabolite of dichlobenil (Health Canada 2011).

Typical aerobic soil half-lifes are 140 to 270 days.

Solubility in water is about 2.8 mg/L over a wide pH range. The octanol/water partition coefficient Log(Kow) is about 3.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of fluopicolide.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2014).

### Health considerations

The chronic RfD and PAD is 0.2 mg/kg/d; there is no ARfD. Fluopicolide is not likely to be carcinogenic to humans (USEPA 2007). The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluopicolide is 1.4 mg/L (no acute one-day value available.)

An ADI of 0–0.08 mg/kg bw was established for fluopicolide based on the NOAEL of 7.9 mg/kg bw per day, identified on the basis of organ weight increases and gross and microscopic changes in the liver and kidneys in an 18-month dietary study of toxicity and carcinogenicity in mice, supported by the NOAEL of 8.4 mg/kg bw per day identified on the basis of histopathological changes in the liver and increased kidney weights in a two-year dietary study of toxicity and carcinogenicity in rats, and with a safety factor of 100. An ARfD of 0.6 mg/kg bw was established for women of child-bearing age based on a NOAEL of 60 mg/kg bw per day identified on the basis of a marginally increased incidence of skeletal defects of the vertebrae and sternebrae, which might be attributable to a single exposure to fluopicolide at 700 mg/kg bw per day in a study of developmental toxicity in rats, and with a safety factor of 100. An ADI of 0–0.02 mg/kg bw was established for the fluopicolide metabolite M-01 2,6‑dichlorobenzamide, and an ARfD of 0.6 mg/kg bw (JMPR 2009; FAO/WHO 2009). Several metabolites that are also crop residues have been investigated, but only M-01 (2,6-dichlorobenzamide) was more toxic than fluopicolide in a single dose and a long-term study. M-04, or 2,6-dichloro-3-hydroxybenzamide, is found on rotational crops; it has very low acute toxicity. M-05, or 3-(methylsulfinyl)-5-(trifluoromethyl)pyridine-2-carboxylic acid, is found on rotational crops; it too has very low acute toxicity.

APVMA adopted an ADI of 0.08 mg/kg/d for Australia (<https://apvma.gov.au/>). The ARfD is 0.6 mg/kg. The ARfD for fluopicolide only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary.

EFSA (2013, 2014 and 2015) reports that the toxicological profile of fluopicolide was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.08 mg/kg bw per day and an ARfD of 0.18 mg/kg bw. For the metabolite 2,6-dichlorobenzamide (M-01 or BAM) separate toxicological reference values were set (ADI: 0.05 mg/kg bw per day; ARfD: 0.3 mg/kg bw). EC (2010) had established the same values for fluopicolide.

The JMPR 2009 meeting concluded that fluopicolide was unlikely to be carcinogenic or cause neurotoxicity in humans.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2010. *Final Review Report for the Active Substance Fluopicolide*. European Commission, Health & Consumers Directorate-General. *SANCO*/10164/09 – final [10 pp]. Available at: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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Health Canada. 2011. *Evaluation Report ERC2011-08: Fluopicolide*. <http://www.hc-sc.gc.ca/cps-spc/pubs/pest/_decisions/erc2011-08/index-eng.php>

JMPR. 2009. Pesticide residues in food. *FAO Plant Production and Protection Paper* 196. 5.12 Fluopicolide (235): 141–64. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and WHO the Core Assessment Group. <http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report09/Fluopicolide.pdf> or <http://www.who.int/foodsafety/chem/jmpr/en/>

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USEPA. 2007. *Pesticide Factsheet: Fluopicolide* [11 pp]. <http://www.epa.gov/opprd001/factsheets/> or <http://www.epa.gov/opp00001/chem_search/reg_actions/registration/fs_PC-027412_01-Mar-07.pdf>

# Fluopyram

CAS No. 658066-35-4. The IUPAC name for fluopyram is N-{2-[3-chloro-5-(trifluoromethyl)-2-pyridyl]ethyl}-α,α,α-trifluoro-o-toluamide. The CAS name is N‑[2‑[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide.

### Maximum Acceptable Value

Fluopyram does not have a MAV in the DWSNZ; fluopyram is not mentioned in the WHO Guidelines.

### Sources to water

Fluopyram is a benzamide or pyridine or pyridylethylamide broad spectrum fungicide used for the control of fungal diseases mainly on kiwifruit, grapes, tomatoes and strawberries.

Fluopyram appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

In soil laboratory incubations under aerobic conditions in the dark, fluopyram exhibited high to very high persistence, with a half-life up to around 700 days. In anaerobic soil incubations fluopyram was essentially stable. Fluopyram exhibited medium mobility in soil. The metabolite M08 7-hydroxy exhibited high soil mobility. It was concluded that the adsorption of fluopyram and M08 7-hydroxy was not pH dependent (EFSA 2013).

In laboratory incubations in dark aerobic natural sediment water systems, fluopyram slowly partitioned from water to sediment where it exhibited very high persistence. The potential for groundwater contamination is low (EFSA 2013).

Fluopyram was stable in sterile aqueous buffered solutions at pH 4, 7 and 9 when stored at 50°C in the dark for five days (JMPR 2010).

Solubility in water is about 16 mg/L over a wide pH range. The octanol/water partition coefficient Log(Kow) is 3.3. Henry’s Law constant is 2.98 x 10-5 Pa m3 mol-1 at pH 7.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of fluopyram.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Fluopyram is rapidly and extensively absorbed after oral administration (93 percent in 48 hours). After absorption it is widely distributed and extensively metabolised, and almost completely excreted after 168 hours.

The 2010 JMPR meeting established an acceptable daily intake (ADI) for fluopyram of 0–0.01 mg/kg bw, based on a NOAEL of 1.2 mg/kg bw per day for changes in the liver (hepatocellular hypertrophy, eosinophilic foci) at 6.0 mg/kg bw per day in a two-year rat study. A safety factor of 100 was applied. The ADI provides a margin of at least 860‑fold relative to the NOAEL for liver tumours in rats. The meeting established an acute reference dose (ARfD) for fluopyram of 0.5 mg/kg bw, based on the NOAEL of 50 mg/kg bw for decreases in measures of motor and locomotor activities at 100 mg/kg bw in an acute neurotoxicity study in rats. A 100-fold safety factor was applied (FAO/WHO 2010). These values were reaffirmed in JMPR (2012 and 2014).

The agreed Acceptable Daily Intake (ADI) is 0.012 mg/kg bw per day based on the NOAEL of the two-year study applying an Uncertainty Factor (UF) of 100. The Acute Reference Dose (ARfD) is 0.5 mg/kg bw based on the acute neurotoxicity NOAEL with an UF of 100. There is limited evidence of a carcinogenic effect (EFSA 2013/2014). EC (2013) also adopted the ADI and ARfD values.

The JMPR 2010 meeting reported an ADI of 0.01 mg/kg bw and an ARfD of 0.5 mg/kg bw for fluopyram. FAO/WHO (2013 and 2017) quote the same values.

The USEPA developed a chronic dietary RfD of 0.012 mg/kg/d for fluopyram, and an acute RfD of 0.50 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluopyram is 5.0 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for fluopyram is 0.01 mg/kg body weight, with a NOEL of 1.2 mg/kg bw. There is no ARfD. In July 2015 APVMA developed an ARfD of 0.5 mg/kg based on an acute neurotoxicity rat study; a NOAEL of 50 mg/kg bw/d was based on slightly lower motor and locomotor activity at the next higher dose (<https://apvma.gov.au/>).

Fluopyram is classified as Likely to be Carcinogenic to Humans and a unit risk, Q1\*, of 1.55 x 10-2 (mg/kg/day)-1 was used for the linear low dose extrapolation of cancer risk based on liver tumours in female rats; thyroid tumours were also observed in male mice. Fluopyram is not genotoxic or mutagenic (USEPA 2012).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2013. *Review Report for the Active Substance Fluopyram*. European Commission, Health & Consumers Directorate-General. *SANCO*/11456/2013 rev 2 [8 pp]. Available at: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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JMPR. 2010. Pesticide residues in food. *FAO Plant Production and Protection Paper* 206. Fluopyram (243): 1415–701. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and WHO the Core Assessment Group. <http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation10/2010_Evaluation.pdf> or <http://www.who.int/foodsafety/chem/jmpr/en/>

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USEPA. 2012. Fluopyram: pesticide tolerances. *Federal Register* 77(37) 24 February. [www.gpo.gov/fdsys/pkg/FR-2012-02-24/html/2012-4321.htm](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\INetCache\Content.Word\www.gpo.gov\fdsys\pkg\FR-2012-02-24\html\2012-4321.htm)

# Fluoxastrobin

CAS No. 361377-29-9. The IUPAC name for fluoxastrobin is (E)-{2-[6-(2-chlorophenoxy)-5-fluoropyrimidin-4-yloxy]phenyl}(5,6-dihydro-1,4,2-dioxazin-3-yl)methanone O-methyloxime. The CAS name is (1E)-[2-[[6-(2-chlorophenoxy)-5-fluoro-4-pyrimidinyl]oxy]phenyl](5,6-dihydro-1,4,2-dioxazin-3-yl)methanone O‑methyloxime.

Fluoxastrobin is also called HEC5725. It appears to consist of 93.73 percent E-isomer, 1.12 percent Z-isomer, and the rest various process-related impurities.

### Maximum Acceptable Value

Fluoxastrobin does not have a MAV in the DWSNZ; fluoxastrobin is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.0001 mg/L (0.1 µg/L) for fluoxastrobin in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Fluoxastrobin is a systemic stobilurin fungicide for the control of fungal diseases such as early blight, late blight, leaf spots, leaf rust, and Rhizoctonia solani.

Fluoxastrobin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Fluoxastrobin is a persistent compound. Terrestrial field dissipation studies conducted in New York State yielded half-lifes of 533 days and 347 days in bare ground and turf plots, respectively. At study termination, after roughly 18 months, 35 percent and 17 percent of the applied material remained in the two study plot types as parent compound. Parent fluoxastrobin will likely exhibit low to moderate mobility post-application. Persistent metabolites produced are more mobile than the parent. EFSA (2012) stated it was demonstrated in several degradation studies that fluoxastrobin is persistent in soil and that DT90 values exceed the trigger value of 100 days.

The slow biodegradation, compounded with low mobility in soils, low water solubility, and a relatively low octanol/water partition coefficient suggest that fluoxastrobin may have limited potential for run-off and low bioaccumulation. The low vapour pressure and low Henry’s Law Constant suggest that this compound is not expected to volatilise from water or soils in natural environments.

Solubility in water is about 2.5 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

USEPA (2005) states: for all populations, the dose and endpoint for establishing a cRfD is a LOAEL of 7.7 mg/kg/day (NOAEL for females) from the one year toxicity study in dogs. The NOAEL is 1.5 mg/kg/day (NOAEL for females) based on body weight reductions and liver toxicity (cholestasis) in both sexes. An uncertainty factor (UF) of 100 was selected (10x inter-species extrapolation, 10x intra-species variability) and the cRfD is 0.015 mg/kg/day. No acute toxicity endpoint was identified for either females age 13–49 years or the general population. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.015 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluoxastrobin is 0.105 mg/L (no acute one-day value available.)

The USEPA’s Cancer Assessment Review Committee (CARC) stated “… that there was no evidence of carcinogenicity for fluoxastrobin” and classified this chemical as “not likely to be carcinogenic to humans.” This classification of carcinogenic potential was based on the fact that the observed increase in uterine adenocarcinomas and thyroid follicular cell adenomas did not exceed the historical control values for these two tumour types, which are 24 percent and 9 percent, respectively. By comparison, the respective highest percent tumour incidences in female rats fed fluoxastrobin were 20 percent and 5 percent. Furthermore, fluoxastrobin gave negative results in a number of genotoxicity studies. The CARC also noted that two structurally-related strobilurin compounds, azoxystrobin and trifloxystrobin, did not cause oncogenic effects. The only strobilurin compound they indicated was associated with causing oncogenic effects was kresoxim-methyl, which caused liver tumours.

EC (2008) established an ADI of 0.015 mg/kg bw/day, and an ARfD 0.3 mg/kg bw/day. Reaffirmed by EFSA (2012); both toxicological reference values were established for fluoxastrobin (E-isomer) but were considered to apply to different ratio’s of E and Z isomer.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2008. *Final Review Report for the Active Substance Fluoxastrobin*. European Commission, Health & Consumers Directorate-General. *SANCO*/3921/07 – final [8 pp]. Available at: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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PMEP. Accessed 2011. *Pesticide Active Ingredient Information: Fungicides and Nematicides*. <http://pmep.cce.cornell.edu/profiles/index.html>

USEPA. 2003. Fluoxastrobin: Notice of filing a pesticide petition to establish a tolerance for a certain pesticide chemical in or on food. *Federal Register* 68(78): 19991–4. Notices, 23 April, Accessed via <http://pmep.cce.cornell.edu/profiles/index.html>

USEPA. 2005. *Pesticide Factsheet: Fluoxastrobin*. [47 pp]. <http://www.epa.gov/opprd001/factsheets/>

# Flupropanate-sodium

CAS No. 756-09-2. The IUPAC name for flupropanate is 2,2,3,3-tetrafluoropropionic acid. The CAS name is 2,2,3,3-tetrafluoropropanoic acid. Flupropanate may be sold as salts or esters, mainly flupropanate-sodium, also called sodium tetrafluoropropionate, CAS No. 22898-01-7.

### Maximum Acceptable Value

Flupropanate-sodium does not have a MAV in the DWSNZ; flupropanate-sodium is not mentioned in the WHO Guidelines.

### Sources to water

Flupropanate-sodium (trade name in New Zealand is Taskforce) is a halogenated aliphatic herbicide used in New Zealand to control Chilean needlegrass, Nassella tussock (AgResearch 2014), and kangaroo grass (the latter in vineyards). Flupropanate is slowly translocated from the soil into the growing plant (ie, systemic activity) where it inhibits a biochemical pathway resulting in brown out in about three months and death (up to 16 months). The plant then decays and the residual flupropanate is released into the soil and together with remnant flupropanate, will act upon and kill seedlings for the next three to five years.

Flupropanate-sodium appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Flupropanate-sodium binds tightly to the clay portion of the soil. Its typical half-life is quoted as one year. It does not leach unless soil erosion occurs.

Solubility of flupropanate-sodium in water is well over 100 percent.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of flupropanate-sodium in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

A short-term dietary study in rats (90 days) found increases in liver weights at ≥300 ppm with reduced haemoglobin concentration and increased kidney weights at 1,000 ppm. In a developmental study in mice no teratogenic effects were attributed to flupropanate and no details of maternal effects were recorded. In a developmental study in rats no effects of flupropanate were found in the foetuses, however, decreased maternal body weight was seen from day 15 onwards. This study was barely adequate because of the number of animals used in each group and the low dose levels. Two bacterial studies found flupropanate to be non-mutagenic. The 90-day dietary rat study in which an increase in liver weights was observed was at the dose level of 15 mg/kg bw/day. The NOEL was set at 5 mg/kg bw/day based on the end point of the liver effects in this study. Consequently, the NOEL of 5 mg/kg bw/d in the dietary study in rats is considered to be the most appropriate for brief, intermittent, infrequent and possible short-term occupational exposure risk assessment. Given that no information is available on the GI tract absorption rate, an adjustment factor is not applied to establish the acceptable internal dose (APVMA 2007).

The Acceptable Daily Intake (ADI) adopted for flupropanate in Australia is 0.002 mg/kg body weight, with a NOEL of 5 mg/kg bw. There is no ARfD.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

AgResearch. 2014. Experimental protocol to test pasture species susceptibility to the herbicide flupropanate. By Shona Lamoureaux for Hawke’s Bay Regional Council. Client report number: RE400/2014/514 [10 pp]. *Envirolink Report* 1446. <http://www.envirolink.govt.nz/Envirolink-reports/>

Agrivet Services. 2012. *Evaluation of a Single Autumn Spray of Taskforce (Flupropanate) Herbicide for Controlling Kangaroo Grass in Marlborough* [19 pp]. <http://www.epa.govt.nz/search-databases/HSNO%20Application%20Register%20Documents/APP201170_Kangaroo%20Grass%20Evaluation%20Report%20(Agrivet)%20Provided%20by%20Applicant.pdf>

APVMA. 2007. *Application for Registration of a Chemical Product: GP Flupropanate 100 Granular Herbicide* [5 pp]. <http://www.apvma.gov.au/advice_summaries/41383.pdf>

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# Fluquinconazole

CAS No. 136426-54-5. The IUPAC name for fluquinconazole is 3-(2,4-dichlorophenyl)-6-fluoro-2-(1H-1,2,4-triazol-1-yl)quinazolin-4(3H)-one. The CAS name is 3‑(2,4‑dichlorophenyl)-6-fluoro-2-(1H-1,2,4-triazol-1-yl)-4(3H)-quinazolinone. Fluquinconazole is sometimes sold mixed with other pesticides, eg, prochloraz.

### Maximum Acceptable Value

Fluquinconazole does not have a MAV in the DWSNZ; fluquinconazole is not mentioned in the WHO Guidelines.

### Sources to water

Fluquinconazole is a conazole, or triazole, fungicide which can be used as a seed dressing to control blackleg in canola. It inhibits ergosterol biosynthesis.

Fluquinconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

In soil laboratory incubations under aerobic conditions in the dark, fluquinconazole exhibited high to very high persistence, forming the major breakdown products dione (maximum 29 percent AR) and 1,2,4-triazole (maximum 19 percent AR), which exhibited high to very high and low to moderate persistence, respectively. The available data indicate that breakdown of fluquinconazole in soil to these two compounds is primarily an abiotic process.

In anaerobic soil incubations the same pattern of breakdown was observed, though the levels of the two breakdown products formed were higher than under aerobic conditions. Fluquinconazole and dione exhibited low mobility in soil. 1,2,4-triazole exhibited high to very high soil mobility. There were no indications that the adsorption of these three compounds was pH dependent.

In sterile aqueous hydrolysis studies at pH 7 and 25ºC the half-life of fluquinconazole was estimated to be 21.9 days. Under more alkaline conditions (pH 9) fluquinconazole was more labile. Under acidic conditions (pH 5) it was more stable. The hydrolytic breakdown products dione and 1,2,4-triazole were demonstrated to be essentially stable to further hydrolytic breakdown at environmentally relevant pH and temperatures. Aqueous photolyic investigations indicated that light did not enhance the breakdown of fluquinconazole but that light energy can enhance the breakdown of dione in aqueous solution.

Groundwater exposure assessments showed that the potential for groundwater exposure from the representative uses by fluquinconazole and 1,2,4-triazole to be low, whereas for the breakdown product dione, contamination of groundwater might be expected in vulnerable situations.

Solubility of fluquinconazole in water is about 1 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2011).

### Health considerations

Fluquinconazole is acutely toxic by inhalation and if swallowed. The relevant short-term NOAEL is 0.2 mg/kg bw/day derived from one-year and 90-day dog studies.

Long-term administration of fluquinconazole resulted in the same target organs affecting rats and mice; liver tumours were observed in both species. The thyroid was also affected in rats, leading to the formation of thyroid tumours in both sexes, these tumours are considered rat specific due to the mechanism of action and not relevant to humans. The relevant long-term toxicity and carcinogenicity NOAEL is 0.44 mg/kg bw/day derived from the two-year rat study. No effect on the reproduction was observed up to the highest dose tested of 6.8 mg/kg bw/day showing parental and offspring toxicity; young rats were more sensitive to fluquinconazole toxicity than the adults and the offspring NOAEL is 0.3 mg/kg bw/day based on clinical signs and reduced pup viability observed at higher dose levels. Developmental toxicity as increased post-implantation loss in rats and increased variant sternebrae in rabbits was associated with maternal toxicity; a NOAEL of 2 mg/kg bw/day for both maternal and developmental toxicity is found in both species. No neurotoxic potential is attributed to the active substance.

Toxicological studies were presented on a minor rat metabolite, dione, showing that the metabolite is less acutely toxic than the parent compound, the short-term (28-day) toxicity was also lower than fluquinconazole. No toxicological information was presented in the dossier on the triazole derivative plant metabolites (1,2,4-triazole, triazolyl alanine and triazolyl acetic acid) and a data gap is identified.

The acceptable daily intake (ADI) of fluquinconazole is set at 0.002 mg/kg bw/day, based on the overall NOAEL from the one-year and 90-day dog studies and applying a safety factor of 100; the acceptable operator exposure level (AOEL) is 0.001 mg/kg bw/day, based on the same NOAEL from the dog studies, 100 safety factor and 60 percent correction for limited oral absorption (in rats). The acute reference dose (ARfD) is 0.02 mg/kg bw based on both developmental toxicity studies in rat and rabbit. These values were reaffirmed by EFSA (2018).

The Acceptable Daily Intake (ADI) adopted for fluquinconazole in Australia is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EFSA. 2011. Conclusion on the peer review of the pesticide risk assessment of the active substance fluquinconazole. *EFSA Journal* 9(5): 2096 [112 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/2096.pdf>

EFSA. 2018. *Review of the Existing Maximum Residue Levels for Fluquinconazole according to Article 12 of Regulation (EC) No 396/2005*. September [16 pp]. <https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5409>

# Fluroxypyr

CAS No. 69377-81-7. The IUPAC name for fluroxypyr (sometimes called fluroxypyr acid) is 4-amino-3,5-dichloro-6-fluoro-2-pyridyloxyacetic acid. The CAS name is [(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]acetic acid. Sometimes called fluoroxypyr (in France), and has been misspelt as fluoxypyr. Fluroxypyr may be sold as the methylheptyl ester (fluroxypyr-meptyl, CAS No. 81406-37-3, which is sometimes referred to as just fluroxypyr).

### Maximum Acceptable Value

Fluroxypyr does not have a MAV in the DWSNZ; fluroxypyr is not mentioned in the WHO Guidelines.

### Sources to water

Fluroxypyr is a post-emergence pyridine herbicide commonly used on cereals and around trees to control broadleaf plants. Fluroxypyr ranked number nine for “Most widely used pesticides in the UK (by area treated)”.

Fluroxypyr appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Available data indicate that fluroxypyr (the acid) is mobile to very mobile in the submitted laboratory studies. However, dissipation by hydrolysis and microbial degradation reduced persistence and limited downward transport (ie, leaching) in the submitted field studies. Half-lifes in soil and water range from one to five weeks. 4‑Amino-3,5-dichloro-6-fluoro-2-pyridinol and 4-amino-3,5-dichloro-6-fluoro-methoxypyridine are the main metabolites in soil.

Fluroxypyr-meptyl is present as a mixture of two enantiomers. However, in all environmental compartments it is rapidly transformed (D90 of six days) to fluroxypyr (EFSA 2011). Fluroxypyr is low to moderate persistent in soil and degrades into two major metabolites: fluroxypyr pyridinol (maximum 23.9 percent after 28 d) and fluroxypyr methoxypyridine (maximum 38.2 percent after 56 d). The DT90 values reported from laboratory studies for fluroxypyr and its relevant soil metabolites (fluroxypyr pyridinol and fluroxypyr methoxypyridine) are up to 163, 283 and 2,663 days, respectively (EFSA 2011).

EFSA (2011) states that potential for groundwater contamination above the limit of 0.1 μg/L by the metabolites fluroxypyr pyridinol (only when formed in alkaline soils) and fluroxypyr methoxypyridine was identified for some uses in vulnerable scenarios.

Solubility in water is about 0.1 mg/L (fluroxypyr-meptyl), or about 6,000 mg/L (fluroxypyr).

### Removal methods

GAC is likely to be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The dog appears to be more sensitive than rats and mice. In a range-finding feeding study in dogs, dogs at 500 mg/kg/day exhibited ataxia and hind limb weakness as well as decreases in body weight and food consumption. Histopathology showed moderate acute tubular nephrosis and a slight to moderate acute gastroenteritis. Some early signs of acute tubular nephrosis were also seen in both sexes of dogs at 150 mg/kg/day. The NOEL for the study was 50 mg/kg/day, the LOAEL was 150 mg/kg/day based on histopathological lesions in the kidneys, decreased testes weights, and increased adrenal weights in both sexes. The Reference Dose (RfD) was established at 0.5 mg/kg/day (USEPA 1998). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 1.0 mg/kg/d for fluroxypyr and fluroxypyr acid. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluoxypyr and fluoxypyr acid is 7.0 mg/L (no acute one-day value available.)

EC (1999) states that the lowest long-term NOAEL is 80 mg/kg bw/d, based on a two-year oral study on rats (fluroxypyr). Fluroxypyr showed no evidence of genotoxicity, teratogenicity or carcinogenicity. EC (1999) established an ADI of 0.8 mg/kg bw based on a two-year rat study (oral) and a safety factor of 100; an ARfD was not considered to be necessary.

The Acceptable Daily Intake (ADI) adopted for fluroxypyr in Australia is 0.2 mg/kg body weight, with a NOEL of 20 mg/kg bw.

The acceptable daily intake (ADI) of fluroxypyr is 0.8 mg/kg bw/day, based on the NOAEL of 80 mg/kg bw/day found in the two-year rat study and applying a safety factor of 100. The acute reference dose (ARfD) was not set and was considered not necessary (EFSA 2011 and 2013).

Fluroxypyr is classified as a “not likely” human carcinogen. It does not demonstrate developmental or reproductive toxicity (USEPA 1998).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 1999. *Final Review Report for the Active Substance Fluroxypyr*. European Commission, Health & Consumers Directorate-General. 6848/VI/98-Final [35 pp]. Available at: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2011. Peer Review of the pesticide risk assessment of the active substance fluroxypyr. *EFSA Journal* 9(3): 2091 [91 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/2091.pdf>

EFSA. 2013. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for fluroxypyr according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 11(12): 3495 [49 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm>

PMEP. 1997. *Fluroxypyr 1-methylheptyl ester (Starane) Pesticide Petition Filing 12/97* (USEPA). <http://pmep.cce.cornell.edu/profiles/herb-growthreg/fatty-alcohol-monuron/fluroxypyr/fluroxypyr_pet_1297.html>

PMEP. 1998. *Fluroxypyr 1-methylheptyl ester (Starane) Approval of Pesticide Product Registrations* (USEPA). <http://pmep.cce.cornell.edu/profiles/herb-growthreg/fatty-alcohol-monuron/fluroxypyr/fluroxypyr_prod_reg_1198.html> or <http://pmep.cce.cornell.edu/profiles/index.html>

USEPA. 1998. *Pesticide Factsheet: Fluroxypyr*. Office of Prevention, Pesticides and Toxic Substances [13 pp]. <http://www.epa.gov/opprd001/factsheets/>

# Flusilazole

CAS No. 85509-19-9. The IUPAC name for flusilazole is either bis(4‑fluorophenyl)(methyl)(1H-1,2,4-triazol-1-ylmethyl)silane or 1‑{[bis(4‑fluorophenyl)(methyl)silyl]methyl}-1H-1,2,4-triazole. The CAS name is 1‑[[bis(4-fluorophenyl)methylsilyl]methyl]-1H-1,2,4-triazole. Sometimes called NuStar in the US.

### Maximum Acceptable Value

Flusilazole does not have a MAV in the DWSNZ; flusilazole is not mentioned in the WHO Guidelines.

### Sources to water

Flusilazole is a systemic conazole (or triazole) fungicide. Flusilazole is a sterol synthesis inhibitor, which interferes with fungal membrane structure and function. A common use is to protect fruit from scab and powdery mildew. NZFSA has a residue limit of 0.1 mg/kg in citrus fruit. It is used use on cereals, maize, oilseed rape and sugarbeet in Europe.

Flusilazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Flusilazole degradation is essentially biphasic – initially faster (about 30 percent in 100 days) followed by slow decline (10–15 percent in 250 days); this may be due to reduced availability to soil micro-organisms over time or decline in soil biomass levels (no determination presented, EC 2007). Bis(4-fluorophenyl)metylsilanol is a soil metabolite. Degradation essentially results in intact flusilazole and intermediates or “bound residues”. The half-life in soil is about 100–200 days. It is stable in water as well. EFSA (2013) states the DT90 value of flusilazole is expected to range between  
168–730 days.

Solubility in water is about 40 mg/L.

### Typical concentrations in drinking-water

Flusilazole binds to soil so is not expected to leach to groundwater.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Animal data indicates that flusilazole is a weak carcinogen at high exposure levels. Rat testicular and bladder and mouse liver tumours appeared in the presence of significant chronic toxicity in the target organs and would not be expected to present a significant risk to humans exposed to much lower levels of flusilazole.

Animal data suggest that flusilazole may be a weak developmental toxicant following excessive oral or dermal exposures.

Flusilazole was negative in seven mutagenicity studies, and the JMPR meeting concluded that there was no evidence of genotoxicity (IPCS 1989); an ADI was estimated at 0.001 mg/kg bw on the basis of an NOAEL of 0.14 mg/kg bw per day for liver toxicity in a one-year feeding study in dogs and a safety factor of 100. This was confirmed in 1995. Then the 2007 JMPR established an ADI of 0 to 0.007 mg/kg bw/d and an ARfD of 0.02 mg/kg bw (FAO/WHO 2007).

EC (2007) established an ADI of 0.002 mg/kg bw based on a one-year dog study and a safety factor of 100, and an ARfD (acute reference dose) of 0.005 mg/kg/d, relevant to women of child bearing age. These values were reaffirmed by EFSA (2013).

USEPA. 2007. quotes an acute RfD of 0.02 mg/kg/d, and a chronic RfD of 0.002 mg/kg/d. The oral RfD for NuStar had earlier been 0.0007 mg/kg/d (USEPA 1991). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.002 mg/kg/d, and an ARfD of 0.02 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for flusilazole is 0.66 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for flusilazole is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2007. *Final Review Report for the Active Substance Flusilazole*. European Commission, Health & Consumers Directorate-General. 6850/VI/97 final [24 pp]. Available at: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2013. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for flusilazole according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 11(4): 3186 [62 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm>

DuPont. 2007. *Material Safety Data Sheet, for DuPont Punch Fungicide*. <http://msds.dupont.com/msds/pdfs/EN/PEN_09004a358027241c.pdf>

FAO/WHO. 2007. *Evaluations: Part II – Toxicological* 317–47. Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues. <http://www.inchem.org/> or <http://www.inchem.org/documents/jmpr/jmpmono/v2007pr01.pdf>

FAO. 2008. *FAO Specifications and Evaluations for Agricultural Pesticides*: *Flusilazole* [28 pp]. [www.fao.org/ag/AGP/AGPP/Pesticid/Specs/docs/Pdf/new/Flusilazole08.pdf](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Word\www.fao.org\ag\AGP\AGPP\Pesticid\Specs\docs\Pdf\new\Flusilazole08.pdf)

IPCS. 1989. *Flusilazole*. INCHEM. See: <http://www.inchem.org/documents/jmpr/jmpmono/v89pr09.htm>

IPCS. 1995. *Flusilazole*. INCHEM. See: <http://www.inchem.org/documents/jmpr/jmpmono/v95pr08.htm>

JMPR. 2008. *Flusilazole* [28 pp]. <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/lpe/en/>

NZFSA. 2005. *Proposed Amendment to the New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards 2005 (No. 2)*. <http://www.foodsafety.govt.nz/elibrary/> and copy title into keyword search.

USEPA. 1991. NuStar. *Integrated Risk Information System (IRIS)*. <http://www.epa.gov/iris/subst/0299.htm>

USEPA. 2007. Flusilazole: pesticide tolerances for emergency exemptions. *Federal Register* 72(167): 49654–60. Rules and Regulations, 29 August. Accessed via <http://pmep.cce.cornell.edu/profiles/index.html>

# Flusulfamide

CAS No. 106917-52-6. The IUPAC name for flusulfamide is 2′,4-dichloro-α,α,α-trifluoro-4′-nitro-m-toluenesulfonanilide. The CAS name is 4-chloro-N-(2-chloro-4-nitrophenyl)-3-(trifluoromethyl)benzenesulfonamide.

### Maximum Acceptable Value

Flusulfamide does not have a MAV in the DWSNZ; flusulfamide is not mentioned in the WHO Guidelines.

### Sources to water

Flusulfamide is a sulfonanilide (or anilide or benzenesulfonanilide) fungicide, commonly applied to the soil to inhibit fungal spore germination on vegetables, and used to control (sometimes with fluazinam) clubroot of brassicas which is caused by the protozoan Plasmodiophora brassicae.

Flusulfamide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Flusulfamide is slightly mobile in soils. It has a half-life of about 50 days. It is stable in acidic and alkaline media, including water but has a photolysis half life of 3–4 days; it is non-volatile. The partition coefficient (n-octanol/water) logP = 2.8 (ie, moderate). The adsorption coefficient KOC = 3,276.

Solubility in water is about 3 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The manufacturers state that flusulfamide is not mutagenic and is not a reproductive toxin.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Cheah, et al. 1998. *Soil-Incorporation of Fungicides for Control of Clubroot of Vegetable Brassicas*. New Zealand Institute for Crop & Food Research Limited. New Zealand Plant Protection Society (Inc): 130–3. <http://www.nzpps.org/journal/51/nzpp_511300.pdf>

IUPAC. Accessed 2009. *Flusulfamide* (ref: MTF 651). See: <http://sitem.herts.ac.uk/aeru/iupac/351.htm>

# Fluthiacet-methyl

CAS No. 117337-19-6. The IUPAC name for fluthiacet-methyl is methyl{2-chloro-4-fluoro-5-[(EZ)-5,6,7,8-tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylideneamino]phenylthio}acetic acid. The CAS name is methyl-2-[[2-chloro-4-fluoro-5-[(tetrahydro-3-oxo-1H,3H-[1,3,4]thiadiazolo[3,4-a]pyridazin-1-ylidene)amino]phenyl]thio]acetic acid.

Fluthiacet is the acid, fluthiacet-methyl is an ester. The CAS No. for fluthiacet is 149253‑65-6. A trade name for fluthiacet-methyl is Cadet.

### Maximum Acceptable Value

Fluthiacet-methyl does not have a MAV in the DWSNZ; fluthiacet-methyl is not mentioned in the WHO Guidelines.

### Sources to water

Fluthiacet-methyl is a herbicide used to control broadleaf weeds in maize.

Fluthiacet-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2016 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

This commercial pesticide comprises:

|  |  |  |
| --- | --- | --- |
| **Ingredient** | **CAS No.** | **Composition (% weight)** |
| acetophenone | 98-86-2 | 40–50 |
| methyl pyrrolidone | 872-50-4 | 20–30 |
| naphtha (petroleum) | 64742-94-5 | 10–20 |
| fluthiacet-methyl | 117337-19-6 | 10.3 |

### Forms and fate in the environment

If released to soil, fluthiacet-methyl is expected to have slight mobility based upon an estimated Koc of 2,700. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 2.1 x 10-9 atm-cu m/mole. A photolysis half-life on soil of 21 days has been reported. If released into [water](https://pubchem.ncbi.nlm.nih.gov/compound/water), fluthiacet-methyl is expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilisation from [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 160 suggests the potential for bioconcentration in aquatic organisms is high. A hydrolysis half-life in [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) of 18 days (at pH 7) has been reported. Stability in [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) DT50 is 484.8 days (pH 5), 17.7 days (pH 7), 0.2 days (pH 9) (NIH 2016).

Solubility in water of the active ingredient is 0.85 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See USEPA (2006).

### Health considerations

The chronic Reference Dose (RfD) for fluthiacet-methyl is 0.001 mg/kg/day. This value is based on the systemic NOAEL of 0.1 mg/kg/day in the mouse carcinogenicity study with a 100-fold uncertainty factor to account for interspecies extrapolation (10x) and intraspecies variability (10x).

The USEPA (1999) classified fluthiacet-methyl as likely to be carcinogenic to humans based on the presence of pancreatic tumours (exocrine adenomas, islet cell adenomas and combined islet cell adenomas + carcinomas) in male rats and liver tumours (adenomas and combined adenomas + carcinomas) in male and female mice. USEPA (2006) states that the overall cancer dietary risk for the US population is 7.51 x 10-7, based on dietary (food and drinking water exposures).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

NIH. Accessed February 2016. *Fluthiacet-methyl*. National Centre for Biotechnology Information. [https://pubchem.ncbi.nlm.nih.gov/compound/Fluthiacet-methyl#section=Top](https://pubchem.ncbi.nlm.nih.gov/compound/Fluthiacet-methyl%23section=Top)

USEPA. 1999. *Pesticide Factsheet: Fluthiacet-methyl* [21 pp]. <http://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-108803_01-Apr-99.pdf>

USEPA. 2006. Fluthiacet-methyl: pesticide tolerance. *Federal Register* 71 FR 77620–5. EPA‑HQ-OPP-2006-0788. <https://www.federalregister.gov/articles/2006/12/27/E6-22126/fluthiacet-methyl-pesticide-tolerance>

# Flutriafol

CAS No. 76674-21-0. The IUPAC name for flutriafol is (RS)-2,4′-difluoro-α-(1H-1,2,4-triazol-1-ylmethyl)benzhydryl alcohol. The CAS name is α-(2-fluorophenyl)-α-(4‑fluorophenyl)-1H-1,2,4-triazole-1-ethanol.

### Maximum Acceptable Value

Flutriafol does not have a MAV in the DWSNZ; flutriafol is not mentioned in the WHO Guidelines.

### Sources to water

Flutriafol is a broad spectrum, systemic and contact conazole (or triazole) fungicide. It can be applied as a foliar spray or mixed with fertiliser. It can also be used for seed treatment. Flutriafol was introduced in 1981, and since then it has attained an important position in the global fungicide market, proving effective in controlling a large number of fungal diseases affecting a wide range of crops. Used on cereals in Australasia. Can be used with other pesticides, eg, imazalil (qv).

Flutriafol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of flutriafol in soil can exceed 12 months, and in some cases, more than two years (USEPA 2007). EFSA (2014) states that soil degradation studies found DT90 values of flutriafol to range between 1051–13,583 days.

It is stable in water as well. It is classified as being moderately mobile, so is likely to contaminate water, including groundwater.

Metabolites include triazolyl alanine, triazolyl acetic acid, and 1H-1,2,4-triazol-1-ylacetic acid (CAS No. 4314-22-1). These metabolites are common to most of the conazole fungicides.

Solubility in water is about 100–180 mg/L.

JMPR (2011) reports: vapour pressure <0.01 x 10-5 Pa at 25°C; water solubility = 95 mg/L at 20°C; partition coefficient = logPow = 2.32 at 20°C; stable to hydrolysis at pH5, 7 and 9 at 50°C over 30 days; photolytically stable in aqueous buffer solution (pH7) at 25°C for periods up to the equivalent of 66 days Florida summer sunlight. Flutriafol is slowly degraded in laboratory incubated soils. Approximately 85 percent remained after 252 days in a loamy sand and a sandy clay loam. In aerobic soil the DT50 is >1,000 days.

### Typical concentrations in drinking-water

PSD (1996) reports that traces have been found in UK drinking-water (0.0001 mg/L).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The chronic dietary reference dose (RfD) was established by the USEPA (2007) at 0.01 mg/kg/d bw, based on a NOAEL of 10 mg/kg/d and an uncertainty factor of 1,000. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.075 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for flutriafol is 2.48 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

Based on lack of evidence of carcinogenicity in both rats and mice studies, the chemical was considered as “not likely” to be carcinogenic to humans (USEPA 2007).

Flutriafol is on the endocrine disruptor list.

The Acceptable Daily Intake (ADI) adopted in Australia for flutriafol is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw in a one-year study in dogs and a two-year study in rats.

The FAO/WHO 2011 meeting established an acceptable daily intake (ADI) of  
0–0.01 mg/kg bw on the basis of the NOAEL of 1.0 mg/kg bw per day in the two-year rat study, based on increases in fatty changes and increased weights of the liver in males at 10 mg/kg bw per day. A safety factor of 100 was applied. The ADI is supported by the NOAEL in the carcinogenicity study in mice of 1.2 mg/kg bw per day, based on the increased incidence and severity of hepatic centrilobular fatty change in males at 6 mg/kg bw per day. The meeting also established an acute reference dose (ARfD) of 0.05 mg/kg bw on the basis of the NOAEL of 5 mg/kg bw per day in the 90‑day and one-year toxicity studies in dogs based on reduced body weight gain (males) or body weight loss (females) after one week (the first time of measurement) and subsequently reduced body weight gain during the early part of the study, although feed consumption was unaffected by treatment. A safety factor of 100 was applied. This provides a margin of greater than 1,000 between the ARfD and the LOAEL for cleft palate in rats (75 mg/kg bw per day). JMPR (2011) reaffirmed these values.

The toxicological profile of flutriafol was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI value of 0.01 mg/kg bw per day and an ARfD of 0.05 mg/kg bw (EFSA 2013/2014/2016). See datasheet for triazole metabolites for latest ADI and ARfD.

1,2,4-triazole, triazole acetic acid and triazole lactic acid: ADI = 0.02 mg/kg/d; ARfD = 0.06 mg/kg.

Triazole alanine: ADI = 0.1 mg/kg/d; ARfD = 0.1 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EFSA. 2013. Reasoned opinion on the modification of the existing MRLs for flutriafol in pome fruits, peaches, cherries and plums. *EFSA Journal* 11(10): 3446 [25 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm>

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USEPA. 2007. Flutriafol: time-limited pesticide tolerance. *Federal Register* 72(167): 49660–6, Rules and Regulations, 29 August. <http://pmep.cce.cornell.edu/profiles/fung-nemat/febuconazole-sulfur/flutriafol/index.html> or <http://pmep.cce.cornell.edu/profiles/index.html>

# Fluxapyroxad

CAS No. 907204-31-3. The IUPAC name for fluxapyroxad is 3-(difluoromethyl)-1-methyl-N-(3′,4′,5′-trifluorobiphenyl-2-yl)pyrazole-4-carboxamide. The CAS name is 3‑(difluoromethyl)-1-methyl-N-(3′,4′,5′-trifluoro[1,1′-biphenyl]-2-yl)-1H-pyrazole-4-carboxamide.

### Maximum Acceptable Value

Fluxapyroxad does not have a MAV in the DWSNZ; fluxapyroxad is not mentioned in the WHO Guidelines.

### Sources to water

Fluxapyroxad is a broad spectrum [anilide, carboxamide](http://www.alanwood.net/pesticides/class_fungicides.html#anilide_fungicides) or [pyrazole](http://www.alanwood.net/pesticides/class_fungicides.html#pyrazole_fungicides) fungicide. It is registered in the US for both foliar and seed treatment uses on a wide range of crops (cereal grains, legume vegetables, oil seed crops, peanuts, pome fruit, stone fruit, root and tuber vegetables, fruiting vegetables and cotton).

Fluxapyroxad appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The impurity toluene is of toxicological concern and must not exceed 1 g/kg in the technical material (EC 2012).

### Forms and fate in the environment

Fluxapyroxad degrades slowly in soil and aquatic systems. Fluxapyroxad is stable to hydrolysis at pH values of 5, 7 and 9, and is stable to both soil and aqueous photolysis. Fluxapyroxad does not readily undergo aerobic or anaerobic degradation in soil (half-lifes ranging from 213 to 1,827 days) or in aquatic systems (half-lifes ranging from 420 to 731 days), and therefore may persist in soil, water, and in benthic sediment once transported or partitioned to these environmental compartments. Fluxapyroxad has a moderate potential to reach aquatic environments, including surface and groundwater, for several months or more following terrestrial application. The available fate data indicate that fluxapyroxad is likely to dissipate to some extent through various mechanisms, including run-off, erosion, and leaching to groundwater. Based on its mobility and environmental persistence, fluxapyroxad has the potential to leach to groundwater, particularly where high water tables are present, high rainfall/irrigation occurs, and where sandy soils with low organic matter exist. Fluxapyroxad is not expected to volatilise (USEPA 2012).

Fluxapyroxad is stable in water at pH 7 with and without the influence of light. Fluxapyroxad is stable in aqueous solution at pH 4, 5, 7 and 9 (50°C) for five days. Henry’s Law constant = 3.028 × 10-7 Pa × m3 × mol-1. Solubility in water is about 3.5 mg/L. The n-octanol/water partition coefficient is log Kow = 3.13 at pH 7 and 20°C (JMPR 2012) – which also discusses a host of metabolites, as does EFSA (2012). EFSA (2015) states that the soil degradation rate of fluxapyroxad and its soil metabolite M700F002 is slow. The DT90 value in soil exceeds one year (DT90field >1,000 days) and fluxapyroxad is likely to accumulate in soils. The plateau concentration in soil following several years of consecutive applications could not be established during the peer review, but is expected to be reached after 13 years.

Under aerobic laboratory conditions at 20–27°C fluxapyroxad degrades at a moderate to slow rate with DT50 values ranging from 69 to 689 days and DT90 values from >120 to >1,000 days. There was no apparent correlation between half–lifes and soil characteristics of pH and organic carbon. Metabolite M700F001 degraded rapidly with DT50 values ranging from 2–9 days while DT50 values for M700F002 ranged from  
77–197 days (FAO/WHO 2013).

### Typical concentrations in drinking-water

Treatment processes that remove particulate matter will reduce the concentration of fluxapyroxad.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

JMPR (2012) quotes an ADI for fluxapyroxad of 0.02 mg/kg bw, and an ARfD of 0.3 mg/kg bw. FAO/WHO (2013) quote the same values.

EC (2012) quotes an ADI of 0.02 mg/kg bw, and an ARfD of 0.25 mg/kg bw. EFSA (2012, 2015 and 2016) allocated an ADI of 0.02 mg.kg bw/d for fluxapyroxad, based on the NOAEL of 2.1 mg/kg bw/day from the two-year rat study and applying the standard AF of 100. The ARfD is 0.25 mg/kg bw, based on the NOAEL of 25 mg/kg bw/day for developmental effects in rabbits and decreased maternal body weight gain in rats with an AF of 100 applied.

USEPA (2012) derived an acute PAD (aPAD) of 1.25 mg/kg/day based on the observation of decreased motor activity and decreased rearing in the rat acute neurotoxicity study at a LOAEL of 500 mg/kg/day [NOAEL = 125 mg/kg/day]. The chronic PAD (cPAD) of 0.021 mg/kg/day was based on the observation of non-neoplastic changes in the liver (foci and masses) in the chronic toxicity/carcinogenicity study in rats at a LOAEL of 11 mg/kg/day [NOAEL = 2.1 mg/kg/day]. The cPAD will adequately account for all chronic effects, including carcinogenicity, likely to result from exposure to fluxapyroxad. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fluxapyroxad is 12.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for fluxapyroxad is 0.02 mg/kg body weight based on a NOAEL of 2.1 mg/kg bw/d in a two-year oral study in rats and using a 100-fold safety factor. An acute reference dose (ARfD) has not been established because no significant treatment related findings have been observed in the experimental animal database evaluated following a single dose administration of fluxapyroxad, which would be likely to present an acute hazard to humans (APVMA 2012 and <https://apvma.gov.au/>).

FAO/WHO (2013) concluded that fluxapyroxad was unlikely to be genotoxic. Fluxapyroxad is classified by the USEPA as “Not likely to be Carcinogenic to Humans” based on convincing evidence that carcinogenic effects are not likely below a defined dose range.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Folpet

CAS No. 133-07-3. The IUPAC name for folpet is either N‑(trichloromethylthio)phthalimide or N-(trichloromethanesulfenyl)phthalimide. The CAS name is 2-[(trichloromethyl)thio]-1H-isoindole-1,3(2H)-dione. Can be called N‑(trichloromethylmercapto)phthalimide. Has also been called folpel.

### Maximum Acceptable Value

Folpet does not have a MAV in the DWSNZ; folpet is not mentioned in the WHO Guidelines.

### Sources to water

Folpet is a broad spectrum phthalimide fungicide which acts by denaturing fungal proteins. It is used to control cherry leaf spot, rose mildew, rose black spot, apple scab and grapes and fruit. Used on berries, flowers, ornamentals, fruits and vegetables, and for seed- and plant- bed treatment. Also used, in a minor way, as a fungicide in paints, sealants, adhesives and plastics. No longer sold in the US.

Folpet appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

EC (2008) states that the carbon tetrachloride maximum level in the manufactured product should not exceed 4 g/kg, and perchloromethylmercaptan should not exceed 3.5 g/kg.

Technical folpet is usually about 90 percent pure. The main impurity is phthalimide (up to 4.0 percent).

### Forms and fate in the environment

Degradation is probably the same as that of captan (the parent chemical), in which three chlorine atoms are removed under the influence of endogenous thiol compounds, with the formation of the trithiocarbonate, thiophosgene, phthalic acid and phthalimide. Folpet is considered to be not persistent and small quantities of the compound are readily hydrolysed in soil and surface waters. However, it is highly toxic for aquatic organisms. DT90 values of folpet, phthalimide and their relevant soil metabolites (phthalic acid and phthalamic acid) are all less than 100 days; folpet and phthalimide half lives are <3 days under field conditions (EFSA 2014).

One of the other metabolites formed in the breakdown of folpet is thiophosgene, however its tendency to hydrolyse rapidly and its high reactivity with other substances likely to be present in wash-waters, leachates, drains and sewers mean that it is unstable and that exposure of biota in aquatic and terrestrial compartments of the environment to thiophosgene will not occur (ECHA 2014).

Solubility in water is about 1 mg/L.

### Removal methods

GAC is likely to be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Folpet is a member of the N-trihalomethylthio group of compounds which are highly reactive with biological tissues. The labile N-trichloromethylthio (S-CCl3) side chain is the reactive portion of the molecule and degrades rapidly under neutral/alkaline conditions in the presence of tissue or blood thiols (such as cysteine and glutathione) to form a key short-lived intermediate, thiophosgene. Thiophosgene is highly reactive and severely irritating to tissues. Thiophosgene causes irritation to mucus membranes and is a skin irritant and sensitiser. The thiophosgene moiety is most likely responsible for folpet’s activity as a surface fungicide and is responsible for the predominant toxicity in mammals, although the rest of the molecule (ie, phthalimide, phthalamic acid) may also contribute to folpet’s toxicity.

Based on changes in body weight and clinical biochemistry in a one-year chronic oral toxicity study in dogs the Lowest Observed Effects Level (LOEL) was 60 mg/kg/day, and the No Observable Effect Level (NOEL) was 10 mg/kg/day. The NOEL led to a RfD of 0.1 mg/kg/d (USEPA 1991/1999), using an uncertainty factor of 100 to account for intra- and interspecies differences in sensitivity. In general, the RfD is an estimate of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.09 mg/kg/d, and an ARfD of 0.10 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for folpet is 3.30 mg/L.

The following environmental degradates of folpet have been detected: phthalic acid, phthalimide, and phthalamic acid. Phthalimide and phthalic acid are also animal and plant metabolites. In addition, a fish bioconcentration study shows that the phthalic anhydride accumulates and concentrates in fish. No human health toxicology data are available for these degradates or metabolites. However, USEPA (1999) states that none of these environmental degradates or metabolites are expected to be of human toxicological concern.

Carcinogenic tumours of the gastrointestinal tract were produced in mice from continuous administration of 437 mg/kg for two years (EXTOXNET 1995). Another study found that feeding folpet to rats at 3,200 mg/kg or to dogs at 1,500 mg/kg for 17 months produced no adverse effects. WHO (1992) stated that tumours were not observed in similar studies on rats, and therefore the evidence for the carcinogenicity of this compound in experimental animals is inadequate. As at September 2008 the USEPA has classified folpet in Group B: a probable human carcinogen, based on induced carcinoma and adenoma of the duodenum (an unusual site) in both sexes of both CD-1 and B6C3F1 mice. Folpet is also mutagenic in several in vitro assays and is a structural analogue of captan, which has been shown to induce carcinoma in the duodenum of two mouse strains. Folpet appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

In 1995 JMPR established an ADI of 0–0.1 mg/kg bw based on a NOAEL of 10 mg/kg bw per day in a two-year study of toxicity and carcinogenicity in rats, a one-year study of toxicity in dogs, and studies of reproductive toxicity in rats and rabbits, and using a safety factor of 100. In 2004, the meeting established an ARfD for folpet of 0.2 mg/kg bw for women of childbearing age only, based on a NOAEL of 20 mg/kg bw per day for increased incidences of hydrocephalus at 60 mg/kg bw per day in rabbits and using a safety factor of 100. These values were reconfirmed in JMPR (2007) and EFSA (2011 plus 2013/2014).

On the basis of the study of developmental study with phthalimide in rabbits, the 2004 JMPR meeting considered that it is unlikely that phthalimide (or its metabolites, including phthalamic acid) is a teratogenic agent.

The concentration of folpet in drinking-water that would lead to an increase of one cancer per 100,000 (10-5 risk) is 0.1 mg/L (USEPA 1999).

The WHO and the EC estimated that the acceptable daily intake (ADI) for man is  
0–0.1 mg/kg. EC (2008) also established an ARfD of 0.1 mg/kg/d.

USEPA (2015) found that based on weight of evidence considerations, a mammalian EDSP Tier 2 testing is not recommended for folpet since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Foramsulfuron

CAS No. 173159-57-4. The IUPAC name for foramsulfuron is 1‑(4,6‑dimethoxypyrimidin-2-yl)-3-[2-(dimethylcarbamoyl)-5-formamidophenylsulfonyl]urea. The CAS name is 2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-4-(formylamino)-N,N-dimethylbenzamide. Some formulations contain isoxadifen-ethyl as a crop safener.

### Maximum Acceptable Value

Foramsulfuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Foramsulfuron is a pyrimidinylsulfonylurea foliar post-emergence herbicide, which works by inhibition of acetolactate synthase ALS (acetohydroxyacid synthase AHAS). It is commonly used to control annual and perennial grasses and broadleaf weeds, particularly in corn/maize.

Foramsulfuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of foramsulfuron in soil is about a month. Parent foramsulfuron is only weakly sorbed to soils, but is relatively unstable and represents a low potential to leach to groundwater. Parent and a suite of structurally similar transformation products have low sorptivity to soil, and, judging by this measure alone, are prone to leach and to run off. However, relatively short environmental life times and progressive formation of large fractions of by-products which resist extraction (or bound residues) make leaching and running off less likely. The degradation products are generally more stable than the parent, but are more likely to bind to soil, and are therefore still unlikely to run off or leach (USEPA 2002; PMEP 2003).

EFSA (2016) found that foramsulfuron and its major metabolites exhibited very high to medium mobility in soil. In laboratory incubations in dark aerobic natural sediment water systems, foramsulfuron exhibited moderate persistence. The potential for groundwater exposure from the representative uses by foramsulfuron above the parametric drinking water limit of 0.1 μg/L was concluded to be low.

Metabolites include 4-amino-2-[3-(4,6-dimethoxypyrimidin-2-yl)ureidosulfonyl]-N, N‑dimethylbenzamide, and 4,6-dimethoxypyrimidin-2-amine (IUPAC name) or 2‑amino-4,6-dimethoxypyrimidine (CAS name) – CAS No. 36315-01-2 (SITEM). These are not persistent in soil, but are persistent in water. Recently, foramsulfuron concentrations have been found to be increasing rapidly in Lake Geneva (Chevre et al 2008).

Water solubility is about 37 mg/L at pH 5; 3,300 mg/L at pH 7; 94,500 mg/L (9.5 percent) at pH 8. Henry’s Law constant is 5.8 x 10-12 Pa x m3 x mol-1 (20°C). Partition coefficient = log POW = 0.60 at 20°C (pH 5.42 to pH 5.71).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Foramsulfuron is classified as a not likely human carcinogen. No adverse effects were observed in any of the submitted toxicological studies regardless of the route of exposure, and there were no observed adverse effects at the highest dose tested (500 mg/kg/day or higher) in any of the subchronic or chronic toxicity tests conducted. Therefore, an exemption from the requirements of a tolerance is warranted (USEPA 2002).

There were no observed adverse effects at the highest dose tested (500 mg/kg/day or higher) in any of the subchronic or chronic toxicity tests conducted (USEPA 2002a). Consequently the USEPA established an exemption from the requirement of a tolerance for residues of foramsulfuron on corn when applied/used as a herbicide.

The lowest relevant oral NOAEL quoted by EC (2002) is 434 mg/kg/d. An ADI of 0.5 mg/kg is stated, based on development studies in rabbits; an ARfD was considered unnecessary; reaffirmed by EFSA (2012). For the derivation of the reference values, the Acceptable Daily Intake (ADI) value of 0.5 mg/kg bw per day based on the rabbit developmental study in the first peer review is changed to an ADI of 0.25 mg/kg bw per day based on the two-year rat study (UF 100); an ARfD is still unnecessary (EFSA 2016).

EC (2002) stated that foramsulfuron showed no genotoxic or carcinogenic concerns.

### Derivation of Maximum Acceptable Value

No MAV.

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# Forchlorfenuron

CAS No. 68157-60-8. The IUPAC name for forchlorfenuron is 1-(2-chloro-4-pyridyl)-3-phenylurea. The CAS name is N-(2-chloro-4-pyridinyl)-N′-phenylurea.

### Maximum Acceptable Value

Forchlorfenuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Forchlorfenuron is a phenylurea plant growth regulator or stimulator. Forchlorfenuron is a cytokinin, which improves fruit size, fruit set, cluster weight and cold storage in grapes and kiwifruit. Forchlorfenuron acts synergistically with natural auxins to promote plant cell division and lateral growth. This plant growth regulator causes an increase in berry or fruit size, including varieties not tolerant to gibberellic acid (certain grape varieties and kiwifruit). Application rates are extremely low. For grapes, lower use rates minimise harvest delay, while the higher use rates of 8 to 10 grams active ingredient (a.i.) per acre (A) maximises berry size and harvest delay. For kiwifruit, application rate ranges from 2 to 8 grams a.i./A.

Forchlorfenuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Often used on grapes and kiwifruit.

### Forms and fate in the environment

Forchlorfenuron sorbed on to soil did not degrade significantly based on the sum of extractable, bound, and water residues. The calculated half-life of 226 days in anaerobic flooded sandy loam soil was based on extractable residues. The parent compound appeared to be relatively stable in the water and soil phases from 60 to 90 days post-treatment (anaerobic incubation 30–60 days). Forchlorfenuron was essentially stable in sandy loam soil incubated in darkness at 25°C for up to 12 months. The calculated half-lifes for extractable residues were 578 days and 1659 days for the sum of extractable and bound, respectively.

Forchlorfenuron was seen to have low mobility in silt loam, sandy loam and sand, and slight mobility in clay. These values would also indicate that forchlorfenuron in waterbodies should adsorb to sediment rather than staying in the water column.

A predominant metabolite in soil and water is 4-amino-2-chloropyridine (CAS No. 14432-12-3).

Water solubility is about 40 mg/L.

### Removal methods

Water treatment processes that remove particulate matter should be effective in reducing the concentration of forchlorfenuron.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The acute RfD is based on a rabbit developmental study. The study NOAEL of >100 mg/kg/day is considered to be a conservative dose for acute dietary risk assessment. The NOAEL of 200 mg/kg/day in the rat developmental study supports the assertion that the rabbit developmental study is a conservative endpoint for risk assessment. The acute RfD = 1.0 mg/kg/day (USEPA 2004).

The chronic RfD is based on a two-year rat feeding study. The NOAEL of 7.0 mg/kg/day and an uncertainty factor (UF) of 100 are based on decreases in bodyweight/body weight gain/food consumption, as well as kidney toxicity (suppurative inflammation in males; non-suppurative interstitial nephritis in females) at the LOAEL of 93 and 122 mg/kg/day in males and females, respectively. The chronic RfD = 0.07 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.07 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for forchlorfenuron is 0.49 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for forchlorfenuron is 0.07 mg/kg body weight, with a NOEL of 7 mg/kg bw.

EC (2005) established an ADI of 0.05 mg/kg/d, and an ARfD of 1 mg/kg/d. These values were confirmed by EFSA (2012).

Carcinogenicity studies indicated no evidence of an increase in the incidence of tumours in either the rat or the mouse, and forchlorfenuron has been classified as not likely to be a human carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Formetanate

CAS No. 22259-30-9. The IUPAC name for formetanate is 3‑[(EZ)‑dimethylaminomethyleneamino]phenyl methylcarbamate. The CAS name is N,N‑dimethyl-N′-[3-[[(methylamino)carbonyl]oxy]phenyl]methanimidamide. It is generally sold as the hydrochloride, CAS No. 23422-53-9.

### Maximum Acceptable Value

Formetanate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Formetanate is a systemic [formamidine (or N-methyl carbamate) contact insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#formamidine_insecticides), miticide or acaricide, often used on fruit trees and strawberries. Its primary mode of toxic action is through cholinesterase inhibition.

Formetanate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Formetanate appears to degrade rapidly in soil under aerobic conditions; soil degradation laboratory studies suggest a D90 of <43 days (EFSA 2014). This chemical appears to leach in soil and therefore has a potential for groundwater contamination (PMEP 1983).

Formetanate HCl is not a persistent pesticide under most normal use conditions. The primary routes of dissipation appear to be hydrolysis under neutral and alkaline conditions as well as microbial degradation. Formetanate HCl hydrolyses with a half-life of <1 day. The soil photolysis half-life was <3 days. Metabolism data suggest that formetanate HCl is also readily biodegradable, with a half-life of <1 week. Formetanate HCl and degradates were shown in the laboratory to be mobile. Field studies indicate that formetanate HCl degrades rapidly and generally remains within the top six inches of soil.

Formetanate comprises two functional groups: formamidine and carbamate. The half-life of the formamidine group was determined to be 14.4 hours under mildly basic conditions (pH 7.6). The longevity of the carbamate group may exceed six months due its resistance to base-promoted degradation.

Water solubility of the hydrochloride product is extremely high, about 80 percent.

NPIC (1994) quotes for formetanate hydrochloride a soil half-life of 100 days, water solubility of 50 percent and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Formetanate does not result in developmental toxicity in either rats or rabbits or in reproductive effects in the multi-generation rat reproduction study. There was no indication of increased offspring susceptibility in these studies. Formetanate HCl is classified by the USEPA as a group “E” carcinogen (no evidence of carcinogenicity). Formetanate is potentially neurotoxic because of its ability to inhibit cholinesterase (USEPA 2006).

The chronic risk estimate (chronic reference dose, cRfD) for oral intake (food and water) is reported by USEPA (2006) to be 0.00065 mg/kg/d. USEPA (2008) quotes an acute RfD of 0.00065 mg/kg/d, and added that a chronic RfD is not applicable; data on formetanate hydrochloride indicate that the magnitude of cholinesterase inhibition (ChEI) does not increase with continued exposure because of the rapid reversibility of ChEI. Therefore, chronic exposure to formetanate hydrochloride may be considered as a series of acute exposures. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.00032 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for formetanate hydrochloride is 0.003 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for formetanate is 0.004 mg/kg body weight, with a NOEL of 0.37 mg/kg bw.

EC (2006) established an ADI of 0.004 mg/kg/d based on a one-year dog study, and an ARfD of 0.005 mg/kg/d based on rat studies. These values are confirmed in EFSA (2012 and 2014) and relate to formetanate hydrochloride.

Formetanate has a high acute toxicity. The acceptable daily intake (ADI) used in New Zealand is 0.004 mg/kg/d (NZFSA 2008).

In the available toxicity studies on formetanate HCl, there was no evidence of endocrine disruptor effects.

### Derivation of Maximum Acceptable Value

No MAV.

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# Formothion

CAS No. 2540-82-1. The IUPAC name for formothion is either S‑[formyl(methyl)carbamoylmethyl] O,O-dimethyl phosphorodithioate or 2‑dimethoxyphosphinothioylthio-N-formyl-N-methylacetamide. The CAS name is S‑[2‑(formylmethylamino)-2-oxoethyl] O,O-dimethyl phosphorodithioate. Also called O,O-dimethyl dithiophos-phorylacetic acid N-methyl-N-formylamide.

Formothion is metabolised by plants to dimethoate (qv) and omethoate (JMPR 1998).

### Maximum Acceptable Value

WHO (2004 and 2011) states that because formothion is unlikely to occur in drinking-water, a guideline value has not been derived.

### Sources to water

Formothion (an aldehyde derivative of dimethoate) is a systemic and contact organophosphate insecticide used to control spider mites, aphids, psyllids, mealy bugs, whiteflies, jassids, leaf miners, ermine moths, and fruit flies. It is used on tree fruits, vines, olives, hops, cereals, sugar cane, rice.

Formothion does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). Formothion appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Formothion is relatively non-persistent. The half-life of formothion in loamy soils is one to 14 days. There is no danger of formothion residues accumulating in soil, even if plants are subject to repeated treatment. Dimethoate (qv) is said to be a major degradate (SITEM). Dimethoxon, an oxygen analogue metabolite of dimethoate, appears to play a dominant role in its toxicity for insects and mammals. Dimethoxon itself is also used as an insecticide, known as omethoate; after use of dimethoate, formothion is found in the air the day of spraying (ICPS 1989).

Octanol-water partition coefficient at pH 7, 20°C, LogP = 1.48. Formothion has high leachability and is non-volatile.

It is very soluble in water: 700 mg/L (IPCS 1986) or 2,600 mg/L (EXTOXNET 1995).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Formothion is a cholinesterase inhibitor which means it affects normal nervous system function. Formothion is rapidly absorbed by the stomach of rats. It passes through the liver, kidney, pancreas and thymus. Most (96 percent) of a dose of formothion is excreted within 24 hours. The majority of a dose (98–99 percent) is excreted in urine and 2 percent in faeces.

Formothion is one of the least toxic systemic organophosphates. JMPR derived an ADI of 0.02 mg/kg bw in 1973; however, JMPR (1998) states there is now no ADI for formothion. EXTOXNET (1995) quotes an ADI of 0.2 mg/kg.

Studies indicate that organophosphate compounds do not have structures resembling known carcinogens. Though no data is currently available on formothion, it is unlikely that it causes cancer. No evidence of teratogenic or embryotoxic effects was seen in rabbits given formothion from days 6 to 18 of pregnancy at rates of 6 and 30 mg/kg/day (EXTOXNET 1995).

The Australian Government deleted the ADI for formothion in 2003.

### Derivation of Maximum Acceptable Value

No MAV.

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# Fosetyl aluminium

CAS No. 39148-24-8. The IUPAC and CAS names for fosetyl aluminium is aluminium tris(ethyl phosphonate). Fosetyl aluminium is a derivative of fosetyl, CAS No. 15845‑66‑6. Also called ethyl hydrogen phosphonate, aluminium salt; and aluminium tris (o-ethylphosphonate).

### Maximum Acceptable Value

Fosetyl aluminium is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Fosetyl aluminium is a systemic [organophosphorus fungicide](http://www.alanwood.net/pesticides/class_herbicides.html#organophosphorus_herbicides), used to control damping-off and rot of plant roots, stems and fruit. It is applied as a plant dip treatment and a drench for transplants, by incorporating it into the soil prior to planting, and by applying it to foliage.

Fosetyl aluminium appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

EC (2006) and JMPR (2000) state that the maximum inorganic phosphite content is 10 g/kg expressed as aluminium phosphite.

### Forms and fate in the environment

In soil fosetyl aluminium is degraded by microbial action largely to ethanol and phosphorous acid. The half-life in aerobic and anaerobic soils has been reported to be 1 to two days.

Fosetyl aluminium is highly soluble in water (about 13 percent). Since it is soluble in water, susceptible to leaching, and stable to decomposition by water, fosetyl-Al may possibly leach to groundwater through sandy or porous soils in cases where unexpected heavy rainfall closely follows foliar application of the pesticide.

EFSA (2012) stated that it is noted that the main metabolite of fosetyl, which was previously referred to as phosphorous acid in the EFSA conclusion (2005), is actually called phosphonic acid (IUPAC). The lack of information about phosphonates in the environment is linked to analytical problems of their determination at trace concentrations in natural waters. EFSA (2015) states that fosetyl-Al is expected to degrade rapidly in soil to its metabolite phosphonic acid, DT90 <1 day. Phosphonic acid may have a DT90 value in excess of one year (91 to >1,000 days in EFSA 2018) and therefore has the potential to accumulate. Photodegradation studies showed that phosphonic acid was degraded faster under illuminated conditions. The likely product of soil photolysis of phosphonic acid is phosphate.

NPIC (1994) quotes for fosetyl-aluminium a soil half-life of 0.1 days, water solubility of 12 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

USEPA (1990) considers the potential for fosetyl aluminium and its degradates to reach groundwater is low due to rapid degradation in soil. EFSA (2018) assessed the potential for groundwater exposure from the representative uses by fosetyl-Al above the parametric drinking water limit of 0.1 µg/L and was concluded to be low.

### Analytical methods

#### Referee method

No need, because no MAV.

#### Some alternative methods

See EFSA (2018).

### Health considerations

The oral RfD was calculated at 3 mg/kg/d (USEPA 1991). USEPA (2002) quotes a chronic RfD of 2.5 mg/kg/d, adding that no effects attributable to a single exposure (dose) were observed from the oral toxicity studies including developmental toxicity studies in rats and rabbits. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 2.5 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for fosetyl-Al is 17.5 mg/L (no acute one-day value available.)

Fosetyl-Al is not a mutagen and it does not pose developmental or reproductive effects of concern. A NOEL was 250 mg/kg/d was established for fosetyl aluminium based on the two-year dog study. The ADI is 3 mg/kg.

EC (2006) established an ADI of 3 mg/kg/d for fosetyl, and stated that an ARfD was unnecessary because of the low acute toxicity.

The Acceptable Daily Intake (ADI) adopted in Australia for fosetyl aluminium is 1 mg/kg body weight, with a NOEL of 103 mg/kg.

EFSA (2012) states: The toxicological profile of fosetyl was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI of 3 mg/kg bw per day and 3.9 mg/kg bw per day being set for fosetyl-Al and phosphonic acid respectively. It was concluded that fosetyl and phosphonic acid have the same mechanism of toxicity and that an ARfD was not necessary for either compound. Phosphonic acid is considered to be toxicologically relevant and its level is generally expected to be higher than that of the parent compound. This was amended in EFSA (2013, 2015): the ADI for fosetyl-Al is 3 mg/kg bw/day and an ARfD for fosetyl-Al was not set because of the low acute toxicity; an ADI for the metabolite phosphonic acid was set at 2.25 mg/kg bw per day; an ARfD was not necessary. The ADI of 2.8 mg/kg bw/d for fosetyl is calculated from the ADI of fosetyl-Al, by applying a molecular weight conversion factor of 0.93 (EFSA 2015).

The 2017 JMPR meeting established an ADI for fosetyl-Al of 0–1 mg/kg bw based on the NOAEL of 100 mg/kg bw per day for maternal and embryo/fetal toxicity from the rabbit developmental toxicity study. A safety factor of 100 was applied. The meeting concluded that it was not necessary to establish an ARfD for fosetyl-Al in view of its low acute oral toxicity and the absence of embryo/fetal toxicity and any other toxicological effects that would be likely to be elicited by a single dose. Phosphonic acid, the major metabolite, is toxicologically similar to the parent and was considered to be covered by the ADI of fosetyl-Al.

EFSA (2018) modified these values: the acceptable daily intake (ADI) and acceptable operator exposure level (AOEL) for fosetyl-Al are 1 mg/kg bw per day based on the developmental and maternal NOAELs in rabbit and applying an uncertainty factor (UF) of 100. The acute reference dose (ARfD) and the acute AOEL (AAOEL) for fosetyl-Al are 1 mg/kg bw per day based on the maternal decreased body weight gain observed at the beginning of the dosing in rabbit developmental study and applying an UF of 100. No correction for oral absorption is needed. Concerning the metabolites, the toxicological profile of phosphonic acid has been assessed through several studies testing phosphonic acid or its salts (sodium and potassium phosphonates). They have low acute toxicity and show negative results in genotoxic tests. The experts agreed that the reference values for aluminium defined by EFSA in the conclusion on aluminium ammonium sulphate (EFSA 2012a) should be kept, ie, an ADI and ARfD of 0.14 mg/kg bw (per day).

Some laboratory animal feeding studies indicate that fosetyl-Al has a slight degenerative effect on the testes of dogs and shows evidence of cancer effects (urinary bladder tumours) in male rats, when these test animals are fed high doses of the pesticide. Considering these and other available oncogenicity studies, the USEPA has classified fosetyl-Al as a category C oncogen, that is, a possible human carcinogen with limited evidence of carcinogenicity in animals.

The 2017 JMPR meeting concluded that fosetyl-Al is carcinogenic in rats but not in mice. Fosetyl-Al was tested for genotoxicity in an adequate range of in vitro and in vivo assays; no evidence of genotoxicity was found. The meeting concluded that fosetyl-Al is unlikely to be genotoxic.

EFSA (2018) states that fosetyl-Al is unlikely to be carcinogenic or genotoxic.

### Derivation of Maximum Acceptable Value

No MAV.

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# Fuberidazole

CAS No. 3878-19-1. The IUPAC name for fuberidazole is 2-(2′-furyl)benzimidazole. The CAS name is 2-(2-furanyl)-1H-benzimidazole. Also called 2-furan-2-yl-1H-benzoimidazole.

### Maximum Acceptable Value

Fuberidazole is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Fuberidazole is a contact and systemic benzimidazole fungicide. In Europe it is mainly used as a seed treatment for cereals, pre-planting.

Fuberidazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Benzimidazole fungicides include benomyl, carbendazim, fuberidazole, thiabendazole, thiophanate and thiophanate-methyl. They all generate MBC (methyl benzimidazol carbamate), either as the principal active ingredient, or as a breakdown compound formed on mixing with water. They were first introduced into New Zealand in the late 1960s (Beresford 2004).

### Forms and fate in the environment

Fuberidazole is considered hydrolytically stable under environmentally relevant pH and temperature conditions, but undergoes rapid photolysis. The half-life of fuberidazole in aerobic soil is about six days; leachability is low. The half-life of fuberidazole in water is up to 15 days. In natural sediment/water systems parent fuberidazole dissipated rapidly from water by partitioning to the sediment. 1H-benzimidazole-2-carboxylic acid is a major metabolite (SITEM); cis-oxobutenoic acid and trans-oxobutenoic acid form too (ECHA 2010).

The octanol-water partition coefficient at pH 7, 20°C, LogP = 2.71. Fuberidazole is non-volatile. Water solubility is about 70 mg/L.

### Analytical methods

#### Referee method

No need, because no MAV.

### Health considerations

The EC (2008) derived an Acceptable Daily Intake (ADI) for fuberidazole of 0.0072 mg/kg body weight (based on the NOAEL of one-year dog study with a safety factor of 100), and an ARfD of 0.08 mg/kg. These values appear in EFSA (2015) too.

Fuberidazole is not a recognised or suspect carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Furalaxyl

CAS No. 57646-30-7. The IUPAC name for furalaxyl is methyl N-(2-furoyl)-N-(2,6-xylyl)-DL-alaninate. The CAS name is methyl N-(2,6-dimethylphenyl)-N-(2-furanylcarbonyl)-DL-alaninate. Also called furalaxyl-M. Related to metalaxyl (qv).

The enantiomers are called S-furalaxyl and R-furalaxyl.

### Maximum Acceptable Value

Furalaxyl is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Furalaxyl is a systemic acylamino acid (or [furanilide or xylylalanine or acylalanine)](http://www.alanwood.net/pesticides/class_fungicides.html#furanilide_fungicides) fungicide, that inhibits protein and nucleic acid synthesis. It is often used on vegetables and ornamentals.

Furalaxyl does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)), but it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides).

Furalaxyl should not contain more than 0.5 g/kg of 2,6-dimethylaniline.

Furalaxyl is on the “List of active ingredients to be removed in July 2003 under Directive 91/414/EEC”, but with “an essential use exemption”.

### Forms and fate in the environment

The half-life of furalaxyl in soil is about seven weeks (ie, moderately persistent); S‑furalaxyl being slightly more persistent. It is reported to be quite persistent in water, but with a low potential to leach to groundwater (IUPAC). It is non-volatile. Metabolites include 2,6-dimethylaniline, which is also an impurity. The photoderivative, 2(5H)‑furanone (the main photoproduct obtained from furalaxyl) was one-fold more toxic to freshwater crustaceans than the parent compound (Isidori et al 2004).

Water solubility is about 230 mg/L. The octanol-water partition coefficient at pH 7, 20°C, LogP, is 2.7.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

Furalaxyl is rapidly absorbed after oral administration. Within 24 hours 57 to 78 percent of the dose is excreted faecally, and about 33 percent via the kidneys. A NOEL of 1.8 mg/kg/d has been quoted for dogs.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Isidori, et al. 2004. *Environmental Toxicity of Three Fungicides and their Photoderivatives on Freshwater Crustaceans*. PW215. The Society of Toxicology and Chemistry (SETAC). 25th annual meeting in North America. <http://abstracts.co.allenpress.com/pweb/setac2004/document/41847>

IUPAC. Accessed 2009. *Furalaxyl* (ref: IPE 134). <http://sitem.herts.ac.uk/aeru/iupac/366.htm>

# Furathiocarb

CAS No. 65907-30-4. The IUPAC name for furathiocarb is butyl 2,3-dihydro-2,2-dimethylbenzofuran-7-yl N,N′-dimethyl-N,N′-thiodicarbamate. The CAS name is 2,3‑dihydro-2,2-dimethyl-7-benzofuranyl 2,4-dimethyl-5-oxo-6-oxa-3-thia-2,4-diazadecanoate.

### Maximum Acceptable Value

Furathiocarb is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Furathiocarb is a systemic benzofuranyl methylcarbamate (or more simply, thiocarbamate or carbamate) insecticide, inhibiting acetylcholinesterase. It is used as a seed coating for clover in New Zealand.

Furathiocarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). It is not approved for use in the UK, Europe or the US.

### Forms and fate in the environment

Compounds based on carbofuran (eg, furathiocarb) are completely converted to carbofuran within a few days (DEFRA (2002). Carbofuranphenol (CAS No. 1563-38-8) has been found in human urine (ATSDR 2003). Carbofuran is a major metabolite (SITEM).

Water solubility is about 10 mg/L.

### Analytical methods

#### Referee method

No need, because no MAV.

### Health considerations

The Acceptable Daily Intake (ADI) adopted in Australia for furathiocarb is 0.003 mg/kg body weight, with a NOEL of 0.35 mg/kg based on a rat study.

EFSA (2014) stated that furathiocarb has never been evaluated by JMPR; EFSA established an ADI of 0.003 mg/kg bw/d and an ARfD of 0.006 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

ATSDR. 2003. *Health Consultation: Analysis of Human Exposure Pathways for Pesticide Use in Churchill County*. US Department of Health And Human Services. Agency for Toxic Substances and Disease Registry. [www.atsdr.cdc.gov/sites/fallon/fallonleukemia062503-ne-pesticide.pdf](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Word\www.atsdr.cdc.gov\sites\fallon\fallonleukemia062503-ne-pesticide.pdf)

DEFRA. 2002. *Development and Improvement of Methods for the Wildlife Incident Investigation Scheme*. Department for Environment, Food and Rural Affeirs (UK). <http://randd.defra.gov.uk/Document.aspx?Document=PS2508_1997_FRP.doc>

EFSA. 2014. Reasoned opinion on the review of the existing MRLs for carbofuran, carbosulfan, benfuracarb and furathiocarb and the setting of an import tolerance for carbofuran in cultivated mushrooms. *EFSA Journal* 12(2): 3559 [38 pp]. http://www.efsa.europa.eu/en/efsajournal/doc/3559.pdf

SITEM. Accessed January 2011. *Furathiocarb*. <http://sitem.herts.ac.uk/aeru/footprint/en/Reports/367.htm>

# Gibberellic acid

CAS No. 77-06-5. The IUPAC name for gibberellic acid is (3S,3aS,4S,4aS,7S,9aR,9bR,12S)-7,12-dihydroxy-3-methyl-6-methylene-2-oxoperhydro-4a,7-methano-9b,3-propenoazuleno[1,2-b]furan-4-carboxylic acid or (3S,3aR,4S,4aS,6S,8aR,8bR,11S)-6,11-dihydroxy-3-methyl-12-methylene-2-oxo-4a,6-ethano-3,8b-prop-1-enoperhydroindeno[1,2-b]furan-4-carboxylic acid. The CAS name is (1α,2β,4aα,4bβ,10β)-2,4a,7-trihydroxy-1-methyl-8-methylenegibb-3-ene-1,10-dicarboxylic acid 1,4a-lactone.

Most authorities consider the following compounds collectively under the term “gibberellic acids”: gibberellic acid (GA3); related isomers known as gibberellins (GA4 +GA7); and the salt of the acid, potassium gibberellate.

CAS No. 77-06-5 usually relates to the mixture of GA3, GA4 and GA7, whereas CAS No. 125-67-7 relates to potassium gibberellate. CAS No. 8030-53-3 refers to the mixture of gibberellins (GA4) and (GA7). CAS No. 468-44-0 refers to GA4. CAS No. 510-75-8 refers to GA7.

### Maximum Acceptable Value

Gibberellic acid is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Gibberellic acid is a plant growth regulator, a hormone in the family of gibberellins. Since gibberellic acid regulates growth, applications of very low concentrations can have a profound effect while too much will have the opposite effect. Gibberellins can stimulate rapid stem and root growth, induce [mitotic division](http://en.wikipedia.org/wiki/Mitotic_division) in the leaves of some plants, and increase seed germination rate. They are also widely used in the grape-growing industry as a hormone to induce the production of larger bundles and bigger grapes, especially [Thompson seedless](http://en.wikipedia.org/wiki/Sultana_(grape)) grapes.

Gibberellic acid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 11.6 tonnes were used in New Zealand in 2004, at an application rate of 2,000 grams of active ingredient per hectare. The main New Zealand use appears to be on fruit crops; also used on pasture. Trade names in New Zealand are Express and ProGibb.

### Forms and fate in the environment

Gibberellic acid is expected to be transformed rapidly to compounds other than CO2 in soil, but there is no information on what these compounds might be. Gibberellic acid exhibits very high mobility in soil. There was no indication that soil adsorption of gibberellic acid was pH dependent in the range of pH of agricultural soils (the pKa of 4.1 indicates significant dissociation would be expected across this range). Gibberellic acid was estimated to exhibit moderate persistence under the conditions of a sterile aqueous hydrolysis study. Investigations of the route and rate of degradation in microbially active natural sediment water systems were not available in the dossier evaluated.

Water solubility of gibberellic acid: about 4,600 mg/L; gibberellins about 120 mg/L.

### Analytical methods

#### Referee method

No need, because no MAV.

### Health considerations

The USEPA (1995) plans to propose to exempt from tolerance many plant regulators, including gibberellic acids, when used in low doses. This exemption will apply only when application rates do not exceed 250 grams of ai/acre/year. The Agency believes this action does not present unreasonable risks because it is based on gibberellic acid’s low acute mammalian toxicity, low use rates, naturally occurring exposure in the diet from numerous plant sources, and minimal exposure in the diet derived from consumption of treated commodities under the proposed maximum label use rate.

Two developmental toxicity studies for gibberellic acids were reviewed for this RED (USEPA 1995). In the first study, rats were dosed at 0, 100, or 1,000 mg/kg/day for eight weeks without significant chemical, haematological or pathologic evidence of toxicity. The maternal toxicity NOEL was greater than 1,000 mg/kg/day (HTD). In the second study, rabbits were dosed at 0, 300, or 1,000 mg/kg/day; the highest concentration caused increased mortality, abortion rates, clinical signs of toxicity, and gross pathological observations. The maternal and developmental NOELs were established at 300 mg/kg/day.

EC (2008) stated that there are clear indications that it may be expected that gibberellic acid and gibberellins do not have any harmful effects on human or animal health or on groundwater or any unacceptable influence on the environment.

The Acceptable Daily Intake (ADI) adopted for gibberellic acid in Australia is 5 mg/kg body weight, with a NOEL of 550 mg/kg.

Based on the available data and the toxicological profile of gibberellic acid the agreed acceptable daily intake (ADI) is 0.68 mg/kg bw/d, based on the NOAEL of 680 in the 90-day study in rats and applying a standard safety factor of 100 plus an additional safety factor of 10 because of the use of short-term toxicity and also due to a general database weakness. The setting of an acute reference dose (ARfD) is considered not justified. The weight of evidence suggests that gibberelic acid is unlikely to be genotoxic (EFSA 2012).

Based on available data and the toxicological profile of gibberellins GA4/GA7 the agreed acceptable daily intake (ADI) is 0.3 mg/kg bw/d, based on the parental NOAEL of 300 mg/kg bw/d in the multigeneration study and applying a standard uncertainty factor of 100 plus an additional uncertainty factor of 10 because of the use of short-term toxicity and also due to a general database weakness. The setting of an acute reference dose (ARfD) is considered not justified (EFSA 2012a).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2008. *Review Report for the Active Substance Gibberellic Acid*. European Commission, Health & Consumer Protection Directorate-General. *SANCO*/2613/08 – rev. 1 [7 pp]. See: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EC. 2008. *Review Report for the Active Substance Giberelline*. *SANCO*/2614/08 – rev. 1 [9 pp]. <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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EFSA. 2002a. Conclusion on the peer review of the pesticide risk assessment of the active substance gibberellins (GA4, GA7) (approved as giberelline). *EFSA Journal* 10(1): 2502 [50 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/2502.pdf>

USEPA. 1995. Gibberellic acid. *Re‑registration Eligibility Decision (RED)*. EPA 738‑R‑96‑005 [136 pp]. See: <http://www.epa.gov/pesticides/reregistration/status.htm> refer also to <http://www.epa.gov/pesticides/biopesticides/#factsheet>

# Glufosinate-ammonium

CAS No. 77182-82-2. The IUPAC name for glufosinate-ammonium is ammonium (2RS)‑2-amino-4-(methylphosphinato)butyric acid. The CAS name is 2-amino-4-(hydroxymethylphosphinyl)butanoic acid monoammonium salt. Is also known as DL‑phosphinothricin.

Glufosinate ammonium is a racemic mixture of the D- and L-isomers of the ammonium salt of ammonium-DL-homoalanin-4-yl(methyl)phosphinate or ammonium-(3-amino-3-carboxypropyl) methyl phosphinate. JMPR (2012).

### Maximum Acceptable Value

Glufosinate-ammonium is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Glufosinate-ammonium is an [organophosphorus herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#organophosphorus_herbicides), and is a broad-spectrum contact herbicide which is used to control a wide range of weeds after the crop emerges or for total vegetation control on land not used for cultivation. Glufosinate herbicides are also used to desiccate (dry off) crops before harvest. It is also a component in human hygiene biocidal products. Glufosinate is a natural compound isolated from two species of Streptomyces fungi. It inhibits the activity of an enzyme, glutamine synthetase, which is necessary for the production of glutamine and for ammonia detoxification. The application of glufosinate leads to reduced glutamine and increased ammonia levels in the plant tissues. This causes photosynthesis to stop and the plant dies within a few days. Glufosinate also inhibits the same enzyme in animals.

Glufosinate-ammonium appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 11.6 tonnes were used in New Zealand in 2004, at an application rate of 2,000 grams of active ingredient per hectare. The main New Zealand use appears to be on fruit crops.

### Forms and fate in the environment

In soil glufosinate-ammonium is degraded by microbial action to 3‑methylphosphinicopropionic acid (MPP) and 2-methylphosphinicoacetic acid (MPA), and eventually to carbon dioxide under dark aerobic conditions. See JMPR (1999 and 2012) for a discussion on metabolites.

Glufosinate has been found in Canadian soils after 113 days; and in greenhouse soils after 172 days. The half-life in Californian vineyard soils has been reported as 12 to 70 days, with an average of 40 days. Other reported half-lifes vary from 3 to 20 days, with degradation occurring more rapidly at higher temperatures.

DT90 values of glufosinate range between 19–35 days which is far below the trigger value of 100 days. However, DT50 values of its relevant soil metabolites MPP and MPA range between 6–50 days (EFSA, 2005). Assuming a first order decline of residues in soil, this would correspond to DT90 values that are approximately 3.32 times higher, hereby significantly exceeding the trigger values of 100 days. According to the European guidelines on rotational crops (EC 1997b), further investigation of residues in rotational crops is therefore relevant.

Glufosinate is highly soluble in water (over 100 percent), and is also classified as persistent and mobile. Degradation of glufosinate is largely by microbial activity. The half-life has been determined in numerous laboratory studies and varies from 3 to 42 days in some studies and up to 70 days in others.

NPIC (1994) quotes for glufosinate ammonium a soil half-life of seven days, water solubility of 137 percent and a sorption coefficient (soil Koc) of 100. This resulted in a pesticide movement to groundwater rating of low.

Henry’s Law constant = 4.48 × 10-9 Pa m3/mole; water solubility at pH 5.4, 7 and 8.9: >500 g/L (>50 percent) at 20°C; partition coefficient (n-octanol/water) = log Pow at pH 5, 7, 9: –3.77, –4.01, –4.07 respectively; hydrolysis half-life in sterile water at 25°C and pH 5, 7 and 9: >300 days; photolysis: stable under abiotic conditions, at pH5, 7, 9 (JMPR 2012).

### Analytical methods

#### Referee method

No need, because no MAV.

#### Some alternative methods

See JMPR (2012).

### Health considerations

Low doses of glufosinate have been found to affect central nervous system development in young rats. Sub-lethal doses of glufosinate ammonium were found to cause abnormalities in the development of embryos in mammals both in vitro and in vivo. Commercial formulations are more toxic to humans and the aquatic environment than the active ingredient alone, but little information is publicly available on the inert, or adjuvant, ingredients in the formulated products.

The surfactant, AES (sodium polyoxyethylene alkyl ether sulphate), which is used in formulations, has also been found to cause toxic effects and may be a cause of some of the clinical symptoms observed in suicide cases involving glufosinate. The metabolite, MPPA-3, is, like glufosinate, a neurotoxin. 1-Methoxy-2-propanol is also present in some products. The USEPA reported that MPPA-3 injected into the brain of rats caused severe convulsions.

JMPR (1999) established an ADI of 0.02 mg/k/d for glufosinate-ammonium, N‑acetylglufosinate and 3-[hydroxy(methyl)phosphinoyl]propionic acid (alone or in combination). The meeting also concluded that an acute RfD for glufosinate-ammonium is unnecessary, based on a determination that the pesticide is unlikely to present an acute toxicological hazard and residues are therefore unlikely to present an acute risk to consumers. The WHO Panel of the 2012 JMPR established an Acceptable Daily Intake (ADI) of 0–0.01 mg/kg bw for glufosinate and established an Acute Reference Dose (ARfD) of 0.01 mg/kg bw (JMPR 2012 and 2014; FAO/WHO 2013).

The USEPA (1992) developed a RfD of 0.0004 mg/kg/d using a NOEL of 0.4 mg/kg/d which was based on increased absolute and relative kidney weights in male rats in a 13‑week feeding study. An uncertainty factor of 100 was used to account for intra- and interspecies differences in sensitivity. An additional factor of 10 was used because the study was only of 90 days duration. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.006 mg/kg/d, and an ARfD of 0.063 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for glufosinate-ammonium is 2.08 mg/L.

In 1992 the WHO/FAO recommended acceptable daily intake (ADI) for glufosinate is 0.02 mg/kg. The ADI set by the European Food Safety Authority = 0.021 mg/kg bw/day, based on the NOEL (no observed effects levels) of 6.3 mg/kg bw/day in rabbits. EFSA (2012) quote the same value but called it a NOAEL (no observed adverse effects level).

EC (2007) established an ADI and ARfD of 0.021 mg/kg/d. These values were affirmed by EFSA (2015). Both toxicological reference values apply to glufosinate ammonium and glufosinate.

The Acceptable Daily Intake (ADI) adopted in Australia for glufosinate ammonium is 0.02 mg/kg body weight, with a NOEL of 2.1 mg/kg, and the ADI for glufosinate is 0.007 mg/kg body weight, with a NOEL of 0.67 mg/kg. An ARfD for glufosinate ammonium was considered unnecessary.

FAO/WHO (2012) established an estimate of acceptable daily intake for humans of  
0–0.01 mg/kg bw (ADI for glufosinate-ammonium, also applies to NAG, MPP and MPA); and an estimate of acute reference dose of 0.01 mg/kg bw (ARfD for glufosinate-ammonium, again also applies to NAG, MPP and MPA).

Glufosinate-ammonium is not carcinogenic in mice or rats and no evidence for genotoxicity was observed in any test (FAO/WHO 2013).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Glyphosate

Glyphosate CAS No. 1071-83-6. The IUPAC and CAS name for glyphosate (which is the acidic form) is N-(phosphonomethyl)glycine. A common trade name is Roundup.

Some other glyphosate products are marketed as the:

* monoammonium salt (CAS No. 40465-66-5)
* diammonium salt (CAS No. 69254-40-6)
* dimethylamine (CAS No. 34494-04-7)
* isopropylamine (CAS No. 38641-94-0) – the commonest product
* potassium salt (CAS No. 39600-42-5)
* monosodium salt (CAS No. 34494-03-6)
* sesquisodium salt (CAS No. 70393-85-0)
* trimesium salt (CAS No. 81591-81-3)

The impurity and metabolite aminomethyl phosphonic acid (AMPA) CAS No. 1066-51-9 is covered in this datasheet as well. Glyphosate usually contains a surfactant or wetting agent.

Another impurity is N-nitro-glyphosate (which belongs to a group of impurities of particular concern as they can be activated to genotoxic carcinogens) (EFSA 2015).

Note: The glyphosate tolerant crops with the gat trait have been inserted with a glyphosate N-acetyltransferase gene which inactivates glyphosate by converting it to N-cetylglyphosate, making it the main metabolite in plant commodities (JMPR (2013).

### Maximum Acceptable Value

WHO (2005/2011/2017) states that because glyphosate occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

WHO (2017) developed a health-based value of 0.9 mg/L for AMPA alone or in combination with glyphosate. Other impurities can include formaldehyde (maximum, 1.3 g/kg), N-nitrosoglyphosate (maximum, 1 mg/kg), and N-nitroso-N-phosphonomethylglycine. Surfactants and sulfuric and phosphoric acids may be added to formulations of glyphosate, with type and concentration differing by formulation.

The maximum contaminant level or MCL (USEPA 2004/2009/2011) is 0.7 mg/L.

The maximum acceptable concentration for glyphosate in Canada is 0.28 mg/L.

The Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency (2007) has a public health goal of 0.9 mg/L based on an updated exposure calculation for adult females, on whom the PHG value is based.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 1 mg/L; excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for glyphosate in water (set by an approval under Part 5 of the HSNO Act) of 0.37 mg/L (370 µg/L).

### Sources to water

Glyphosate is a broad-spectrum non-selective post-emergence N-(phosphonomethyl) glycine (an aminophosphonic amine) systemic herbicide used in both agriculture and forestry, and for aquatic weed control. It is approved for use in the UK (MAFF 1985) for control of emergent and bankside plants including trees, and for some floating leaved plants; the maximum permitted water concentration is 0.2 mg/L. By weight, it is the third most heavily used pesticide in the UK as at 2012. When used in smaller quantities, glyphosate can act as a plant growth regulator.

Glyphosate is usually formulated as an isopropylamine salt. A common trade name in New Zealand is Roundup (the isopropylammonium form). Glyphosate can enter surface and subsurface waters after direct use near aquatic environments or by run-off or leaching from terrestrial applications. Glyphosate isopropylamine should be applied to actively growing target plants and is effective against emergent and marginal plants and trees such as willows (Auckland City 2013). It is also used to control pampas grass.

Glyphosate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 344.3 tonnes of glyphosate were used in New Zealand in 2004, at an application rate of 7,200 grams of active ingredient per hectare. The degradation product aminomethyl phosphonic acid (AMPA) has no commercial use. Glyphosate should not contain more than 28 g/kg of N-methylglyphosate, 17 g/kg of aminomethylphosphonic acid (AMPA), 12 g/kg of hydroxymethylphosphonic acid, 10 g/kg of (phosphonomethylimino)di(acetic acid), and 1 mg/kg of N‑nitrosoglyphosate. Technical glyphosate may contain up to 1.3 g/kg formaldehyde.

In a survey conducted in 1988–1989 in the Netherlands, surface water contained 0.0005–0.001 mg of glyphosate per litre and 0.006 mg of the metabolite AMPA per litre, and up to 1.7 mg/L of glyphosate has been found in ponds in the US, usually due to poor application practices.

### Forms and fate in the environment

If released to water, glyphosate is expected to adsorb to suspended solids and sediment in the water column based upon the Koc values. Volatilisation from water surfaces is not expected to be an important fate process.

In Canada, direct spraying of glyphosate on lakes and ponds at 1 kg/ha resulted in an initial concentration of 1.10 mg/L, dropping to 0.15 mg/L at two days and 0.055 mg/L after five days. After forestry operations, glyphosate concentrations in water declined to a few μg/litre or to non-detectable levels hours or days post-treatment, depending on the extent of vegetation present. A half-life in water of <24 hours is often used. The concentration of AMPA in water without substantial vegetation was about 0.003 mg/L.

Microbial biodegradation of glyphosate occurs in soil, aquatic sediment and water, the major metabolite being AMPA, whose chemical structure is very similar to that of glyphosate. Glyphosate is chemically stable in water and is not subject to photochemical degradation; the median half-life of glyphosate in water varies from a few days to 91 days depending on soil conditions. The low mobility of glyphosate in soil indicates minimal potential for the contamination of groundwater. Water solubility of pure glyphosate is quite high: about 12,000 mg/L (1.2 percent), or about 100 percent for the trimesium salt. Solubility will increase with pH and be dependant upon ionic strength.

Glyphosate is highly adsorbed on most soils, especially those with high organic content. The compound is so strongly attracted to the soil that little is expected to leach from the applied area. The median half-life of glyphosate in soil has been widely studied; values between 2 and 197 days have been reported in the literature. A typical field half-life of 47 days has been suggested (NPIC). Microbes are primarily responsible for the breakdown of the product, and of AMPA. The time it takes for half of the product to break down ranges from 1 to 174 days. Because glyphosate is bound so tightly to the soil, little is transferred by rain or irrigation water. One estimate showed less than two percent of the applied chemical was lost to run-off. The herbicide could move when attached to soil particles in erosion run-off. Photodecomposition plays only a minor role in environmental breakdown. Glyphosate that enters water is stable.

If released to soil, glyphosate is expected to have slight mobility, based on Koc values in the range of 2,600 to 4,900. Volatilisation from moist soil surfaces is not expected to be an important fate process because glyphosate exists as a zwitterion (dipolar ion) at environmental pH (5–9) and ionic species do not volatilise. Volatilisation from dry soil surfaces is not expected to be an important environmental fate process based on the vapour pressure. The biodegradation half-lifes of glyphosate in a sandy loam and silt loam soil were 1.85 and 2.06 days, respectively under laboratory controlled (25°C) aerobic conditions. In 8 field studies in which glyphosate was applied at maximum usage rates to bare ground plots, the median dissipation half-time (DT50) was 13.9 days. If released to water, glyphosate is expected to adsorb to suspended solids and sediment in the water column based upon the Koc values. Volatilisation from water surfaces is not expected to be an important fate process because ionic compounds do not volatilise. The aerobic and anaerobic biodegradation half-lifes of glyphosate in a flooded silty clay loam sediment was 7 and 8.1 days, respectively. Glyphosate was stable to hydrolysis at pH 5, 7, and 9 at 5 to 35°C. According to a classification scheme, BCF values of 0.2 to 0.63 measured in fish, suggest bioconcentration in aquatic organisms is low. EAWAG. Accessed February 2015. However, EFSA (2015) states that glyphosate exhibits high to very high persistence under anaerobic conditions (DT50 anaerobic = 135–>1,000 d). The same major metabolite AMPA, as identified under aerobic conditions, was also formed under anaerobic conditions.

EFSA (2015) states that glyphosate is not readily biodegradable according the available OECD studies. Degradation and dissipation of glyphosate in the aquatic environment under aerobic conditions was investigated in eight water/sediment systems. Glyphosate partitioned in the sediment to a substantial extent (maximum 61.4 percent AR after 14 days). The persistence of glyphosate in these systems was relatively variable going from moderate to high persistence (DT50 whole system (SFO) = 13.82 days to >301 days). Two major metabolites were found in the water phase: AMPA (maximum 15.7 percent AR after 14 days) and HMPA (maximum 10.0 percent AR after 61 days).

For glyphosate (in the acid form): Octanol-Water Partition Coefficient (log Kow): <2 (but note: EFSA 2005 says -3.2). Henry’s constant: 4.1 x 10-19 atm·m3/mol (EFSA 2015 says 2.1 x 10-7 Pa.m3 per mol at 25°C). Soil Sorption Coefficient (Koc): 300 to 20,000. Water solubility 1.16 percent (ie, 11,600 mg/L). The alkali-metal and amine salts are readily soluble in water.

The vapour pressure of glyphosate is negligible (1.3 x 10-2 mm Hg at 25°C) suggesting little volatilisation from soil is expected. The low Henry’s Law constant (<2 x 10-7 Pa m3 per mol) suggests little volatilisation from water surfaces is expected. The octanol-water partition coefficient (log Kow or log P) is <-3.2. Glyphosate is stable to hydrolysis (pH 3 to 9) and relatively stable to photodegradation. From IARC (2015).

NPIC (1994) quotes for glyphosate isopropylamine a soil half-life of 47 days, water solubility of 90 percent and a sorption coefficient (soil Koc) of 24,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

Intensive monitoring studies over a number of years in Denmark have identified glyphosate and AMPA in the root zone and in groundwater at monitoring sites; however, the concentrations in groundwater were less than 0.0001 mg/L.

Twelve water utilities in the US reported detecting glyphosate in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.095 mg/L.

USEPA (2002) states glyphosate monitoring data of both surface water and groundwater sources for 7,800 PWSs has been conducted. Occurrences of detectable levels of glyphosate in groundwater or surface water were very infrequent. All detections of glyphosate were below 10 percent of the Maximum Contaminant Level (MCL), which is the health-based maximum permissible level of a contaminant in water that is delivered to any user of a PWS. Only 0.1 percent of the PWSs reported any detection of glyphosate at a level above 1 percent of the MCL.

### Removal methods

Being strongly adsorbed to soil suggests many water physical treatment processes such as chemical coagulation processes, may reduce the concentration of glyphosate in the water; activated carbon should enhance this removal.

Oxidants used in water treatment, particularly Cl2 and O3, are highly effective in degrading glyphosate and AMPA. UV treatment is ineffective for glyphosate and AMPA degradation but the combination of UV/H2O2 provided significant degradation of glyphosate, but not AMPA, under the conditions investigated. Removal or degradation by bank filtration, slow sand filtration, ClO2 and membranes is variable but can provide significant removal under the right conditions (Jönsson et al 2013).

### Analytical methods

#### Referee method

No need, because no MAV.

#### Some alternative methods

Various analytical methods for the determination of glyphosate have been described, including thin-layer chromatography, high-performance liquid chromatography and gas chromatography–mass spectrometry. The limits of determination were  
0.00002–0.05 mg/L in water. The limit of determination of AMPA in water is reported to be 0.0012 mg/L (IPCS 1994). See also IARC (2017).

### Health considerations

Glyphosate and AMPA have similar toxicological profiles, and both are considered to exhibit low toxicity. While it can be described as an organophosphorus compound, glyphosate is not an organophosphate ester but a phosphanoglycine, and it does not inhibit cholinesterase activity (WHO 2017).

Glyphosate is absorbed poorly from the digestive tract and is excreted largely unchanged by mammals. Ten days after treatment there were only minute amounts in the tissues of rats fed glyphosate for three weeks.

Subchronic and chronic tests with glyphosate have been conducted with rats, dogs, mice, and rabbits in studies lasting from 21 days to two years. With few exceptions there were no treatment-related gross (easily observable) or cellular changes. In a chronic feeding study with rats, no toxic effects were observed in rats given doses as high as 31 mg/kg/day, the highest dose tested. No toxic effects were observed in a chronic feeding study with dogs fed up to 500 mg/kg/day, the highest dose tested. Mice fed glyphosate for 90 days exhibited reduced body weight gains. The lifetime administration of very high amounts of glyphosate produced only a slight reduction of body weight and some microscopic liver and kidney changes. Blood chemistry, cellular components, and organ function were not affected even at the highest doses.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.3 mg/kg body weight, with a NOEL of 30 mg/kg bw from a long-term (three-generation reproduction) study. This NOEL is based on no adverse effects observed at the highest dose in rats. The ADI incorporates a safety factor of 100. In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EC (2002) established an ADI for glyphosate of 0.3 mg/kg/d; an ARfD was considered unnecessary; reaffirmed in EFSA (2013). EC (2002) established an ADI for glyphosate trimesium of 0.2 mg/kg/d, and an ARfD of 0.25 mg/kg.

The reference dose or RfD (USEPA 2006/2009/2011) is 2 mg/kg/d (rounded from 1.75). The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 70 mg/L. The oral RfD had previously been 0.1 mg/kg/d (USEPA 1990). The USEPA has set a One-Day Health Advisory of 20 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.25 mg/kg/d, and an ARfD of 1.0 mg/kg/d for glyphosate-trimesium. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for sulfosate (glyphosate-trimesium) is 10 mg/L.

AMPA is considered to be of no greater toxicological concern than its parent compound. JMPR (1997) quotes an ADI of 0–0.3 mg/kg bw for aminomethylphosphonic acid. The 2004 meeting (JMPR 2005) concluded that the metabolite AMPA is of no greater toxicological concern than the parent glyphosate and established an ADI for the sum of glyphosate and AMPA of 0–1 mg/kg bw. The same meeting considered an ARfD unnecessary.

USEPA (2002) states: most toxicology studies are conducted using glyphosate alone, not the formulations that are in commercial products, which contain so-called inert ingredients. Roundup, which contains glyphosate and the surfactant POEA, is three times as acutely toxic to rats as glyphosate alone. This deficiency in regulation needs to be corrected. Subchronic and chronic studies also reflect toxicity from glyphosate, and commercial products are more toxic than just glyphosate. This action establishes a tolerance for glyphosate, not the inert polyethylated tallow amines (POEA). The developmental toxicity of the surfactant POEA has been evaluated and found not to be a teratogen or a developmental toxicant in rats. Subchronic toxicity studies with the surfactant and/or Roundup herbicide have also been conducted in rats, rabbits, and dogs. In these studies, gross and microscopic pathology examinations were conducted on several reproductive tissues including ovaries, uterus, testes, and epididymis. No developmental effects or changes in reproductive tissues were found in any of these evaluations. There is no evidence that the surfactant or Roundup herbicide adversely impacts reproductive function. The Agency has concluded that the use of glyphosate and glyphosate products do not pose unreasonable risks or adverse effects to humans.

The FAO/WHO 2011 meeting concluded that the group ADI of 0–1 mg/kg bw established by the 2004 JMPR for glyphosate and AMPA may also be applied to N‑acetyl-glyphosate and N-acetyl-AMPA, as the available toxicological data showed that these plant metabolites have no greater toxicity than the parent glyphosate.

The 2004 JMPR decided that an ARfD for glyphosate was unnecessary. The present Meeting confirmed that it is not necessary to establish an ARfD for N-acetyl-glyphosate or N-acetyl-AMPA in view of their low acute toxicity and the absence of any toxicological effects that would be likely to be elicited by a single dose. JMPR (2013/2016) reaffirms these values.

EFSA (2015) quotes an ADI of 0.5 mg/kg bw/d and ARfD of 0.5 mg/kg bw for glyphosate.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for glyphosate since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

Glyphosate was consistently without mutagenic effect in a range of genotoxicity assays in vitro and in vivo. As at September 2008 the USEPA has classified glyphosate in Group E: evidence of non-carcinogenicity for humans.

JMPR (2016) states that in view of the absence of carcinogenic potential in rodents at human-relevant doses and the absence of genotoxicity by the oral route in mammals, and considering the epidemiological evidence from occupational exposures, the meeting concluded that glyphosate is unlikely to pose a carcinogenic risk to humans via exposure from the diet.

IARC (2017) reports that there is limited evidence in humans for the carcinogenicity of glyphosate. A positive association has been observed for non-Hodgkin lymphoma. There is sufficient evidence in experimental animals for the carcinogenicity of glyphosate. Their overall evaluation is that glyphosate is probably carcinogenic to humans (Group 2A).

EFSA (2017) reports: Glyphosate effects on reproductive parameters were observed in some ecotoxicology studies. However, these effects were not consistently observed and no indication was found that the effects are related to an androgenic, estrogenic, steroidogenic or thyroidal mode of action. No evidence was found in the available ecotoxicology studies which would contradict the conclusion of mammalian toxicology that there is no evidence of endocrine mode of action of glyphosate. All the experts agreed that the weight of evidence indicates that glyphosate does not have EATS-mediated endocrine disrupting properties.

### Derivation of Maximum Acceptable Value

No MAV.

WHO (2005/2011/2017) states that a health-based value of 0.9 mg/L could be derived (1 mg/L for 70 kg body weight), based on the group ADI for AMPA alone, or in combination with glyphosate of 0.3 mg/kg of body weight, based upon a NOAEL of 32 mg/kg of body weight per day, the highest dose tested, identified in a 26-month study of toxicity in rats fed technical-grade glyphosate and using an uncertainty factor of 100 (for interspecies and intraspecies variation) and allocating 10 percent of the ADI to drinking-water.

Because of their low toxicity, the health-based value derived for AMPA alone, or in combination with glyphosate, is orders of magnitude higher than concentrations of glyphosate or AMPA normally found in drinking-water. Under usual conditions, therefore, the presence of glyphosate and AMPA in drinking-water does not represent a hazard to human health. For this reason, the establishment of a guideline value for glyphosate and AMPA is not deemed necessary. Because of its sorption to particulate matter and its microbial degradation in the aquatic environment, the major source of exposure to glyphosate is expected to be food.

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# Guazatine

CAS No. 108173-90-6, or 115044-19-4 for guazatine acetates; 19010-48-1 and 79956‑56-2 seem to be used as well. There is no IUPAC or CAS name because the commercial product is a mixture of chemicals. IUPAC describes guazatine as “a mixture of the reaction products from polyamines, comprising mainly octamethylenediamine, iminodi(octamethylene)diamine, octamethylenebis(imino-octamethylene)diamine, and carbamonitrile”. The ISO common name [iminoctadine](http://www.alanwood.net/pesticides/iminoctadine.html) has been given to the pure compound. The name “guanoctine” was formerly approved by the British Standards Institution. The acetate product has also been called GTA. EFSA (2010) discusses the components identified as NGN, GNN, GGN, GNNG, GGGN and GGGG.

### Maximum Acceptable Value

Guazatine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for guazatine in fresh water (set by an approval under Part 5 of the HSNO Act) of 0.00013 mg/L (0.13 µg/L).

### Sources to water

Guazatine is a aliphatic nitrogen fungicide and bird repellent. Guazatine is a non-systemic contact guanidine fungicide which disturbs the membrane function of fungi, decreasing the cellular permeability. Guazatine controls a wide range of seed-borne diseases of cereals. It is used on citrus fruits as a bulk dip after harvest, in the packing line as a spray and in washing installations to disinfect the process water. It seems to be used on timber in New Zealand.

Guazatine is a mixture of products resulting from the amidination of technical iminodi(octamethylene)diamine, containing numerous guanidines and polyamines. Diamine derivatives account for 40 percent of the constituents, triamines for 46 percent, tetramines for 11 percent and other amine derivatives for 3 percent. The most abundant individual components are the fully guanidated triamine (30.6 percent) and the fully guanidated diamine (29.5 percent) followed by the monoguanidated diamine (9.8 percent) and a diguanidated triamine.

Guazatine does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, guazatine is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …).

The technical material used in plant protection product comprises ca. 70 percent w/w of guazatine acetates in water.

The use of guazatine is no longer authorised within the EU (EFSA 2013).

### Forms and fate in the environment

Half-lifes of the components of guazatine have been calculated as 62 days in loamy sand, 104 days in clay loam, 106 days in loamy sand with low organic matter, and 176 days in sandy loam. In leaching trials, after the equivalent of 50 cm of rain the guazatine components were still associated with the seeds or the soil surrounding them.

Guanoctine (CAS No. 3658-25-1) and iminoctadine (CSA No. 13516-27-3) are breakdown products, and are also used as a fungicide in some countries (not New Zealand). EFSA (2014) includes a list of components and metabolites with related structural formulae.

Solubility in water is very high.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

Such a complex mixture as guazatine presents a problem in choosing a residue analytical method. It is not practical to attempt analysis for all the components so some alternative is necessary; see FAO (1997).

### Health considerations

Studies on rats and lactating cows showed poor absorption from the gastrointestinal tract, rapid elimination mainly in the faeces (>90 percent), excretion largely as the unchanged parent mixture and no accumulation in any organs, tissues or milk.

Guazatine was first evaluated by the Joint Meeting (JMPR) in 1978, when an ADI of  
0–0.03 mg/kg bw was established on the basis of an NOAEL of 200 ppm (equivalent to 3 mg/kg bw per day) in a two-year dietary study in dogs. The 1997 meeting concluded that it could not establish an ADI for guazatine owing to the inadequate information on its composition and concerns about the production of rare malignant tumours in mice. The dog appears to be the most sensitive animal; the level causing no toxic effect being equal to 0.8 mg/kg bw per day (one-year study of toxicity). The ADI is now considered to be a guideline value.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.006 mg/kg body weight, with a NOEL of 0.625 mg/kg bw.

<http://ec.europa.eu/sanco_pesticides/public/index.cfm> quotes an ADI of 0.0048 mg/kg/d and an ARfD of 0.04 mg/kg, referring to an EFSA source. EFSA (2013 and 2014) confirms these values, being for guazatine acetates which is the variant used in plant protection products.

The meeting (JMPR) concluded that guazatine is not genotoxic (FAO 1998), and was not carcinogenic in two two-year studies in rats given up to 350 ppm (16.3 mg/kg/d bw).

### Derivation of Maximum Acceptable Value

No MAV.

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# Halauxifen-methyl

CAS No. 943831-98-9. The IUPAC name is methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)pyridine-2-carboxylate, or methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)picolinate. The CAS name is methyl 4-amino-3-chloro-6-(4-chloro-2-fluoro-3-methoxyphenyl)-2-pyridinecarboxylate. This substance is a derivative of [halauxifen](http://www.alanwood.net/pesticides/halauxifen.html) [943832-60-8].

### Maximum Acceptable Value

Halauxifen-methyl does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Halauxifen-methyl, a ([picolinic acid](http://www.alanwood.net/pesticides/class_herbicides.html#picolinic_acid_herbicides) or [pyridine herbicide)](http://www.alanwood.net/pesticides/class_herbicides.html#pyridine_herbicides), is usually used as a wettable granule herbicide containing 200 g/kg halauxifen-methyl and 200 g/kg florasulam (qv) for the control of broadleaf weeds in cereals.

As at June 2015, neither product appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM), but they are in the process of applying.

### Forms and fate in the environment

In soil laboratory incubations under aerobic conditions in the dark, halauxifen-methyl exhibited low persistence, forming the major metabolite (halauxifen) which exhibited low to moderate persistence.

In an aqueous photolysis study in both sterile pH 7 buffer and natural water, halauxifen-methyl degraded extremely quickly under irradiated conditions with complete disappearance of the a.s. within one hour after the start of the study in both water systems. Over the whole of the study, four separate metabolites were found to exceed 10 percent AR in individual replicates: halauxifen (X11393729) accounting for 10.7 percent AR, Deg 10 accounting for 12.6 percent AR; Deg 11 accounting for 15.7 percent AR and Deg 14 accounting for 11.5 percent AR.

The water/octanol partitioning coefficient for halauxifen-methyl is 3.76 at pH 7. Solubility in water is about 1.7 mg/L; Henry’s Law constant is about 1.22 × 10-6 Pa m3/mol – both over a range of pH.

Halauxifen-methyl is not considered persistent (DT50 of 1.74 days in soil, four days in water in aerobic conditions) or bioaccumulative. (EPA 2018).

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2014).

### Health considerations

In toxicokinetics studies, halauxifen-methyl was extensively and rapidly absorbed. Oral absorption was estimated to be greater than 80 percent. There was no evidence for accumulation. Excretion of halauxifen-methyl was predominantly through urine and faeces.

The relevant short-term oral NOAEL (no observed adverse effect level) is 10 mg/kg bw per day (28- and 90-day rat studies) for halauxifen-methyl and 11 mg/kg bw per day for X11393729 (halauxifen) (28-day dog study).

Based on available genotoxicity studies halauxifen-methyl and X11393729 (halauxifen), are unlikely to be genotoxic. Halauxifen-methyl is unlikely to be carcinogenic up to dose level of 10 mg/kg bw per day. Maternal toxicity in rabbits treated with halauxifen-methyl included liver toxicity for which a NOAEL of 5.78 mg/kg bw per day was identified.

APVMA adopted an ADI of 0.1 mg/kg/d for Australia (<https://apvma.gov.au/>).

The agreed acceptable daily intake (ADI) is 0.058 mg/kg bw per day, on the basis of the relevant maternal NOAEL of 5.8 mg/kg bw found in the developmental study in rabbits on halauxifen-methyl, based on liver toxicity effects at 18.5 mg/kg bw per day. An uncertainty factor of 100 was applied (EFSA 2014).

Mechanistic data indicated that liver toxicity effects are produced during the initial exposure period and rabbits showed to be more sensitive than the rat to liver effects. Therefore, the experts agreed to set the acute reference dose (ARfD) of 0.058 mg/kg based on the maternal NOAEL of 5.8 mg/kg bw in the developmental study in rabbits on halauxifen-methyl. An uncertainty factor of 100 was applied (EFSA 2014).

New Zealand’s EPA set an ARfD for halauxifen-methyl at 0.058 mg/kg bw/day.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EFSA. 2014. Conclusion on the peer review of the pesticide risk assessment of the active substance halauxifen-methyl (XDE-729 methyl). *EFSA Journal* 12(12): 3913 [93 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/3913.pdf>

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# Halosulfuron-methyl

CAS No. 100784-20-1. The IUPAC name for halosulfuron-methyl is methyl 3-chloro-5-(4,6-dimethoxypyrimidin-2-ylcarbamoylsulfamoyl)-1-methylpyrazole-4-carboxylate. The CAS name is methyl 3-chloro-5-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-1-methyl-1H-pyrazole-4-carboxylate.

Also called methyl 5-[((4,6-dimethoxy-2-pyrimidinyl)amino)carbonylaminosulfonyl]-3-chloro-1-methyl-1H-pyrazole-4-carboxylate.

This substance is a derivative of [halosulfuron](http://www.alanwood.net/pesticides/halosulfuron.html): CAS No. 135397-30-7.

### Maximum Acceptable Value

Halosulfuron-methyl does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Halosulfuron-methyl is a pyrazole (or [pyrimidinylsulfonylurea) herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#pyrimidinylsulfonylurea_herbicides). Halosulfuron-methyl is a systemic selective herbicide used at low dosage for pre- and post-emergence control of sedges and other weeds in turf and cereals.

Halosulfuron-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of halosulfuron-methyl in soils is 55 days. Halosulfuron is a breakdown product.

When applied pre-emergence, or to the paddy water, unchanged halosulfuron-methyl was either not detected or was recovered in extremely low amounts. The metabolites chlorosulfonamide and chlorosulfonamide acid have been detected in paddy water, plants and groundwater. Aminopyrimidine is a minor metabolite (EFSA 2012).

Halosulfuron-methyl solubility in water is about 15 mg/L at pH 5, and 1,600 mg/L at pH 7. Halosulfuron-methyl is not stable in water at pH 9. Henry’s Law constant for halosulfuron is 3.5 x 10-6 Pa m3 mol-1. The partition coefficient for halosulfuron-methyl is log POW = -0.0186 at 22.8°C and pH = 7. The hydrolysis rate (half-life) for halosulfuron-methyl in water is 14.4 days at pH 7 (EFSA 2012).

### Typical concentrations in drinking-water

Halosulfuron-methyl has high potential to leach into surface water and groundwater when applied to normal to basic soils (greater than pH 7). However, at the low dosage used, there should be no problem in groundwaters.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The dog is the most sensitive mammalian species where decreased body weight was seen in the chronic oral toxicity study and decreased body weight gain was observed in females in the subchronic oral toxicity study. Halosulfuron-methyl is classified as “not likely to be carcinogenic to humans” based on a lack of evidence for carcinogenicity in mice and rats following long-term dietary administration. Halosulfuron-methyl is negative for mutagenicity in a battery of mutagenicity studies. There is no evidence of immunotoxicity or neurotoxicity in the available studies for halosulfuron-methyl (USEPA 2009).

The USEPA Office of Pesticide Programs previously established a chronic reference dose (RfD) for halosulfuron-methyl of 0.1 mg/kg/d bw based on a no-observed-effect level (NOEL) of 10 mg/kg/day in a one-year dog feeding study and an uncertainty factor of 100. More recently (USEPA 2002), they revised the chronic RfD to 0.03 mg/kg/day based on the same NOEL (10 mg/kg/day) and an uncertainty factor of 300. The uncertainty factor was increased from 100 to 300 because of concern for lack of a developmental neurotoxicity study on halosulfuron-methyl. The acute RfD was set at 0.17 mg/kg/d. Neither RfD has yet been adopted by the USEPA’s *Integrated Risk Information System (IRIS)*; PMEP (2003). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.10 mg/kg/d, and an ARfD of 0.50 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for halosulfuron methyl is 16.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for halosulfuron-methyl is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

IUPAC quote an ADI of 0.1 mg/kg bw.

The main metabolite, chlorosulfonamide acid, has lower toxicity than the parent. The acceptable daily intake (ADI) of halosulfuron-methyl is 0.063 mg/kg bw per day, based on the offspring’s NOAEL of 6.3 mg/kg bw per day from the multigeneration study in rat, applying the standard uncertainty factor (UF) of 100. The acute reference dose (ARfD) is 0.5 mg/kg bw, based on the NOAEL of 50 mg/kg bw/day from the maternal effects observed in the developmental toxicity study in rabbits, 100 UF applied (EFSA 2012).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Haloxyfop

CAS No. 69806-34-4. The IUPAC name for haloxyfop is (RS)-2-{4-[3-chloro-5-(trifluoromethyl)-2-pyridyloxy]phenoxy}propionic acid. The CAS name is 2‑[4‑[[3‑chloro-5-(trifluoromethyl)-2-pyridinyl]oxy]phenoxy]propanoic acid.

The R-isomer is the biologically active form, and is sold as haloxyfop-p, CAS No. 95977-29-0 – this once was sometimes called haloxyfop-R or haloxyfop acid. The methyl ester is also available, CAS No. 72619-32-0.

### Maximum Acceptable Value

Haloxyfop does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* NHMRC, NRMMC 2011) include a guideline value of 0.001 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.00084 mg/L (0.84 µg/L) for haloxyfop-R methyl in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Haloxyfop is an aryloxyphenoxypropionic herbicide, used for selective post-emergent control of grass weeds in broadleaf crops. Haloxyfop and its R-isomer appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Four herbicides (metsulfuron methyl, haloxyfop methyl, imazapyr isopropylamine and triclopyr triethylamine (TEA)) have been approved by the New Zealand Environmental Protection Agency (EPA) for restricted use over water, by authorised agencies, under a set of conditions (Auckland City 2013; EPA 2014). It is also used to control pampas grass.

The EU (2007) found that the use of haloxyfop-R, in the scenarios presented by the notifier, led to the appearance of a number of metabolites which are persistent and can leach easily into the water table, with potentially negative effects on drinking water. This raised concerns which could not be resolved on the basis of the data presented within the legal deadlines by the notifier. Moreover, based on the available data, concerns remain as regards the risk assessment for mammals. Member states shall ensure that: (a) authorisations for plant protection products containing haloxyfop-R are withdrawn by 19 December 2007 (b) no authorisations for plant protection products containing haloxyfop-R are granted or renewed from the date of publication of this decision.

### Forms and fate in the environment

Haloxyfop is active on leaves, with minimal soil activity, and low volatility. The half-life of haloxyfop in soil is 55–100 days depending on the soil type. In soil incubation studies under aerobic conditions at 20°C, parent haloxyfop-P-methyl disappeared with a half-life of approximately 0.5 days. Haloxyfop-P-methyl was hydrolysed just as quickly in a sterile soil as in a fresh soil, demonstrating that the methyl ester is chemically labile. Haloxyfop-P acid was persistent in the sterile soil. Under aerobic soil incubation, the first metabolite was haloxyfop-P acid, which mostly disappeared with half-lifes in the range of 9–21 days (n = 8), but in subsoils with low organic carbon its disappearance half-lifes were 28 and 129 days (JMPR 2009). Leaching is moderate.

The half-life of haloxyfop in water is 33 days for haloxyfop at pH 5, five days at pH 7, and a few hours at pH 9. Haloxyprop solubility in water is 43 mg/L at pH 2.6, 25ºC; 1.6 mg/L at pH 5 and 7 mg/L at pH 9 (both 20ºC). Haloxyfop-p solubility in water is 375 mg/L at 20ºC.

NPIC (1994) quotes for haloxyfop-methyl a soil half-life of 55 days, water solubility of 43 mg/L and a sorption coefficient (soil Koc) of 75. This resulted in a pesticide movement to groundwater rating of high.

The metabolites pyridinol and pyridinone may be found in groundwater (EC 2006), for which a trigger level of 0.00075 mg/L has been set.

### Removal methods

Depending on the product used and the soil type, treatment processes that remove particulate matter may be effective at reducing the concentration of haloxyfop in water.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The USEPA (1991) derived an oral reference dose of 0.00005 mg/kg/d bw (the intake likely to be without an appreciable risk of causing deleterious effects during a lifetime).

JMPR developed an ADI for haloxyfop of 0.0003 mg/kg body weight (IPCS 1995) on the basis of the NOAEL of 0.03 mg/kg bw per day in the two two-year studies in mice producing increased incidence of liver tumours, and using a safety factor of 100. The most recent toxicological review by JMPR was in 2006 when a group ADI of  
0–0.0007 mg/kg bw and a group ARfD of 0.08 mg/kg bw were established for racemic haloxyfop, haloxyfop-R and their methyl esters.

EC (2006) established an ADI of 0.00065 mg/kg/d and an ARfD of 0.075 mg/kg for haloxyfop-P. These values were adopted by EFSA (2014 and 2016) too.

The Acceptable Daily Intake (ADI) adopted in Australia for haloxyfop is 0.0003 mg/kg body weight, with a NOEL of 0.03 mg/kg bw from a long-term (two-year) dietary study in mice. The NOEL is based on the presence of liver tumours at 0.065 mg/kg bw/day. The ADI incorporates a safety factor of 100.

As at September 2008 the USEPA has classified haloxyfop in Group B: a probable human carcinogen.

The EC (2006) stated that the information available is insufficient, in particular with regard to the environmental fate and ecotoxicology of the substance, and a finalised assessment of consumers’ exposure.

### Derivation of Maximum Acceptable Value

No MAV.

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# Heptachlor and Heptachlor epoxide

Heptachlor CAS No. 76-44-8. The IUPAC name for heptachlor is 1,4,5,6,7,8,8‑heptachloro-3a,4,7,7a-tetrahydro-4,7-methanoindene. The CAS name is 1,4,5,6,7,8,8‑heptachloro-3a,4,7,7a-tetrahydro-4,7-methano-1H-indene. Also called heptachlorodicyclopentadiene.

Heptachlor epoxide CAS No. 1024-57-3. Heptachlor epoxide is the common name for 2,3,4,5,6,7,7-heptachloro-1a,1b,5,5a,6,6a-hexahydro-2,5-methano-2H-indene(1,2b)oxirene.

### Maximum Acceptable Value

WHO (2004/2011/2017) states that because heptachlor and heptachlor epoxide occur at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

WHO (2017) derived a health-based value of 0.03 μg/L for heptachlor and heptachlor epoxide.

In DWSNZ 2005, the provisional MAV for heptachlor plus heptachlor epoxide in drinking-water had been 0.00004 mg/L (0.04 g/L, or 40 ng/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.0004 mg/L for heptachlor and 0.0002 mg/L for the epoxide. The 2004 version of the *Australian Drinking Water Guidelines* stated that heptachlor should not be detected in drinking water. If present in drinking water, heptachlor would not be a health concern unless the concentration exceeded 0.0003 mg/L. If it is detected, remedial action should be taken to stop contamination. The limit of determination is 0.00005 mg/L (50 ng/L).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0003 mg/L, however, heptachlor has not been used in Australia since 1994.

Heptachlor and heptachlor epoxide are “priority pollutants” under the US Clean Water Act.

Heptachlor is one of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention (see <http://chm.pops.int/>). Heptachlor appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical) (see <http://www.pic.int/home.php?type=s&id=77>).

### Sources to water

Heptachlor, a chlorinated cyclodiene or organochlorine, may enter source waters as a result of its application as a broad spectrum non-systemic contact and stomach insecticide used for soil treatment and seed treatment, or if it is applied directly to foliage to control a wide variety of insects. It had also been used for malaria control. Heptachlor epoxide is an oxidation product of heptachlor.

Chlordane and heptachlor were considered together (IARC 1991) because of their close structural similarity and because technical-grade products each contain approximately 20 percent of the other compound. Technical-grade heptachlor contained about 72 percent heptachlor and 28 percent related compounds (20 to 22 percent γ‑chlordane and 4 to 8 percent γ-nonachlor). Hexachlorocyclopentadiene was often an impurity, up to 1 percent.

Heptachlor is not currently (2005) used in New Zealand. It was never fully registered and its highest status was provisional B, which was cancelled in the early 1970s.

Heptachlor was used in Australia until September 1994 to protect wooden structures against termites. Its other former uses were withdrawn in the late 1970s and early 1980s.

### Forms and fate in the environment

Heptachlor is moderately persistent in soil where it is transformed (by hydrolysis) mainly to its epoxide and to 1-hydroxychlordene. They bind to soil particles and migrate and volatilise slowly. Heptachlor epoxide is resistant to further chemical or biological changes in soil and also binds to soil and migrates very slowly. The epoxide half-life in soil ranges from nine months to four years.

The water solubility is about 0.05–0.06 mg/L for heptachlor and 0.30–0.35 mg/L for heptachlor epoxide.

NPIC (1994) quotes for heptachlor a soil half-life of 250 days, water solubility of 0.056 mg/L and a sorption coefficient (soil Koc) of 24,000. This resulted in a pesticide movement to groundwater rating of extremely low.

USGS (2006) give the following values for heptachlor epoxide: log Kow = 5.0; log Koc (where Koc is in mL/g) = 4.0; water solubility = 0.35 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.51; half-life in aerobic soil = NA days; half-life in water = NA days.

Heptachlor and its epoxide are not expected to leach to groundwater.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of heptachlor and heptachlor epoxide (limit of detection = 0.00001 mg/L or 10 ng/L) (ESR 2001).

Heptachlor and heptachlor epoxide have been found in drinking-water at levels of nanograms per litre (WHO 2004/2017).

Twenty water utilities in the US reported detecting heptachlor in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0002 mg/L.

Sixty-two water utilities in the US reported detecting heptachlor epoxide in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0004 mg/L.

### Removal methods

No information is available on methods of removing heptachlor or heptachlor epoxide from water. However, the strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of heptachlor and heptachlor epoxide in water; also isotherm adsorption data also indicate that removal by adsorption on to granular activated carbon should be possible. WHO (2017) states that concentrations below 0.0001 mg/L are generally not achievable using conventional treatment technology.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 505).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

### Health considerations

Heptachlor is absorbed rapidly from the gastrointestinal tract of rats following intragastric administration. Heptachlor is metabolised to heptachlor epoxide and other metabolites which are distributed throughout the body, including human milk.

The liver appears to be the target organ for heptachlor toxicity and oral administration of heptachlor enhanced the incidence of liver tumours induced in mice by oral administration of N-nitrosodiethylamine.

Clinical case studies of humans subject to acute exposure of chlordane-containing heptachlor (via ingestion, skin or inhalation routes) report central nervous system effects such as irritability, salivation, laboured respiration, muscle tremors and convulsions.

JMPR (1994) quoted a provisional tolerable daily intake (PTDI) of 0.0001 mg/kg/d.

The Tolerable Daily Intake (TDI) adopted in Australia for heptachlor is 0.0005 mg/kg body weight.

The oral reference dose or RfD for heptachlor (USEPA 1991/2006/2009) is 0.0005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009) is 0.02 mg/L.

The reference dose or RfD for heptachlor epoxide (USEPA 1991/2006/2009/2011) is 0.00001 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.0004 mg/L.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) for heptachlor of:

* 0.0006 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.0001 mg/kg/day for intermediate-duration oral exposure (15–364 days).

Prolonged exposure to heptachlor has been associated with damage to the liver and central nervous system toxicity. The International Agency for Research on Cancer (IARC) has classed heptachlor in Group 2B (possibly carcinogenic to humans).

As at May 2002 the USEPA classified heptachlor and heptachlor epoxide in Group B2: probable human carcinogens, but they did not appear on the September 2008 list. The USEPA (2009/2011) quotes a health advisory of 0.0008 mg/L for heptachlor and 0.0004 mg/L for heptachlor epoxide, representing a 10-4 cancer risk.

These chemicals appear on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Heptachlor is one of the Substances from the Carcinogenic Potency Database which are of particular concern even if ingested at doses at or below 0.0025 μg/kg body weight per day (EFSA 2016).

### Derivation of Maximum Acceptable Value

WHO (2017) states that because heptachlor and heptachlor epoxide occur at concentrations in drinking-water well below those at which toxic effects are expected to be observed, it is not considered necessary to derive a guideline value.

In the 1995 and 2005 DWSNZ, the provisional MAV had been derived as follows (WHO 2011/2017 now calls this a health-based value):

The Joint FAO/WHO Meetings on Pesticide Residues (JMPR) have evaluated heptachlor on several occasions and in 1991 established as Acceptable Daily Intake (ADI) of  
0.1 g/L of body weight on the basis of a no-observable-adverse effect level of 0.025 mg/L:

0.025 mg/kg body weight/day x 70 kg x 0.01 = 0.000044 mg/L (0.044 g/L)

2 L/day x 200

(rounded to 0.00004 mg/L, or 0.04 g/L, or 40 ng/L)

where:

* no-observable-adverse-effect level = 0.025 mg/kg body weight per day from two studies in the dog
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01
* uncertainty factor = 200 (100 for inter and intra-species variation and 2 for the inadequacy of the data base).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for heptachlor is 0.00008 mg/L, and 0.00004 mg/L for heptachlor epoxide.

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# Hexachlorobenzene

CAS No. 118-74-1. The IUPAC and CAS name is hexachlorobenzene. IUPAC also calls it perchlorobenzene. Also known as HCB or pentachlorophenyl chloride.

### Maximum Acceptable Value

WHO (2004) stated that because the health-based values are considerably higher than the concentrations at which HCB is detected in drinking-water (ie, sub-nanograms per litre), when it is detected, it is not considered necessary to establish a guideline value for HCB in drinking-water. WHO (2011) states that hexachlorobenzene occurs in drinking-water at concentrations well below those of health concern.

WHO (2017) derived a health-based value of 0.001 mg/L.

In the 2005 DWSNZ, the provisional MAV for hexachlorobenzene in drinking-water had been 0.0001 mg/L (0.1 g/L). In the 1995 DWSNZ, the MAV for hexachlorobenzene in drinking-water had been 0.001 mg/L (1 g/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.001 mg/L.

Hexachlorobenzene is one of the “priority pollutants” under the US Clean Water Act.

Hexachlorobenzene is one of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention; see <http://chm.pops.int/>. It also appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

### Sources to water

Hexachlorobenzene may enter source waters as a result of its application as a selective organochlorine fungicide, used to control dwarf bunt in wheat. The major agricultural application for HCB used to be as a seed dressing for crops such as wheat, barley, oats and rye to prevent growth of fungi. The use of HCB in such applications was discontinued in many countries in the 1970s owing to concerns about adverse effects on the environment and human health.

Levels of HCB in fresh water in Europe and North America are generally below 0.000001 mg/L, although higher values have been reported in aquatic systems that receive industrial discharges and surface run-off.

Hexachlorobenzene is not presently (2011/2017) registered in New Zealand and never reached full registration, although it did gain experimental use status.

HCB is produced as a by-product or waste material in the production or use of tetrachloroethylene, trichloroethylene, carbon tetrachloride, chlorine, dimethyl tetrachloroterephthalate, vinyl chloride, atrazine, propazine, simazine, pentachloronitrobenzene (quintozene), and mirex. It is a contaminant in several pesticides including dimethyl tetrachlorophthalate and pentachloronitrobenzene.

Technical grade HCB can contain up to 2 percent impurities, about half of which is pentachlorobenzene, the remainder including hepta- and octa-chlorodibenzofurans, octachlorodibenzo-p-dioxin, and decachlorobiphenyl.

At present, it appears mainly as a by-product of several chemical processes or an impurity in some pesticides. Small amounts of hexachlorobenzene can also be produced during combustion processes such as burning of city wastes.

### Forms and fate in the environment

HCB is distributed throughout the environment because it is mobile and resistant to degradation. It bioaccumulates in organisms because of its physicochemical properties and its slow elimination. Hexachlorobenzene photolyses slowly in the atmosphere with a half-life of about 80 days. It has a very low solubility in water (about 0.005 mg/L, although ICPS (2001) reports 8 mg/L) and, despite its relatively low vapour pressure, volatilises from water at a significant rate. Biotransformation in surface water, sludge, or soil suspensions is extremely slow. Hexachlorobenzene is adsorbed strongly by soil. HCB completely degraded to pentachlorophenol in hydrosoil samples (EXTOXNET 1993).

In water, it is a persistent chemical not readily degraded by either abiotic or biotic processes. The half-life value of hexachlorobenzene is estimated to range from 2.7 to 5.7 years in surface water and from 5.3 to 11.4 years in groundwater. Volatilisation from the water column is moderately rapid; however, the compound’s strong adsorption to particulates and organic matter in water can result in lengthy persistence in the sediment. Hexachlorobenzene bioaccumulates significantly in both terrestrial and aquatic food chains.

NPIC (1994) quotes for hexachlorobenzene a soil half-life of 1,000 days, water solubility of 0.005 mg/L and a sorption coefficient (soil Koc) of 50,000. This resulted in a pesticide movement to groundwater rating of extremely low.

USGS (2006) give the following values: log Kow = 5.31; log Koc (where Koc is in mL/g) = 4.7; water solubility = 0.0062 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 1.69; half-life in aerobic soil = NA days; half-life in water = >26,000 days.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of hexachlorobenzene (limit of detection = 0.0001 mg/L) (ESR 2001).

It has been detected only infrequently, and at very low concentrations (below 0.0001 mg/L), in drinking-water supplies (WHO 2004/2017).

Samples of drinking-water collected in 1980 from Canadian cities in the vicinity of Lake Ontario contained from 0.00000006 to 0.0000002 mg/L, with a mean of 0.0000001 mg/L.

Twenty-one water utilities in the US reported detecting hexachlorobenzene (HCB) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00065 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of hexachlorobenzene in water. Aeration may enhance the removal. Isotherm adsorption data also indicate that removal by adsorption on to granular activated carbon should be possible.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (EPA 525).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

2. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 505).

### Health considerations

Animal studies have shown that following administration, hexachlorobenzene was detected in adipose tissue, bone marrow, skin, the Harderian gland, nasal mucosa and the preputial gland. It is metabolised slowly into lower chlorinated benzenes, chlorinated phenols and other metabolites, and excreted principally in faeces.

Symptoms observed with acute exposure in animals include convulsions, tremors, weakness, loss of coordination, paralysis and pathological changes in organs. Short-term exposure studies in animals reported symptoms principally affecting the spleen, liver and kidneys.

The reference dose or RfD (USEPA 1991/2006/2009/2011) is 0.0008 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.03 mg/L.

As at August 2015 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.008 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.0001 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.00007 mg/kg/day for chronic-duration oral exposure (>364 days).

The International Agency for Research on Cancer has evaluated the evidence for carcinogenicity of hexachlorobenzene in animals and humans and have classed it in Group 2B (possibly carcinogenic to humans). Hexachlorobenzene has been shown to induce tumours in three animal species and at a variety of sites.

No report of a direct association between hexachlorobenzene and human cancer is available. Hepatocellular carcinoma has been associated with porphyria (abnormal porphyrin metabolism). However, while this persisted at least 20 years after an epidemic of porphyria cutanea tarda in Turkey, caused by consumption of grain treated with hexachlorobenzene, no excess cancer occurrence was reported in this population 25 years after the accident.

As at May 2002 the USEPA classified hexachlorobenzene in Group B2: a probable human carcinogen, but it did not appear on the September 2008 list. The USEPA (2009/2011) quotes a health advisory of 0.002 mg/L for hexachlorobenzene, representing a 10-4 cancer risk.

Hexachlorobenzene appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Hexachlorobenzene is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

A health-based value of 0.001 mg/L in drinking-water, corresponding to an upper-bound excess lifetime cancer risk of 10-5, can be calculated by applying the linearised multistage low-dose extrapolation model to liver tumours observed in female rats in a two-year dietary study. An alternative (tumorigenic dose05, or TD05) a TDI of 0.16 μg/kg body weight can be calculated, which corresponds to a health-based value of approximately 0.00005 mg/L, if one assumes a 1 percent allocation of the TDI to drinking-water. It should be noted that concentrations in food have been falling steadily, and this allocation factor may be considered very conservative (WHO 2017).

WHO (2004) states that because the health-based values derived from both of these approaches are considerably higher than the concentrations at which HCB is detected in drinking-water (ie, sub-ng/litre), when it is detected, it is not considered necessary to establish a guideline value for HCB in drinking-water.

In the 2000 DWSNZ, the provisional MAV had been based on the alternative approach for deriving exposure values when dealing with neoplastic effects, based on the TD05 approach (IPCS 1997). Using this approach, IPCS (1997) derived a health-based guidance value of 0.16 μg/kg of body weight per day. If one were to assume a 1 percent allocation of this guidance value to drinking-water (IPCS 1997), then this would correspond to a 60-kg adult consuming two litres of drinking-water containing approximately 0.05 μg/litre (0.00005 mg/L). Allowing for a 70 kg person and rounding off, this became a provisional MAV of 0.0001 mg/L.

In DWSNZ 1995, the MAV had been based on the following:

Hexachlorobenzene has been shown to induce tumours in three animal species and at a variety of sites. A linear low-dose extrapolation model was therefore used to calculate a reference dose. On the basis of liver tumours observed in female rats in a two-year dietary study, and applying the linearised multistage model, the concentration of hexachlorobenzene associated with an excess lifetime cancer risk of one per 100,000 (10-5) is 0.001 mg/L (1 g/L).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for hexachlorobenzene is 0.0002 mg/L.

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# Hexachlorocyclohexane

The CAS No. of the technical grade hexachlorocyclohexane is 608-73-1. The IUPAC and CAS name is 1,2,3,4,5,6-hexachlorocyclohexane. Also called benzene hexachloride (incorrectly), or HCH or BHC. The four main isomers are:

* α–HCH CAS No. is 319-84-6
* β-HCH CAS No. is 319-85-7. Also called benzene-cis-hexachloride.
* δ-HCH CAS No. is 319-86-8
* γ-HCH CAS No. is 58-89-9. This is lindane (qv).

A minor isomer is epsilon-hexachlorocyclohexane, or ε-HCH (CAS No.6108-10-7).

### Maximum Acceptable Value

WHO (2004 and 2011) states that because hexachlorocyclohexane is unlikely to occur in drinking-water, a guideline value has not been derived.

The USEPA concluded on 22 September 2009 that α-hexachlorocyclohexane is known or anticipated to occur in PWSs and may require regulation. Therefore they added α‑hexachlorocyclohexane to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

Also see datasheet for lindane.

α-Hexachlorocyclohexane, β-hexachlorocyclohexane and lindane were added to the Persistent Organic Pollutants (POP) Stockholm Convention list in May 2009 (ICS 2009, <http://chm.pops.int/>). HCH and mixed isomers appear on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

### Sources to water

Hexachlorocyclohexane (HCH) is a manufactured organochlorine chemical that exists in eight chemical forms called isomers; one is lindane and the other three main isomers are discussed here. Hexachlorocyclohexane does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Technical-grade HCH was used as an insecticide and typically contained 10–15 percent γ-HCH as well as 60–70 percent as the alpha (α), 5–12 percent as beta (β), 6–10 percent as the delta (δ), and 3–4 percent as the epsilon (ε) forms of HCH. Virtually all the insecticidal properties resided in the γ-HCH isomer. Technical-grade HCH has not been produced or used in the United States in over 20 years, although γ-HCH is still imported there.

Lindane (γ-HCH) is still used to treat and/or control scabies (mites) and head lice in humans, but generally without the isomers. For each ton of lindane produced, around 6–10 tons of the other isomers including alpha- and beta-HCH are created. Large stockpiles of alpha- and beta-HCH are therefore present in the environment.

### Forms and fate in the environment

α-, β-, γ-, and δ-HCH have been found in at least 146, 159, 189, and 126, respectively, of the current or former 1,662 National Priority List sites identified by the Environmental Protection Agency (USEPA).

Water solubility for α–HCH is about 10–50 mg/L (temperature dependant); β-HCH is about 5 mg/L; δ-HCH is about 10 mg/L.

Biodegradation is believed to be the dominant degradative process for the HCH isomers in aquatic systems. Hydrolysis is not considered an important degradation process for the HCHs in aquatic environments under neutral pH conditions. However, under alkaline conditions, hydrolysis is more rapid.

Biodegradation and abiotic degradation (dechlorination) of α–HCH by ultraviolet radiation occurs in the environment, with the production of delta-3,4,5,6-tetrachlorohexene, and pentachlorocyclohexene, respectively. The breakdown process is slower than in the case of lindane. The persistence of alpha-HCH in soils is determined by environmental factors, such as the action of micro-organisms, organic matter content, and co-distillation and evaporation from soils. No isomerisation occurred from lindane into alpha-HCH (IPCS 1991).

Biodegradation and abiotic degradation (dechlorination) of β-HCH by UV light occurs in the environment, with the production of pentachlorocyclohexane, but the degradation rate is much slower than that for lindane (gamma-HCH). ß-HCH is the most persistent HCH isomer (IPCS 1991).

If released to soil, beta-hexachlorocyclohexane is expected to have slight to no mobility based upon log Koc values of 3.4–4.1 measured in two oil contaminated soils. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 4.4 x 10-7 atm-cu m/mole. beta-Hexachlorocyclohexane is not expected to volatilise from dry soil surfaces based upon its vapour pressure. This compound is expected to be highly persistent in the environment with observed half-lifes of 184 and 100 days on cropped and uncropped soils, respectively. If released into water, beta-hexachlorocyclohexane is expected to adsorb to suspended solids and sediment in the water column based upon its measured Koc values. Volatilisation from water surfaces is not expected to be an important environmental fate process given its Henry’s Law constant. This compound has the potential to undergo hydrolysis, but the kinetics of this reaction are unknown for this isomer. Hydrolysis is likely to occur slowly based on hydrolysis half-lifes of 1.2 years, 0.8 years, and 30 days at pH values of 7, 8, and 9, respectively, for the alpha isomer. An average log BCF value of 2.8 (BCF = 631) reported for fish suggests that bioconcentration in aquatic organisms is high (EAWAG accessed February 2015).

The Stockholm Convention meeting stated that:

“Lindane was used as a broad-spectrum insecticide for seed and soil treatment, foliar applications, tree and wood treatment and against ectoparasites in both veterinary and human treatments. Lindane production has decreased rapidly in recent years and only a few countries still produce it. Although the intentional use of alpha- and beta-HCH as an insecticide was phased out years ago, these chemicals are still produced as an unintentional by-product of lindane. Approximately 6–10 tons of other isomers including alpha- and beta-HCH result from each ton of lindane produced.”

### Typical concentrations in drinking-water

One water utility in the US reported detecting alpha-HCH (wrongly called alpha-lindane) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

Three water utilities in the US reported detecting beta-HCH (wrongly called beta-lindane) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00009 mg/L.

One water utility in the US reported detecting delta-HCH (wrongly called delta-BCH) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00002 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See Table 7-2 in ATSDR (2005).

### Health considerations

Food is the main source of alpha-HCH and beta-HCH for the general population.

Among the HCH isomers, β-HCH leaves the body the most slowly. α-HCH, δ-HCH, and γ-HCH, and the products formed from them in the body, are more rapidly excreted in the urine; small amounts leave in the faeces and expired air. HCH breaks down in the body to many other substances; these include various chlorophenols, some of which have toxic properties.

Animal studies have reported that ingestion of α-, β-, and γ-HCH isomers, individually or as technical-grade HCH, has resulted in some degree of liver toxicity including increased microsomal activity, increased liver weight, mild-to-moderate liver necrosis and fatty degeneration, and liver cancer.

The International Agency for Research on Cancer (IARC) has classified HCH (all isomers) as possibly carcinogenic to humans. The USEPA has classified technical HCH and α‑HCH as probable human carcinogens (Class B2), β-HCH as a possible human carcinogen (Class C), and δ- and ε-HCH as not classifiable as to human carcinogenicity (Class D). These chemicals appear on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

HCH isomers differ quantitatively and qualitatively in biological activity. The alpha and gamma HCH isomers are central nervous system stimulants causing violent epileptiform convulsions. The beta and delta isomers are mainly depressant (INCHEM).

The general population is predominantly exposed to HCH by consumption of contaminated food, with minor exposures occurring from drinking water and ambient air.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of 0.008 mg/kg/day for chronic-duration oral exposure (>364 days) to α-HCH.

ATSDR quotes a minimal risk level (MRL) for β-HCH of:

* 0.05 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.0006 mg/kg/day for intermediate-duration oral exposure (15–364 days).

ATSDR quotes a minimal risk level (MRL) for γ-HCH (lindane, qv) of:

* 0.003 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.00001 mg/kg/day for intermediate-duration oral exposure (15–364 days).

### Derivation of Maximum Acceptable Value

No MAV.

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# Hexaconazole

CAS No. 79983-71-4. The IUPAC name for hexaconazole is (RS)-2-(2,4-dichlorophenyl)-1-(1H-1,2,4-triazol-1-yl)hexan-2-ol. The CAS name is α-butyl-α-(2,4-dichlorophenyl)-1H-1,2,4-triazole-1-ethanol.

### Maximum Acceptable Value

Hexaconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Hexaconazole is a broad spectrum systemic conazole (or triazole or azole or imidazole) fungicide particularly effective against [Ascomycetes](http://en.wikipedia.org/wiki/Ascomycetes) and [Basidiomycetes](http://en.wikipedia.org/wiki/Basidiomycetes), and used against powdery mildew, scab and rust of apples and powdery mildew and blackrot of grapes. Also used as a wood preservative.

Hexaconazole does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (both Chemicals and Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals or Pesticides).

### Forms and fate in the environment

Soil half-life of hexaconazole is about 4 to 7 months, ie, persistent. It is stable in water too, but because it has an affinity to bind to soil particles, it is not expected to leach to groundwater.

Water solubility is about 18 mg/L at 20°C.

### Health considerations

#### Acute poisoning

The most common signs of acute toxicity were piloerection, upward curvature of the spine, side pinched-in, hypothermia, decreased activity, urinary incontinence, dehydration, comatosis, reduced righting reflex and decreased respiration rate (IPCS 1990). From acute as well as from short-term studies it appeared that male rats were more sensitive than female rats. Short-term studies with mice, rats and dogs indicated that the liver is the primary target organ. From in vitro studies it can be concluded that hexaconazole inhibits testosterone production.

#### Chronic exposure

In a two-year feeding study in rats, hexaconazole was tested at 0.47, 4.7 and 47 mg/kg/day in females and 0.61, 6.1 and 61 mg/kg/day in males. The no-observed-effect level (NOEL) was established at 0.61 and 0.47 mg/kg/day in males and females, respectively for body weight gain reduction and liver pathology (centrilobular fatty changes and hypertrophy); USEPA (1996). The Reference Dose (RfD) value for use in dietary exposure analysis was 0.02 mg/kg body weight/day, basis of a NOEL of 2 mg/kg/day and an uncertainty factor of 100. This NOEL was derived from a one-year feeding study in dogs that showed increased liver weight accompanied by fatty infiltration of the liver observed at 10 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.02 mg/kg/d, and an ARfD of 0.025 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for hexaconazole is 0.83 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L. See datasheet for triazole metabolites for latest ADI and ARfD.

The Acceptable Daily Intake (ADI) adopted in Australia for hexaconazole is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

The lifetime carcinogenic risk appears to be below the range that the USEPA generally considers to be negligible; tests produced no evidence of mutagenicity due to hexaconazole (USEPA 1996). Later, the USEPA (1999) Cancer Peer Review Committee classified hexaconazole as a Group C (likely) carcinogen based on benign Leydig cell tumours in the male rats.

### Derivation of Maximum Acceptable Value

No MAV.

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# Hexazinone

CAS No. 51235-04-2. The IUPAC and CAS name is 3-cyclohexyl-6-dimethylamino-1-methyl-1,3,5-triazine-2,4(1H,3H)-dione.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of hexazinone in drinking-water should not exceed 0.4 mg/L (400 μg/L).

Hexazinone is not mentioned in WHO (2004 or 2011).

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.4 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Hexazinone is used as a broad spectrum pre- and post- emergence heterocyclic triazine or triazinone herbicide effective against woody and herbaceous weeds, often used selectively in lucerne and radiata pine, and for non-selective control of annual and perennial weeds and brush such as pampas weed in non-cropland areas.

Hexazinone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is available in a variety of formulations, some of which contain terbuthylazine or atrazine as additional active ingredients. Trade names include: Agpro Valzine 500, Agpro Valzine Extra, Forest Mix Special Blend Granular Herbic, Release Ultra, Release, Velgard, and Velpar. ERMA notes that 53.4 tonnes of hexazinone were used in New Zealand in 2004, at an application rate of 7,500 grams of active ingredient per hectare. Hexazinone is understood to have its largest use in forestry (Holland, personal communication).

Hexazinone should not contain more than 50 mg/kg of carbamic acid ethyl ester (the International Agency for Research on Cancer (IARC) lists carbamic acid, ethyl ester, as a carcinogen and the USEPA also considers this impurity to be of toxicological concern).

Hexazinone appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Hexazinone is very soluble in water: about 30 g/L (3 percent or 30,000 mg/L) (JMPR 2006).

Based on laboratory data and confirmed by field and forestry data, hexazinone appears to be persistent and mobile in soil and aquatic environments. Hexazinone was reported in run-off water up to six months post-treatment in a forestry dissipation study. Hexazinone is very poorly adsorbed to soil particles, very soluble in water, and slowly degraded, so it is likely to be mobile in most soils and has the potential to contaminant groundwater. Hexazinone has been detected in groundwater (at levels well below the Health Advisory) in Hawaii, Florida, Maine and North Carolina. Hexazinone also can contaminate surface water by spray drift at application, and for several months post-application via run-off (USEPA 1994). Close et al (1999) have reported a half-life for hexazinone of 113 days and a mobility (Koc) of 50–60 in Horotiu sandy loam, which indicates a moderate level of adsorption to organic soil.

NPIC (1994) quotes for hexazinone a soil half-life of 90 days, water solubility of 3.3 percent and a sorption coefficient (soil Koc) of 54. This resulted in a pesticide movement to groundwater rating of very high. Its GUS score is 4.30, indicating that it will leach to groundwater.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included hexazinone. In the New Zealand national pesticides surveys, conducted every four years between 1990 and 2002, hexazinone has been detected in groundwaters twice, at concentrations of 0.0012 and 0.0023 mg/L.

Pesticide monitoring of groundwater conducted by Environment Canterbury has detected hexazinone at two locations in the Level Plain area in South Canterbury. At the first location the concentration was 0.00018 mg/L, and at the second location the concentrations ranged from 0.00004–0.00079 mg/L (Close et al 2001). Hexazinone has been detected in groundwater at two sites in the Waikato Region. Concentrations ranged from 0.00004–0.00024 mg/L (Hadfield and Smith 1999).

Hexazinone has been detected in groundwater in the Edendale area (Southland) at concentrations ranging between 0.00004–0.00049 mg/L (Hughes 2000). Hexazinone has been found in 33 groundwater samples in Waikato and Southland, ranging from 0.00004 to 0.00024 mg/L (MAF 2006).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Hexazinone occurred at 0.05 to 0.22 µg/L, ie, up to 0.00022 mg/L.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Hexazinone was detected in 3 wells, from 0.093 to 0.74 µg/L, ie, up to 0.00074 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Hexazinone was found in three samples, from 0.039 to 0.21 µg/L, ie, up to 0.00021 mg/L.

In California hexazinone was detected in groundwater and reported in the 1995 well inventory report (DPR 1995). In a Canadian one-year study of hexazinone on short, gravity-irrigated runs in 1991 in southern Alberta, the herbicide was detected in 50 percent of run-off samples and about 27 percent of groundwater samples. No Canadian water quality guideline exists for hexazinone, but all detections were well below the US lifetime health advisory limit for drinking water of 0.21 mg/L (Minister of Public Works and Government Services, Canada 2000).

Seven water utilities in the US reported detecting hexazinone in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0038 mg/L.

### Removal methods

Specific information about the removal of hexazinone from water is unavailable, however, oxidation of triazines (hexazinone is a member of this chemical family) by ozone is reported to be effective. The water chemistry, in particular the alkalinity and pH, will affect the oxidation rate (Chiron et al 2000). Use of activated carbon following ozonisation should be considered to adsorb oxidation products.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of hexazinone, although a guide to the efficiency of the process cannot be provided.

Nanofiltration (membrane technology) in water with a low natural organic matter concentration is reported to remove approximately 50 percent of atrazine and simazine (Agbekodo et al 1996). The percentage is increased to 90–100 percent when 3.6 mg/L of natural organic matter is present. Similar results may be expected for hexazinone as it is from the same chemical family and of comparable size.

### Health considerations

There is no information available regarding the greatest source of exposure to hexazinone for New Zealanders (ie, dermal contact, inhalation, diet: food, water). Based on international studies, the dietary risk posed by hexazinone is expected to be minimal. Exposure to workers and other applicators generally is not expected to pose undue risks, due to hexazinone’s overall low acute toxicity (USEPA 1994).

Hexazinone had not been evaluated by the FAO/WHO JMPR or by WHO/PCS (JMPR 2006).

Almost all of a 14 mg/kg oral dose administered to rats was excreted in three to six days, with the majority in urine. In another study, animals fed 125 mg/kg for two weeks and then given a small single dose, excreted almost all of the product within three days. Less than 1 percent of the parent hexazinone was detected in urine and faeces. There does not appear to be any significant tissue accumulation (USEPA 1987, cited in EXTOXNET 2001).

#### Acute poisoning

In acute toxicity studies using laboratory animals, hexazinone has been shown to be a severe eye irritant and has been placed in Toxicity Category I (the highest of four categories) for primary eye irritation. It is slightly toxic through the acute oral route (Toxicity Category III) (USEPA 1994). It may irritate the eyes, nose and throat of humans (EXTOXNET 2001).

The acute oral LD50 for rats is 1,690 mg/kg, for guinea pigs 860 mg/kg (RSocC 1987), which suggests a moderate acute oral toxicity when compared with other pesticides.

#### Chronic exposure

In a rat study, there was increased survival over all test groups for male rats at 125 mg/kg at two years. Survival at two years in female rats was comparable between control and treated groups. The systemic NOEL was 10 mg/kg (PMEP 1988). USEPA’s Office of Water has issued a lifetime Health Advisory which sets a maximum level of 0.21 mg/L allowable in drinking-water. The critical effect of chronic exposure to hexazinone is decreased body weight (USEPA 1998).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw from a long-term (two-year) dietary rat study. The NOEL is based on decreased bodyweight gain at 125 mg/kg bw/day. The ADI incorporates a safety factor of 100.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.05 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 2 mg/L. The oral RfD had earlier been 0.033 mg/kg/d (USEPA 1990).

The International Agency for Research on Cancer (IARC) has not classified hexazinone for its potential to cause cancer. The USEPA has classified it as a Group D carcinogen, a chemical that is not classifiable as to human carcinogenicity (USEPA 1994), and it is still on their September 2008 list.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH to derive the provisional MAV for hexazinone in drinking-water, as follows:

10 mg/kg body weight per day x 70 kg x 0.1 = 0.35 mg/L, rounded to 0.4 mg/L

2 L x 100

where:

* no observable adverse effect level = 10 mg/kg body weight per day.
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Hexythiazox

CAS No. 78587-05-0. The IUPAC name for hexythiazox is (4RS,5RS)-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-1,3-thiazolidine-3-carboxamide. The CAS name is (4R,5R)-rel-5-(4-chlorophenyl)-N-cyclohexyl-4-methyl-2-oxo-3-thiazolidinecarboxamide. Sometimes called Savey in the US.

### Maximum Acceptable Value

Hexythiazox is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Hexythiazox as a non-systemic mite growth regulator or thiazolidine acaricides, usually used in New Zealand to protect fruit. Hexythiazox is an acaricide which has ovicidal, larvicidal and nymphicidal activities and is applied at any stage of plant growth from budding to fruiting. There are several application timings to protect top fruits, eg, the winter eggs are controlled in early spring, other infection in late spring, and reinfection in summer and occasionally early autumn. Many countries recommend one application a year to avoid the emergence of resistant mites.

Hexythiazox does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Despite that, ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008 lists “a wettable powder containing 100 g/kg hexythiazox”.

### Forms and fate in the environment

The 1991 JMPR reported that hexythiazox is the main residue in crops and its metabolites are present in negligible amounts. Hexythiazox has six major metabolites that are of environmental significance, each is structurally very similar to the parent. All degradates were identified in aerobic soil metabolism, anaerobic aquatic, and aqueous photolysis studies. Degradation is most rapid (half-lifes of a few weeks or less) in aerobic soil and in water when the presence of sunlight enables photolysis. See JMPR (2009) for further discussion. The soil half-life has been measured at four to six weeks.

Water solubility about 0.1–0.4 mg/L.

NPIC (1994) quotes for hexythiazox a soil half-life of 30 days, water solubility of 0.5 mg/L and a sorption coefficient (soil Koc) of 6,200. This resulted in a pesticide movement to groundwater rating of very low.

Hexythiazox is degraded slowly in both crop groups studied; the parent compound was the major component of the residues. The DT90 value of hexythiazox was up to 248 days, and its metabolites PT‐1‐2 up to 877 days, and PT‐1‐3 up to 180 days (EFSA 2019).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The HED Cancer Assessment Review Committee classified hexythiazox as a “possible human carcinogen” in 1988 and established a unit risk of 2.2 x 10-2 based on the increased incidence of liver tumours in female mice. Due to the changes in policy since this 1988 decision, HED plans to re-evaluate the cancer classification in order to be consistent with current policy (USEPA 2007).

The chronic RfD = 0.025 mg/kg, based on a one-year toxicity feeding dog study; LOAEL = 12.5 mg/kg/day, NOEL = 2.5 mg/kg/d (USEPA 1988), based on increased absolute and relative adrenal weights and associated adrenal histopathology. USEPA (2000 and 2007) also quote an acute RfD: 2.4 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.025 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for hexythiazox is 0.175 mg/L (no acute one-day value available.)

The 2008 JMPR meeting established an ADI for hexythiazox of 0–0.03 mg/kg based on the NOAEL of 3.2 mg/kg bw per day, identified in the two-year study in rats on the basis of increases in fatty vacuolation of the adrenals in males and females, the severity of chronic nephritis and the incidence of swollen/withdrawn testes in males at 23 mg/kg bw per day and with a safety factor of 100. This was supported by the NOAEL of 2.9 mg/kg bw per day in the one-year study in dogs. The meeting concluded that the establishment of an ARfD for hexythiazox was unnecessary on the basis of its low acute toxicity, the absence of developmental toxicity in rats and rabbits, the lack of evidence for any acute neurobehavioral effects, and the absence of any other toxicologically relevant effect that would be elicited by a single dose (FAO/WHO 2008). These values were reaffirmed in JMPR (2011).

The Acceptable Daily Intake (ADI) adopted in Australia for hexythiazox is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw. This is the same ADI as adopted by JMPR which was based on NOAELs in the two-year feeding and reproduction studies in rats and a one-year study in dogs, using a 100-fold safety factor (IPCS 1991). In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EFSA (2019) used an ADI of 0.03 mg/kg per day; an ARfD was considered unnecessary.

### Derivation of Maximum Acceptable Value

No MAV.

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# Hydramethylnon

CAS No. 67485-29-4. The IUPAC name for hydramethylnon is 5,5‑dimethylperhydropyrimidin-2-one 4-trifluoromethyl-α-(4-trifluoromethylstyryl)cinnamylidenehydrazone. The CAS name is tetrahydro-5,5-dimethyl-2(1H)-pyrimidinone [3-[4-(trifluoromethyl)phenyl]-1-[2-[4-(trifluoromethyl)phenyl]ethenyl]-2-propenylidene]hydrazone. Has also been called amidine hydrazone or HMN.

### Maximum Acceptable Value

Hydramethylnon is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Hydramethylnon is an unclassified (but sometimes called a trifluoromethyl aminohydrazone) slow-acting insecticide, which acts as a metabolic inhibitor, commonly in cockroach, cricket and ant baits in both indoor and outdoor situations, sometimes substituting for chlorpyrifos.

Hydramethylnon does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), as a plant growth regulator. However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals and Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals or Pesticides).

Hydramethylnon was not allowed to be used as an active ingredient in the EC after 25 July 2003.

### Forms and fate in the environment

Hydramethylnon’s high sorption coefficient causes it to bind tightly to soil and limits its movement and availability in the environment . The soil half-life of hydramethylnon ranges from 375–391 days in aerobic soil although light and biota reduce this. Hydramethylnon photodegrades with a half-life of one hour in water (NPIC). Because hydramethylnon is only slightly soluble in water and is very strongly sorbed by soil organic matter and clay particles, it is not appreciably mobile in most soils. These properties, along with its low persistence, make it unlikely to contaminate groundwater (EXTOXNET 1996).

The reported hydrolysis half-life for hydramethylnon in water is 10 to 11 days over a pH range of 7 to 8.9, and 24 to 33 days at a pH of 4.9. Water solubility is about 0.006 mg/L at 25°C (EXTOXNET 1996).

NPIC (1994) quotes for hydramethylnon (amdro) a soil half-life of 10 days, water solubility of 0.006 mg/L and a sorption coefficient (soil Koc) of 730,000. This resulted in a pesticide movement to groundwater rating of extremely low.

Five breakdown products in water are described in CDPR (undated), and in USEPA (1998).

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of hydramethylnon in water.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In a 26-week study in male and female dogs, doses of up to 3.0 mg/kg/day resulted in increased liver weights and increased liver: body weight ratios. Chronic studies in several animals have shown the testis as a target organ (EXTOXNET 1996).

The available data suggest that reproductive and teratogenic effects are unlikely in humans at expected exposure levels. The data regarding carcinogenic effects are insufficient, but suggest that hydramethylnon is not carcinogenic (EXTOXNET 1996). However, on 28 May 1998, the Cancer Peer Review Committee concluded that the dose levels of 100 ppm in males, and 50 ppm in females were adequate to assess the carcinogenic potential of hydramethylnon in rats. This conclusion was based on significant decreases in body weight at higher doses. The statistically significant increases in tumours observed in the uterus (adenomatous polyps) and adrenals (medullary adenomas) were not considered to be biologically significant since they were seen at excessive doses (ie, at 200 ppm). Under the conditions of this study, the NOAEL was 50 ppm (2.4 mg/kg/day in males, 3.0 mg/kg/day in females), and the LOAEL was 100 ppm (4.9 mg/kg/day in males, 6.2 mg/kg/day in females) based on small, soft testes, decreased testicular weights, and testicular atrophy in males; and decreased body weight gain in females. This study is classified as acceptable and satisfies guideline requirement 83-5 for a chronic feeding/carcinogenicity study in rodents (USEPA 1998).

The long-term NOAEL for systemic toxicity in the chronic dog study was 1 mg/kg/day based on an increased incidence of soft stool, mucoid stool, and diarrhoea observed at 3 mg/kg/day. An uncertainty factor of 100 was applied to account for interspecies extrapolation (10) and intra species variability (10). On this basis the RfD was calculated to be 0.01 mg/kg/day (USEPA 1998). Based on the results of the acute toxicity data, hydramethylnon does not exhibit significant acute toxicity (USEPA 1998a). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.017 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for hydramethylnon is 1.65 mg/L.

A short-term (one to seven days) NOAEL of 250 mg/kg/day was established, based on non-adverse decreased food consumption in males and females, and thrombocytopenia in females (USEPA 1998).

The USEPA (1998) classified hydramethylnon as a possible (group C) human carcinogen due to lung adenomas and carcinomas.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Hydrogen cyanamide

CAS No. 420-04-2. The IUPAC and CAS name for hydrogen cyanamide is cyanamide. It has several trade names and other names, eg, carbodiimide, amidocyanogen, and carbimide. Also sold as the calcium salt (CAS No. 156-62-7).

### Maximum Acceptable Value

Hydrogen cyanamide is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Cyanamide is used as a herbicide and plant growth regulator.

Hydrogen cyanamide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), as a plant growth regulator. It is also used as a herbicide overseas. In New Zealand it is used (late winter) on kiwifruit (and a lesser extent on apples) to promote bud break.

Calcium cyanamide is used as a fertiliser, pesticide, in the steel industry, and in the manufacture of other chemicals. The calcium salt is also called calcium carbamide, nitrolime or lime nitrogen (EA 2010).

There have been suggestions overseas that hydrogen cyanamide could replace methyl bromide as a soil fumigant. It has been used as an alcohol deterrent drug in Canada, Japan and Europe.

Cyanamide is regarded as a key intermediate within chemical evolution on earth billions of years ago.

### Forms and fate in the environment

The half-life of hydrogen cyanamide in sandy loam soil is about three days (the main end-product being CO2), extending to about 35 days if anaerobic and in the dark. It is very mobile in soils, with virtually no adherence to particulate matter, so could enter groundwater where it may persist. A minor degradation product, dicyanodiamide, has a half-life of about four days, breaking down to urea and ammonia. Hydrogen cyanamide is not volatile but reacts with water to form ammonia and the explosive gas acetylene.

If released to soil, cyanamide is expected to have very high mobility based upon estimated Koc values of 4.7 and 7.3. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 2.66 x 10-10 atm-cu m/mole. In soil, cyanamide is converted to nitrogenous compounds which are rapidly taken up. In aqueous soil conditions, cyanamide is expected to decompose by hydrolysis to urea and by dimerisation to dicyanamide. If released into water, cyanamide is not expected to adsorb to suspended solids and sediment based upon the estimated Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. Cyanamide decomposes in water by hydrolysis to urea in acidic conditions and by dimerisation to dicyanamide in alkaline conditions (EAWAG accessed February 2015).

Hydrogen cyanamide is extremely soluble in water.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

As at September 2008, hydrogen cyanamide is classified by the USEPA in Group C: a possible human carcinogen, based on the statistically significant increase in the incidence of ovarian granulosa-theca tumours in mice.

The Acceptable Daily Intake (ADI) adopted in Australia for cyanamide is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw.

Chronic (long-term) occupational exposure of calcium cyanamide has been reported to cause chronic rhinitis with perforation of the nasal septum in workers. The USEPA (2000) has not classified calcium cyanamide with respect to potential carcinogenicity.

EC (2008) quotes an ADI of 0.002 mg/kg/d and an ARfD of 0.05 mg/kg, referring to an EFSA source. Reaffirmed in EFSA (2013).

### Derivation of Maximum Acceptable Value

No MAV.

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# 8-Hydroxyquinoline

CAS No. 148-24-3. The IUPAC name for 8-hydroxyquinolone is 8-quinolinol. Usually sold as the sulphate, CAS No. 134-31-6. The IUPAC name for 8-hydroxyquinoline sulphate is bis(8-hydroxyquinolinium) sulphate, and the CAS name is 8-quinolinol sulphate; also called 8-quinolinol hemisulfate, oxine sulfate, oxyquinoline sulfate, 8‑hydroxychinoline, hydroxybenzopyridine and quinophenol.

Note that the chemical 8-hydroxyquinolone (CAS No. 15450-76-7) exists as well; it is the ketone equivalent of 8-hydroxyquinoline. However, sometimes it appears as a misprint!

### Maximum Acceptable Value

8-Hydroxyquinoline is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

8-Hydroxyquinoline sulphate is a quinoline (coal tar derivative) fungicide and bactericide.

8-Hydroxyquinolone, and some derivatives, was once used as an anti-protozoal agent, for human consumption, as an amoebicide, or to control, eg, giardiasis. Quinolones have also been used to control malarial diseases.

Quinoline family compounds are widely used as a parent compound to make drugs (especially anti-malarial medicines), fungicides, biocides, alkaloids, dyes, rubber chemicals and flavouring agents. They have antiseptic, antipyretic, and antiperiodic properties. They are also used as catalyst, corrosion inhibitor, preservative, and as solvent for resins and terpenes. They are used in transition-metal complex catalyst chemistry for uniform polymerization and luminescence chemistry. Oxyquinoline, hydroxyquinoline at 8-position, is used as a bacteriostatic and fungistatic agent. It is used in preparing antiseptics, deodorants, antiperspirants, and fungicides. The sulfate salt of 8-hydroxyquinoline is used as a complexing agent for pharmaceuticals. A very large number of quinoline-based chemicals are in fairly widespread use; for a list of these, see [http://chemicalland21.com/lifescience/phar/8-hydroxyquinoline%20sulfate.htm](http://chemicalland21.com/lifescience/phar/8-HYDROXYQUINOLINE%20SULFATE.htm).

8-Hydroxyquinoline sulphate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). A common use is as a fungicide/bactericide on glasshouse tomatoes.

8-Hydroxyquinolone is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …). It is in a product containing isothiazolones.

### Forms and fate in the environment

8-Hydroxyquinoline is expected to have slight mobility in many soil types. Volatilisation of 8-hydroxyquinoline from moist soil surfaces is not expected to be an important fate process given an estimated Henry’s Law constant of 5.7 x 10-7 atm-cu m/mole, based upon its vapour pressure, 1.66 x 10-3 mm Hg, and water solubility, 556 mg/L. 8‑Hydroxyquinoline is not expected to volatilise from dry soil surfaces based upon its vapour pressure.

In soil laboratory incubations under aerobic conditions in the dark (8-hydroxyquinoline sulfate was dosed) 8-hydroxyquinoline salts exhibited low to moderate persistence, forming no metabolites. EFSA (2013/16) states that soil studies demonstrated that the degradation rate of 8-hydroxyquinoline is rapid with the maximum DT90 value of 34 days. 8-Hydroxyquinoline sulfate is stable towards photolytic degradation. In laboratory incubations in aerobic natural sediment water systems the majority of 8‑hydroxyquinoline partitioned to sediment very quickly (maximum occurrence has been reached within one day). That was followed by a slow degradation (estimated biphasic whole system period required for 50 percent dissipation (DT50) 230 days) with formation of no major metabolites. The potential for groundwater exposure from the representative uses for 8-hydroxyquinoline sulfate was concluded to be low.

8-Hydroxyquinoline is expected to adsorb to suspended solids and sediment. The half-life for the photolytic degradation of 8-hydroxyquinoline in water ranged from 40 to 64 hours. Biodegradation in water is not an important environmental fate process.

Water solubility of 8-hydroxyquinoline is about 550 mg/L. Water solubility of 8-hydroxyquinoline sulphate is about 30 percent.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2016).

### Health considerations

In short-term toxicity studies, haematological alterations and increased relative weight of the kidneys and spleen were observed in rats (NOAEL 97.7 mg/kg bw/day) whereas no adverse effect was observed in dogs at the highest dose tested (NOAEL 100 mg/kg bw/day) (EFSA 2011).

EC Risk Classification for 8-hydroxyquinoline: mutagenic category: may cause heritable genetic damage; carcinogen category: limited evidence of a carcinogenic effect. IARC classified 8-hydroxyquinoline as Group 3: not classifiable as to human carcinogenicity.

8-Hydroxyquinoline sulfate is labelled as a mutagen by the National Institute for Occupational Safety and Health (NIOSH 2003) because it caused genetic damage in human blood cells.

Based on the available genotoxicity studies, 8-hydroxyquinoline shows genotoxic properties in vitro but no genotoxic potential in vivo relevant to humans. From the long-term studies with rats and mice, it can be concluded that 8-hydroxyquinoline has no carcinogenic properties, but important drawbacks related to limited investigations of systemic toxicity parameters were highlighted (EFSA 2011).

<http://ec.europa.eu/sanco_pesticides/public/index.cfm> quotes an ADI and ARfD of 0.05 mg/kg/d, referring to an EFSA source. The Acceptable Daily Intake (ADI), Acceptable Operator Exposure Level (AOEL) and Acute Reference Dose (ARfD) are 0.05 mg/kg bw/day, based on the rabbit developmental study and applying a safety factor of 100. EFSA (2011 and 2016). 8-Hydroxyquinoline is to be classified as toxic for reproduction category 1B, and 8-hydroxyquinoline may be considered to have endocrine-disrupting properties.

### Derivation of Maximum Acceptable Value

No MAV.

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# Imazalil

CAS No. 35554-44-0 (73790-28-0 has also been used). The IUPAC name for imazalil is (RS)-1-(β-allyloxy-2,4-dichlorophenethyl)imidazole, or allyl (RS)-1-(2,4-dichlorophenyl)-2-imidazol-1-ylethyl ether. The CAS name is 1-[2-(2,4-dichlorophenyl)-2-(2-propenyloxy)ethyl]-1H-imidazole.

The name “enilconazole” (a pharmaceutical) is approved by the World Health Organization.

### Maximum Acceptable Value

Imazalil is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Imazalil is a systemic conazole fungicide, used as an agricultural fungicide on citrus trees, for seed dressings and pre- and post-harvest application to crops. Imazalil is often found in oranges, sometimes above the NZFSA MRL. It has also been used as a disinfectant to sterilise chicken processing facilities by spraying or fumigation.

Imazalil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Imazalil was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in mandarins and oranges.

### Forms and fate in the environment

Imazalil undergoes very little hydrolysis, and has low to moderate volatility. Imazalil is highly persistent in the soil environment, with a reported field half-life of between 120 and 190 days. It adheres to particulate matter, so is not likely to reach groundwater. Any imazalil reaching natural water will be rapidly adsorbed by sediments.

In acid to neutral aqueous solutions, imazalil is stable for at least eight weeks at about 5°C. Decomposition occurs at elevated temperatures and under the influence of light. Water solubility is about 1,000 mg/L at pH 4.9, 700 mg/L at pH 6, and about 200 mg/L at pH 8.

NPIC (1994) quotes for imazalil a soil half-life of 150 days, water solubility of 1400 mg/L and a sorption coefficient (soil Koc) of 4,000. This resulted in a pesticide movement to groundwater rating of very low.

EFSA (2017) reports the geometric mean of the DT50 of imazalil in soil value is 93.2 days, therefore the DT90 value is expected to be much higher.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of imazalil in water.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Imazalil was first evaluated by the JMPR in 1977 when a temporary acceptable daily intake (ADI) of 0–0.01 mg/kg bw was established. The ADI of 0–0.01 mg/kg bw was reaffirmed in 1986 on the basis of the no-observed-adverse-effect level (NOAEL) in a two-year study in dogs. In 1991, the JMPR reconsidered imazalil and a new ADI of  
0–0.03 mg/kg bw was established based on a NOAEL for clinical signs, decreased body-weight gain and food consumption, decreased serum concentration of calcium, increased alkaline phosphatase activity, and increased liver weight in a study in dogs. In 2000, the JMPR reaffirmed the ADI and concluded that an acute reference dose (ARfD) was unnecessary (JMPR 2005).

The JMPR 2005 meeting considered that an ARfD was necessary on the basis of mortality at doses of less than 1,000 mg/kg bw, and acute clinical signs at and above 160 mg/kg bw. On the basis of the data reviewed and previous evaluations, the meeting established an ARfD of 0.05 mg/kg bw, using the NOAEL of 5 mg/kg bw per day for maternal and foetal toxicity in a study of developmental toxicity in rabbits and a safety factor of 100. It was considered that this ARfD would also be protective of the potential effects observed during gestation and lactation.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 2.5 mg/kg bw, and the ARfD is 0.05 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EC (2007) established an ADI of 0.025 mg/kg/d and an ARfD of 0.05 mg/kg. They stated that imazalil showed no potential for genotoxicity or carcinogenicity. These values are also reported in EFSA (2017).

The USEPA (1990) oral Reference Dose (RfD) for chronic exposure is 0.013 mg/kg/day-bw. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for imazalil is 1.65 mg/L.

As at September 2008 imazalil is classified by the USEPA as likely to be carcinogenic to humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Imazapyr

CAS No. 81334-34-1. The IUPAC name for imazapyr is 2-[(RS)-4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl]nicotinic acid. The CAS name is 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-3-pyridinecarboxylic acid. Imazapyr is a 1:1 mixture of the enantiomers.

### Maximum Acceptable Value

Imazapyr is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 9 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.00018 mg/L (0.18 µg/L) for imazapyr in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Imazapyr is a non-selective broad-spectrum systemic imidazolinone herbicide, used for pre- and post-emergence control of a wide range of annual grasses and broadleaf weeds, both on land and in water. It controls plant growth by preventing the synthesis of branched-chain amino acids. Imazapyr is applied either as an acid or as the isopropylamine salt (CAS No. 81510-83-0).

Imazapyr appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Four herbicides (metsulfuron methyl, haloxyfop methyl, imazapyr isopropylamine and triclopyr triethylamine (TEA)) have been approved by the New Zealand Environmental Protection Agency (EPA) for restricted use over water, by authorised agencies, under a set of conditions (Auckland City 2013; EPA 2014).

### Forms and fate in the environment

The herbicide imazapyr is an organic acid that is non-volatile and is both persistent and mobile in soil, even when used in sandy and low organic content soils. Commercial formulations contain either imazapyr acid or the imazapyr isopropylamine salt, both of which are dissolved in a water solution. Imazapyr is mainly in anionic form at typical environmental pH levels, and the behaviour of the acid and salt forms are expected to be similar. Laboratory studies show imazapyr is essentially stable to hydrolysis from pH 5 to 9, aerobic and anaerobic soil degradation, as well as aerobic and anaerobic aquatic metabolism. Field dissipation study observations are consistent with imazapyr’s intrinsic ability to persist in soils and move via run-off to surface water and to leach to groundwater.

The half-life of imazapyr is approximately three to five days in surface water. The major identified metabolites were pyridine hydroxy-dicarboxylic acid, pyridine dicarboxylic acid, and nicotinic acid also called niacin and referred to as Vitamin B3). Quinolinic acid has been detected as well.

JMPR (2013) reports: water solubility is 9,740 mg/L at 15°C, 11,100 mg/L at 25°C and 13,500 mg/L at 35°C, ie, about 1 percent. The octanol/water partition coefficient is -4 at pH 7, 20°C. In distilled water, pH 5 and pH 7 buffers, there was no detectable degradation, thus a hydrolysis half-life could not be calculated because of the stability of the compound. At pH 9 the half-life was calculated to be 325 days. The photolytic half-life is about 2.5 days. A list of metabolites is included.

NPIC (1994) quotes for imazapyr acid a soil half-life of 90 days, water solubility of 1.1 percent and a sorption coefficient (soil Koc) of 100. This resulted in a pesticide movement to groundwater rating of high.

### Removal methods

Despite its persistence in soil, the very high water solubility suggests that treatment processes that remove particulate matter should be ineffective at reducing the concentration of imazapyr in water. The newer advanced oxidation processes and/or activated carbon may be effective.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The main source of public exposure to imazapyr is most likely to be from residues in food.

Imazapyr is not likely to be a carcinogen (USEPA Group E classification) and has no known reproductive effects. In the available toxicity studies on imazapyr, there was no evidence of endocrine disruption.

PMEP (2003) states:

On an acute basis, imazapyr was not very toxic to laboratory animals by the oral, dermal or inhalation routes of exposure. Imazapyr caused very few toxicological effects in subchronic, chronic and developmental/reproductive studies in laboratory animals. The USEPA Office of Pesticide Programs established a reference dose (RfD) of 2.5 mg/kg/day for imazapyr based on a no-observed-effect level (NOEL) of 250 mg/kg/day from the chronic feeding study in dogs and an uncertainty factor of 100. This RfD has not yet been adopted by the USEPA’s *Integrated Risk Information System (IRIS)*.

The Australian Acceptable Daily Intake (ADI) for imazapyr for a human is 2.5 mg/kg/day, set for the public for daily, lifetime exposure, based on the NOEL of 250 mg/kg/day. The NOEL is based on the absence of signs of toxicity at the highest dose tested (250 mg/kg bw/day). The ADI incorporates a safety factor of 100 and was established in 1998. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The chronic dietary RfD = 2.5 mg/kg/day, based on a one-year dog feeding study, and a NOAEL = 250 mg/kg/day and an uncertainty factor of 100 (USEPA 2006). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 2.5 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for imazapyr is 17.5 mg/L (no acute one-day value available.)

EFSA (2014) also quotes an ADI of 2.5 mg/kg/day; no ARfD was deemed necessary.

The 2013 JMPR meeting established an ADI of 0–3 mg/kg bw, and decided that an ARfD is unnecessary. Reaffirmed in 2017.

### Derivation of Maximum Acceptable Value

No MAV.

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# Imazethapyr

CAS No. 81335-77-5. The IUPAC name for imazethapyr is 5-ethyl-2-[(RS)-4-isopropyl-4-methyl-5-oxo-2-imidazolin-2-yl]nicotinic acid. The CAS name is 2-[4,5-dihydro-4-methyl-4-(1-methylethyl)-5-oxo-1H-imidazol-2-yl]-5-ethyl-3-pyridinecarboxylic acid. Sometimes called Pursuit in the US.

### Maximum Acceptable Value

Imazethapyr is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Imazethapyr is a selective imidazolinone or imidazole herbicide used to control grasses and broadleaved weeds in crops. It is sometimes used in conjunction with other pesticides, eg, imazapyr (qv).

Imazethapyr appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The formulated product is stable and persistent, and does not leach through the soil. It is weakly to moderately adsorbed and is not lost from the soil through volitilisation. Soil micro-organisms do not appear to play a significant role in the degradation of the formulated product. The half-life of imazethapyr in soils may exceed a year.

In 1998, 210 water samples were collected during post-application run-off events at 75 surface-water and 25 groundwater sites in the US Midwest (USGS 2004) to gain an understanding of the occurrence of 16 sulfonylurea, sulfonamide, and imidazolinone herbicides, being the newer products for which data is relatively sparse. Imazethapyr was detected most frequently (69 percent of samples) followed by flumetsulam (62 percent) and nicosulfuron (51 percent).

PMEP (2003) reports one major degradate, 5-ethyl-3-pyridine carboxylic acid at 19.8 percent, but it was found during aqueous photolysis; however, aqueous photolysis is not considered to be a significant factor in the breakdown of the parent material.

Water solubility has been reported at about 200 and 1,000 mg/L.

NPIC (1994) quotes for imazethapyr a soil half-life of 90 days, water solubility of 20 percent and a sorption coefficient (soil Koc) of 10. This resulted in a pesticide movement to groundwater rating of very low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

EXTOXNET (1996) quotes an ADI of 0.25 mg/kg/d.

The Australian Acceptable Daily Intake (ADI) for imazethapyr for a human is 2.8 mg/kg/day, set for the public for daily, lifetime exposure, based on the NOEL of 276 mg/kg/day. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The USEPA derived a chronic RfD of 0.25 mg/kg bw based on a NOEL of 25 mg/kg/d bw and an uncertainty factor of 100 and due to the low toxicity of imazethapyr, an acute exposure dietary risk assessment is not warranted. Imazethapyr does not pose a mutagenic or genotoxic risk. The NOAEL for developmental toxicity and teratogenic effects was determined to be >1,000 mg/kg bw/day (USEPA 1990/2003 and PMEP 2003). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 2.5 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for imazethapyr is 17.5 mg/L (no acute one-day value available.)

JMPR (2016) established an ADI of 0–0.6 mg/kg bw on the basis of a NOAEL of 55 mg/kg bw per day for decreased body weight gain in females in a long-term study in rats, with application of a safety factor of 100. Taking into account the close structural similarity of OH-imazethapyr and Glu-OH-imazethapyr with imazethapyr, the meeting concluded that it would be unlikely that OH-imazethapyr and Glu-OH-imazethapyr would be of greater toxicity than imazethapyr and that these metabolites would be covered by the ADI for imazethapyr. The meeting concluded that it was not necessary to establish an ARfD for imazethapyr in view of its low acute oral toxicity and the absence of any toxicological effects, including developmental toxicity, that would likely be elicited by a single dose.

The USEPA classified imazethapyr as negative for carcinogenicity (evidence of non-carcinogenicity for humans, Group E classification) based on the absence of treatment-related tumours in acceptable carcinogenicity studies in both rats and mice.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Imidacloprid

CAS No. 138261-41-3. The IUPAC name for imidacloprid is (E)-1-(6-chloro-3-pyridylmethyl)-N-nitroimidazolidin-2-ylideneamine. The CAS name is (2E)-1-[(6-chloro-3-pyridinyl)methyl]-N-nitro-2-imidazolidinimine.

The name imidacloprid was originally approved for a mixture of (E)- and (Z)-isomers, but in 2007 the sponsor determined that the substance is comprised almost entirely of the (E)-isomer and requested that the definition be changed.

### Maximum Acceptable Value

Imidacloprid is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

In Japan the average annual environmental guideline for imidacloprid in public waters is 0.2 mg/L.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for imidacloprid in water (set by an approval under Part 5 of the HSNO Act) of 0.000038 mg/L (0.038 µg/L).

### Sources to water

Imidacloprid is a first generation [neonicotinoid](http://en.wikipedia.org/wiki/Neonicotinoids), which is a class of neuro-active insecticides, a chlorinated analogue of nicotine, in the chloronicotinyl nitroguanidine chemical family. It is marketed as [pest control](http://en.wikipedia.org/wiki/Pest_control), [seed treatment](http://en.wikipedia.org/wiki/Seed_treatment), an [insecticide](http://en.wikipedia.org/wiki/Insecticide) spray, termite control, flea control, and a [systemic insecticide](http://en.wikipedia.org/wiki/Systemic_insecticide). It is often used in conjunction with other pesticides, eg, cyfluthrin, moxidectin, permethrin, cyproconazole and mancozeb.

Imidacloprid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is a common ingredient in products for treating cats and dogs for fleas. See generic note on page 5/6 of these pesticide datasheets.

Imidacloprid was found in potatoes above the applicable MRL in the 2013/14 FRSP programme. MPI Technical Paper No: 2016/11. <http://www.mpi.govt.nz/news-and-resources/publications>

EFSA (2015) states the uses as seed treatment and soil treatment of plant protection products containing clothianidin, thiamethoxam or imidacloprid have been prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing these active substances have been prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering.

### Forms and fate in the environment

Imidacloprid is very mobile in soil and is classified by the USEPA in category I as having the highest leaching potential. Although imidacloprid is not “persistent” in the technical sense since it does degrade, it can have a half-life in soil under [aerobic](http://en.wikipedia.org/wiki/Oxygen) conditions of as long as 997 days, which is the cause of the concern over possible groundwater contamination. It has a [half-life](http://en.wikipedia.org/wiki/Half-life) of at least 30 days in aerobic water.

The soil DT50 of imidacloprid ranges from 99 to 129 days under laboratory conditions and 104 to 228 days under field conditions (EFSA 2015).

Water solubility is about 500 to 600 mg/L.

Octanol-Water Partition Coefficient (Kow): 0.57 at 21°C. Henry’s constant: 1.7 x 10-10 Pa·m3/mol. Soil Sorption Coefficient (Koc): 156 – 960, mean values 249–336.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In the human body, 96 percent of the chemical is eliminated within 48 hours; the most important degradation product is 6-chloronicotinic acid, another nicotinic neurotoxin with similar properties. Imidacloprid has also been reported to degrade into toxic, persistent, 2-chloropyridine.

A two-year feeding study in rats fed up to 1,800 ppm resulted in a No Observable Effect Level (NOEL) of 100 ppm (5.7 mg/kg body weight in males and 7.6 mg/kg in females). Adverse effects included decreased body weight gain in females at 300 ppm, and increased thyroid lesions in males at 300 ppm and females at 900 ppm. A one-year feeding study in dogs fed up to 2,500 ppm resulted in a NOEL of 1,250 ppm (41 mg/kg). Adverse effects included increased cholesterol levels in the blood, and some stress to the liver (EXTOXNET 1995).

Imidacloprid was evaluated by the JMPR in 2001 for toxicology and in 2002 and 2006 for residues. An ADI of 0–0.06 mg/kg bw/day and an ARfD of 0.4 mg/kg bw/day were established (JMPR 2008 and 2012). Reaffirmed in 2017.

USEPA (2003)quotes an acute RfD of 0.14 mg/kg/d, and a chronic RfD of 0.057 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.057 mg/kg/d, and an ARfD of 0.14 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for imidacloprid is 1.40 mg/L.

EC (2008) established an ADI of 0.06 mg/kg/d, and an ARfD of 0.08 mg/kg. As the current ARfD and AOEL for imidacloprid may not be protective enough for potential developmental neurotoxicity of this active substance, the Panel also recommends to conservatively lower these reference values to the same level as the ADI (0.06 mg/kg bw per day) (EFSA 2013a). Despite that, the ARfD was still 0.08 mg/kg in EFSA (2019).

The Australian Acceptable Daily Intake (ADI) for imidacloprid for a human is 0.06 mg/kg/day, set for the public for daily, lifetime exposure. This is based on the NOEL of 6 mg/kg/day, the level determined to show no effects during long-term exposure for the most sensitive indicators and the most sensitive species (Nufarm 2008).

As at September 2008 the USEPA has classified imidacloprid in Group E: evidence of non-carcinogenicity for humans.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for imidacloprid since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Indaziflam

CAS No. 950782-86-2 (covering both isomers). The IUPAC name for indaziflam is N2‑[(1R,2S)-2,3-dihydro-2,6-dimethyl-1H-inden-1-yl]-6-[(1RS)-1-fluoroethyl]-1,3,5-triazine-2,4-diamine. The CAS name is N-[(1R,2S)-2,3-dihydro-2,6-dimethyl-1H-inden-1-yl]-6-(1-fluoroethyl)-1,3,5-triazine-2,4-diamine. Commercial indaziflam is 95‑100 percent isomer A and 0-5 percent isomer B. The (1R)-1-fluoroethyl diastereoisomer [CAS No. 730979-19-8] and the (1S)-1-fluoroethyl diastereoisomer [CAS No. 730979-32-5] have nearly the same biological activity.

### Maximum Acceptable Value

Indaziflam is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Indaziflam is a fluoroalkyltriazine or alkylazine herbicide. A commercial product used in New Zealand is Alion 500 SC, a herbicide containing 500 g/L (50 percent) indaziflam as the active ingredient for the pre-emergent control of annual grass and broadleaf weeds in apples and grapes, applied at a maximum rate of 200 mL/ha for apples and 150 mL/ha for grapes.

Indaziflam was approved in 2016 and appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Photolysis is not a major route of degradation in soil (DT50: 11 days). Indaziflam is slightly to moderately persistent in soil under laboratory conditions (DT50: 22–176 days) and under field conditions in the United States (DT50: 9.3–71 days). The two stereoisomers showed comparable degradation behaviour in soil. Indaziflam was found to have medium to low mobility in soil (Koc 396–742 L/kg).

Indaziflam is slightly to moderately persistent in soil with biodegradation as the major route of dissipation. Volatilisation is not an important route of dissipation from soil. Indaziflam is moderately mobile in soil and is not expected to leach. Indiziflam can reach aquatic systems by run-off or spray drift. It is stable to hydrolysis but is expected to rapidly photodegrade in clear shallow water. Indaziflam rapidly partitions to sediment where it is persistent.

Three major metabolites were identified in soil: triazine indanone, carboxylic acid and diaminotriazine. Triazine indanone and carboxylic acid were not persistent; however, diaminotriazine is more persistent than its parent indaziflam (DT50: 15–320 days). The major metabolites were more mobile than the parent indaziflam (diaminotriazine Koc 10–47 L/kg; triazine-indanone Koc 183–304 L/kg; carboxylic acid Koc 29–132 L/kg).

Indaziflam is a weak acid and is stable to hydrolysis. Indaziflam is expected to degrade rapidly by photolysis in clear shallow waters (DT50 1.4 days). Two major metabolites were detected in the photolysis study: hydroxyethyl and olefin. In aquatic systems (water/sediment), indaziflam partitions rapidly from water to sediment where it is persistent (water DT50 2.7–4.8 days; whole system DT50 127–651 days). Two major metabolites were formed in the tested aquatic systems: triazine-indanone and carboxylic acid.

Based on the chemical parameters for the parent and the three degradates and the modelling, it does not appear that use of indaziflam as labelled will have a significant negative impact on groundwater (PMEP 2012).

Henry’s Law constant = 2.69 x 10-6 Pa.m3/mol at 20°C. Water/octanol partitioning coefficient: log Pow = 2.8. Water solubility is about 3 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The acute reference dose (aRfD) and Acute Population Adjusted Dose (aPAD) for indaziflam is 0.50 mg/kg body wt, based on the NOAEL of 50 mg/kg body weight from the acute neurotoxicity study in rats and an uncertainty factor of 100. In this study, decreased motor and locomotor activity was observed in females at the “lowest observed adverse effect level” (LOAEL) of 100 mg/kg body wt. The chronic reference dose (cRfD) and chronic Population Adjusted Dose (cPAD) is 0.02 mg/kg body wt/day, based on the NOAEL of 2.0 mg/kg body wt/day from the chronic toxicity study in dogs and an uncertainty factor of 100. In this study, nerve fibre degeneration in the brain, spinal cord and sciatic nerve was observed at the LOAEL of 6/7 (M/F) mg/kg body wt/day (USEPA 2010).

The acute RfD (and aPAD) was changed to 0.075 mg/kg body wt based on a subchronic gavage toxicity study in dogs where the LOAEL = 15 mg/kg/day based on axonal degenerative microscopic findings in the brain, spinal cord and sciatic nerve (USEPA 2014).

APVMA (2015) states that since the current application for registration is not associated with food producing use, no ADI or ARfD for indaziflam is required at this stage.

Fluoroethyldiaminotriazine (FDAT) is a metabolite of indaziflam.

Based on the lack of evidence of carcinogenicity or genotoxicity, the USEPA classified indaziflam as “Not likely to be carcinogenic to humans” (USEPA 2010).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Indolebutyric acid

CAS No. 133-32-4. The IUPAC name for indolebutyric acid is 4-indol-3-ylbutyric acid. The CAS name is 1H-indole-3-butanoic acid. It is also marketed as the potassium salt.

This product has been given a variety of names, including: IBA, 3-IBA, gamma-indolylbutyric acid (ERMA uses this), indolylbutyric acid, indole-3-butyric acid, 3‑indolebutyric acid, indole-3-butyric acid, indole butyric acid, 4-(3-indolyl)butyric acid, beta-indolylbutyric acid, and many trade names.

### Maximum Acceptable Value

Indolebutyric acid is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Indolebutyric acid is a naturally occurring auxin plant growth regulator, and is an ingredient in many commercial plant rooting horticultural products and is used to generate new roots in the cloning of plants through cuttings. This substance is believed to biosynthesise naturally in small concentrations in maize.

Indole-3-butyric acid enhances the growth and development of food crops and ornamentals when applied to soil, cuttings, or leaves. Because it is similar in structure to naturally occurring substances (eg, the naturally occurring plant hormone auxin or indole-3-acetic acid) and is used in tiny amounts, this plant growth regulator poses no known risks to humans or the environment (USEPA 2000).

Indolebutyric acid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

No risks to the environment are expected from use of this active ingredient because: (1) it does not harm animals or plants in the tiny amounts used (2) it acts as a plant growth enhancer (3) it does not persist in the environment (4) it is closely related to naturally occurring substances (USEPA 2000).

Water solubility is about 250 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In animals, indole-3-butyric acid is rapidly broken down to a closely related, harmless chemical that occurs naturally in living organisms.

EFSA (2014) states: A risk assessment for this active substance is in principle not required considering that the pesticide use of indolylbutyric acid is restricted to non-consumable crops within the European Union. Due to the lack of data regarding mammalian toxicology, plant and livestock metabolism and analytical methods for enforcement of residues, EFSA is not in a position to recommend any enforcement measure against the potential illegal use of indolylbutyric acid.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EFSA. 2014. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for indolylbutyric acid according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 12(7): 3748 [8 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/3748.pdf>

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# Indoxacarb

CAS No. 173584-44-6. The IUPAC name for indoxacarb is methyl (S)-N-[7-chloro-2,3,4a,5-tetrahydro-4a-(methoxycarbonyl)indeno[1,2-e][1,3,4]oxadiazin-2-ylcarbonyl]-4′-(trifluoromethoxy)carbanilate, or methyl (S)-7-chloro-2,3,4a,5-tetrahydro-2-[methoxycarbonyl(4-trifluoromethoxyphenyl)carbamoyl]indeno[1,2-e][1,3,4]oxadiazine-4a-carboxylate.

The CAS name for indoxacarb is methyl (4aS)-7-chloro-2,5-dihydro-2-[[(methoxycarbonyl)[4-(trifluoromethoxy)phenyl]amino]carbonyl]indeno[1,2-e][1,3,4]oxadiazine-4a(3H)-carboxylate.

The ISO common name indoxacarb refers to the S-enantiomer solely, being the carrier of insecticidal activity. The R-enantiomer does not carry insecticidal activity.

### Maximum Acceptable Value

Indoxacarb is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Indoxacarb is a new oxadiazine non-systemic insecticide, used for the control of certain sucking insects on (for example) apples, pears, brassica, sweet corn, lettuce and fruiting vegetables. It was developed as an organophosphate replacement. It is also used in fire ant bait in New Zealand.

Indoxacarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Indoxacarb was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007, 2009), exceeding the MRL in spinach and bok choi.

### Forms and fate in the environment

The environmental fate profile indicates no major issues in the areas of soil persistence, mobility, and fish bioaccumulation for indoxacarb or its R-enantiomer which is insecticidally inactive. Indoxacarb is considered to be moderately persistent with aerobic half-lifes ranging from 3 to 693 days and anaerobic range from 147 to 233 days. It is considered to be immobile with Kocs ranging from 3,300 to 9,600 mL/g (USEPA 2000). JMPR (2009) states the low vapour pressure (9.8 x 10-9 Pa) and Henry’s Law constant indicate that volatilisation is not a major route of dissipation. Indoxacarb is expected to be hydrolytically stable in the absence of sunlight. However, a route of degradation in water is accelerated with sunlight. In soil, both indoxacarb and its antipode are expected to be moderately persistent under both anaerobic and aerobic conditions. EFSA (2013) states that soil studies showed the degradation rate of indoxacarb is moderate; the maximum DT90 was 88 days.

See JMPR (2005) and EFSA (2018) for discussion on metabolites.

Indoxacarb hydrolysis rates in water increase with increasing pH. The half-life at pH 5, 7 and 9 were calculated to be approximately 500 days, 38 days, and one day, respectively. Water solubility is about 0.2 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See JMPR (2005).

### Health considerations

Indoxacarb has moderate to low acute and chronic toxicity and does not cause mutagenic, carcinogenic, developmental, or reproductive effects. As at September 2008, the USEPA has classified indoxacarb as “not likely to be carcinogenic to humans”.

USEPA (2004) quotes a chronic RfD of 0.02 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.02 mg/kg/d, and an ARfD of 0.09 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for indoxacarb is 0.90 mg/L.

EC (2005) established an ADI of 0.006 mg/kg/d, and an ARfD of 0.125 mg/kg. These values were confirmed in EFSA (2012 and 2013). EFSA (2018) reports the acceptable daily intake (ADI) for indoxacarb is 0.005 mg/kg bw per day based on the decreased maternal body weight gain in the developmental rat study, and applying an uncertainty factor (UF) of 100. The setting of an acute reference dose (ARfD) is proposed at 0.005 mg/kg bw based on the decreased maternal body weight gain in the developmental rat study applying an UF of 100.

JMPR (2009 and 2013) quotes the ADI as 0–0.01 mg/kg bw, and the ARfD as 0.1 mg/kg bw. It should be recognised that the ADI and ARfD applies to indoxacarb (S‑enantiomer) and its R-enantiomer.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw, and the ARfD is 0.1 mg/kg bw.

After calculating Drinking Water Levels of Concern and comparing them to the Estimated Environmental Concentrations for surface and groundwater, the aggregate exposure and risk did not exceed any of the USEPA’s levels of concern for the US population and any of the population subgroups, in particular children and infants on a chronic or acute basis.

### Derivation of Maximum Acceptable Value

No MAV.

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# Iodocarb

CAS No. 55406-53-6. Occasionally 85045-09-6 has been used. The IUPAC name for iodocarb is 3-iodoprop-2-ynyl N-butylcarbamate. The CAS name is 3-iodo-2-propynyl butylcarbamate. Also called IPBC or [iodopropynyl butylcarbamate](http://msds.chem.ox.ac.uk/IO/iodopropynyl_butylcarbamate.html).

Do not confuse with iodinated activated carbon, which has a trade name of IodocarbTM.

### Maximum Acceptable Value

Iodocarb is not mentioned in the WHO Guidelines, and it does not have a MAV in the DWSNZ.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for iodocarb in water (set by an approval under Part 5 of the HSNO Act) of 0.0001 mg/L (0.1 µg/L).

EPA established an environmental exposure limit of 0.0001 mg/L (0.1 µg/L) for iodocarb in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Iodocarb is a carbamate fungicide (mildew control), is used in wood preservatives and metalworking fluid preservative products, and for use on pruning wounds of various fruit trees, and as a preservative in many other products such as paints, stains, inks, and adhesives. IPBC was approved in 1996 for use up to 0.1 percent concentrations in topical products and cosmetics.

Often used in conjunction with other pesticides, eg, in New Zealand: cyproconazole, propiconazole, permethrin, chlorothalonil, benzalkonium chloride, carbendazim, and orthophenylphenol.

Iodocarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

IPBC is non-persistent, non-volatile and mobile in soil, but because it degrades rapidly, it is not expected to be found in drinking-water. The primary hydrolysis metabolite, propargyl butyl carbamate (PBC), has no iodine and is approximately 1,000 times less toxic to fish and invertebrates than IPBC.

IPBC degrades totally within four hours in a WWTP and IPBC will therefore not be present in the effluent. IPBC quickly degrades to PBC, iodide and iodate within the environmental compartments. Groundwater assessment for iodide and iodate show that they do not pose a risk to groundwater (ECHA 2014).

Water solubility is about 150 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The mode of action of carbamate insecticides is primarily through acetylcholinesterase inhibition. The mode of action of IPBC, a fungicide and antimicrobial ingredient, however, is not clearly known, but may be linked to iodine toxicity (CWQG 1999).

The USEPA (1997) has classified IPBC as not likely to be a human carcinogen. The NOEL for short-term and intermediate-term exposure is 200 mg/kg/d (from the subchronic dermal rat study) and the NOEL for chronic exposure is 20 mg/kg/d (from the chronic rat study). Oral intake is expected to be low because there are no food uses of iodocarb; handling paint is considered to be the main exposure route (USEPA 1997). The LD50 rat oral (female) is 1,100 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Iodomethane

CAS No. 74-88-4. The IUPAC name for iodomethane is iodomethane or methyl iodide. The CAS name is iodomethane. Sometimes called Mel.

### Maximum Acceptable Value

Iodomethane is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Iodomethane is a halogenated aliphatic fungicide, insecticide, nematicide and herbicide, and is used as a pre-plant soil treatment (fumigant). Iodomethane has only recently been approved for such uses, and is designed to replace some applications of bromomethane (methyl bromide, which is banned under the Montreal Protocol).

Iodomethane is naturally emitted by [rice](http://en.wikipedia.org/wiki/Rice) plantations in small amounts. It is also produced in vast quantities estimated to be greater than 214,000 tons annually by algae and kelp in the world’s temperate oceans and in lesser amounts on land due to terrestrial fungi and bacteria.

Iodomethane appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The high vapour pressure and low affinity for sorption on soil of iodomethane suggest that volatilisation is the most important environmental route of dissipation. Field data from iodomethane applied via broadcast shank injection to a bare-ground plot and covered simultaneously with a standard plastic tarpaulin over the treated plot suggests that 54 to 80 percent of iodomethane dissipated to the atmosphere before the tarpaulin was removed. Once volatilised into the atmosphere, iodomethane degrades rapidly due to direct photolysis and the estimated atmospheric residence time is less than 12 days (as compared with two years for methyl bromide). Therefore, iodomethane is unlikely to reach the upper atmosphere to have an impact upon the ozone layer.

The USEPA does not expect iodomethane to adversely impact groundwater or surface water. However, since iodomethane is soluble in water, there is the possibility of leaching to groundwater if slicing or removal of the tarpaulin coincides with, or is followed soon by, a rain event. Consequently, the USEPA requires cautionary language on the label prohibiting the slicing or removal of the tarpaulin if it is raining or if rain is expected within 48 hours after treatment.

Water solubility is about 14,000 mg/L (1.4 percent) at 20-25°C. The octanol/water partition coefficient: log P, = 1.51.

### Typical concentrations in drinking-water

Four water utilities in the US reported detecting iodomethane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest concentration being 0.001 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Plant metabolism studies on strawberries and tomatoes showed that iodomethane is extensively metabolised and incorporated into plant constituents, primarily carbohydrates. Iodide levels in the raw commodities were comparable to background levels found in control samples. Finite residues of toxicological concern are highly unlikely, and the pre-plant fumigant application of iodomethane is considered to be a non-food use and tolerances are not needed. The health risk to humans is related to inhalation routes.

IARC (1999) stated that methyl iodide is not classifiable as to its carcinogenicity to humans (Group 3).

The USEPA (2007) classified iodomethane as “not likely to be carcinogenic to humans in the absence of altered thyroid hormone homeostatis”.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EWG. Accessed 2011. Environmental Working Group. *National Drinking Water Database – Chemical Contaminants*. <http://www.ewg.org/tap-water/chemical-contaminants>

IARC. 1999. *Methyl Iodide* [8 pp]. <http://monographs.iarc.fr/ENG/Monographs/vol71/mono71-106.pdf>

USEPA. 1994. Methyl iodide. *Integrated Risk Information System (IRIS)*. <http://www.epa.gov/iris/subst/0650.htm>

USEPA. 2007. Iodomethane. *Pesticide Factsheet*. Office of Prevention, Pesticides and Toxic Substances [36 pp]. <http://www.epa.gov/opprd001/factsheets/>

# Iodosulfuron-methyl-sodium

CAS No. 144550-36-7. The IUPAC name for iodosulfuron-methyl-sodium is sodium ({[5-iodo-2-(methoxycarbonyl)phenyl]sulfonyl}carbamoyl)(4-methoxy-6-methyl-1,3,5-triazin-2-yl)azanide. The CAS name is sodium salt of methyl 4-iodo-2-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]benzoate. This is a derivative of iodosulfuron, CAS No. 185119-76-0.

### Maximum Acceptable Value

Iodosulfuron-methyl-sodium is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for iodosulfuron-methyl-sodium in water (set by an approval under Part 5 of the HSNO Act) of 0.016 µg/L (0.000016 mg/L).

### Sources to water

Iodosulfuron-methyl-sodium is a triazinylsulfonylurea post-emergence herbicide commonly used on cereals to control grass weeds. Iodosulfuron-methyl-sodium decomposes to iodosulfuron-methyl, the active substance. It acts as an acetolactate synthase (ALS) inhibitor. It is a component of the herbicide with the trade name Hussar which also includes mefenpyr diethyl (qv).

Iodosulfuron-methyl-sodium appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Apart from iodosulfuron-methyl, the other important metabolite is 2-amino-4-methoxy-6-methyl-1,3,5-triazine (CAS No. 1668-54-8). The half-life in soils is about one to two months. Iodosulfuron-methyl does not hydrolyse to iodosulfuron.

In soil laboratory incubations under aerobic conditions in the dark, iodosulfuron-methyl-sodium exhibited very low to moderate persistence, forming the major metabolite metsulfuron-methyl (qv), maximum 88.5 percent AR; the other metabolites are discussed. In anaerobic soil incubations iodosulfuron-methyl-sodium was degraded more slowly than under aerobic conditions. Iodosulfuron-methyl-sodium and some metabolites exhibited very high to medium mobility in soil. In laboratory incubations in dark aerobic natural sediment water systems, iodosulfuron-methyl-sodium exhibited moderate persistence; metsulfuron-methyl was a major metabolite, The potential for groundwater exposure from the representative uses by iodosulfuron-methyl-sodium and its metabolites above the parametric drinking water limit of 0.1 μg/L was concluded to be low (EFSA 2016).

Water solubility is about 20 mg/L at pH 4, 160 mg/L at pH 5, 25,000 mg/L (2.5 percent) at pH 7, and 6.5 percent at pH 9. The half-life in water at neutral pH is about one year.

EFSA (2016) reports vapour pressure = 2.6 × 10-9 Pa at 20°C; Henry’s Law constant (20°C) = 2.29 × 10-11 Pa m3 mol-1.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Following ingestion there is rapid elimination (nearly complete within 72 hours) mainly via urine between 95 percent (low dose) and 70 percent (high dose).

The dog appears to be the most sensitive animal in chronic oral studies (PMEP 2002) with a reported NOAEL of 7.3 mg/kg/day, based on depression of body weight; haematotoxic (dog) and hepatotoxic (rats, mice) effects. PMEP (2002) quotes an acute RfD of 3.15 mg/kg/d, and a chronic RfD of 0.073 mg.kg/d; the cPAD (population adjusted dose) is 0.007 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.073 mg/kg/d, and an ARfD of 3.15 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3a (page 2) – for iodosulfuron-methyl-sodium is 31.5 mg/L.

The Acceptable Daily Intake (ADI) is 0.03 mg/kg body weight (EC 2003); an ARfD was not allocated based on low acute toxicity and on developmental toxicity studies. Confirmed by EFSA (2012, 2016). EFSA (2016) set an acute reference dose (ARfD) of 3.15 mg/kg bw based on the NOAEL of 315 mg/kg bw per day for developmental toxicity (renal pelvis dilation) observed at 1,000 mg/kg bw per day in the developmental toxicity study in rats. An uncertainty factor of 100 was applied.

The Acceptable Daily Intake (ADI) adopted in Australia for iodosulfuron-methyl-sodium is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw.

The mouse carcinogenicity study was negative as was the carcinogenicity study conducted in rats. Iodosulfuron-methyl-sodium was negative for mutagenicity in various assays. The USEPA concludes that the cancer risk from exposure to iodosulfuron-methyl-sodium is negligible. EFSA (2016) stated that based on available genotoxicity studies the substance is unlikely to be genotoxic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2003. *Review Report for the Active Substance Iodosulfuron*. *SANCO*/10166/2003-Final [25 pp]. See <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for iodosulfuron according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 10(11): 2974 [28 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htmFSA>

EFSA. 2016. Peer review of the pesticide risk assessment of the active substanceiodosulfuron-methyl-sodium (approved as iodosulfuron). *EFSA Journal* 14(4): 4453 [111 pp]. <http://www.efsa.europa.eu/en/efsajournal/pub/4453>

PMEP. 2002. Iodosulfuron methyl sodium. *Pesticide Tolerance* 9/02. 40 CFR Part 180 [OPP-2002-0141 FRL-7187-2]. <http://pmep.cce.cornell.edu/profiles/herb-growthreg/fatty-alcohol-monuron/iodosulfuron/iodosulfuron_tol_902.html> or via <http://pmep.cce.cornell.edu/profiles/index.html>

# Ioxynil

CAS No. 1689-83-4. The IUPAC name for ioxynil is 4-hydroxy-3,5-diiodobenzonitrile or 4-hydroxy-3,5-diiodophenyl cyanide. The CAS name is 4-hydroxy-3,5-diiodobenzonitrile. When this substance is used as an ester or a salt, its identity should be stated, for example [ioxynil-lithium](http://www.alanwood.net/pesticides/derivatives/ioxynil-lithium.html) [CAS No. 2961-61-7], [ioxynil octanoate](http://www.alanwood.net/pesticides/derivatives/ioxynil%20octanoate.html) [CAS No. 3861-47-0], [ioxynil-sodium](http://www.alanwood.net/pesticides/derivatives/ioxynil-sodium.html) [CAS No. 2961-62-8]. Sometimes spelt ioxinil.

### Maximum Acceptable Value

Ioxynil is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Ioxynil is a broad spectrum nitrile herbicide commonly used to control broad leaved weeds in cereals, ryegrass seedcrops and turf grasses.

Ioxynil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of ioxynil in various soils at around 20°C is about one to three days, or up to 10 days in some soils; and for ioxynil octanoate about three to 10 days. It is degraded by hydrolysis and de-iodination to less toxic substances such as hydroxybenzoic acid.

Ioxynil, ioxynil octanoate and their relevant soil metabolites (3,5-diiodo-4-hydroxybenzamide and 3,5-diiodo-4-hydroxybenzoic acid) were demonstrated to decline rapidly in soil, with half-lifes (D50) <10 days. D90s are expected to be <33 days (EFSA 2010).

Ioxynil is stable in water from pH 7 to 9 for at least 10 days, at 22°C. Photolysis: ioxynil in water: the half-life is 120 hours of continuous light, with two major by-products: 3‑iodo-4-hydroxybenzonitrile and an isomer of ioxynil. Ioxynil octanoate degrades to ioxynil with a half-life of <4 days.

Henry’s Law constant for ioxynil is 1.5 x 10-5 Pa m3 mol-1 at 25°C. Henry’s Law constant for ioxynil octanoate cannot be calculated. The partition coefficient (log Pow) for ioxynil is logP = 2.2 (pH 5) and 0.23 at pH 8.7, and for ioxynil octanoate logP = 6. The dissociation constant for ioxynil is pKa = 4.1.

The water solubility of ioxynil is about 540 mg/L at pH 5, and 0.55 percent (5,500 mg/L) at pH 9. The water solubility of ioxynil octanoate is <0.03 mg/L at pH 5 to 8.7.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

EC (2004) quotes an ADI for ioxynil of 0.005 mg/kg/d based on a two-year rat study, and an ARfD of 0.04 mg/kg based on teratogenicity studies on the rat. EFSA (2010) reaffirms these values.

Ioxynil was not carcinogenic or mutagenic in animal studies (ie, does not cause cancer in animal tests). Ioxynil octanoate is classified as a category 3 teratogen: substances which cause concern for man owing to possible teratogenic effects but in respect of which the information is not adequate for making a satisfactory assessment.

The Acceptable Daily Intake (ADI) adopted in Australia for ioxynil is 0.004 mg/kg body weight, with a NOEL of 0.04 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2004. *Review Report for the Active Substance Ioxynil*. *SANCO*/4349/2000 final [98 pp]. See <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2010. Review of the existing maximum residue levels (MRLs) for ioxynil according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 8(10): 1831 [32 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/1831.pdf>

FAO. 1996. Ioxinil octanoate. *FAO Specifications for Plant Protection Products* [14 pp]. <http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/Old_specs/IOOC.pdf>

FAO. 1996. Ioxinil. *FAO Specifications for Plant Protection Products* [11 pp]. <http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Specs/Old_specs/IOXI.pdf>

# Ipconazole

CAS No. 125225-28-7. The IUPAC name for ipconazole is (1RS,2SR,5RS;1RS,2SR,5SR)-2-(4-chlorobenzyl)-5-isopropyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol. The CAS name is 2-[(4-chlorophenyl)methyl]-5-(1-methylethyl)-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol.

Ipconazole consists of two diasteroisomer pairs, a 9:1 cis-,cis-,:cis-,trans-mixture of isomers that have significantly different physical properties. The purity of the manufactured product is 955 g/kg: 875 to 930 g/kg of the cis-isomer and 65 to 95 g/kg of the trans-isomer.

CAS No. 115850-69-6 (ipconazole cc, cis isomer); CAS No. 115937-89-8 (ipconazole ct, trans isomer).

### Maximum Acceptable Value

Ipconazole is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Ipconazole, a broad spectrum, systemic conazole (triazole) fungicide, was approved for use in New Zealand in 2016 in a seed treatment fungicide (Rancona Dimension) mixed with metalaxyl. It is used to suppress soil-borne diseases in cereals and maize. Cypermethrin is mixed with ipconazole in other Rancona products.

### Forms and fate in the environment

The physical properties of the isomers are different enough that they will move through the environment at different rates.

Ipconazole degraded with half-lifes of 330 days in pH 5 buffer, 495 days in pH 7 buffer, and 257 days in a buffered pH 9 solution at 25°C. The half-life for ipconazole at 3 μg/mL in a buffered (pH 5) solution under a continuous Xenon lamp irradiated (pH 5) solution is 32 days (equivalent to ca. 64 days of natural sunlight). No degradation was detected in dark control samples (USEPA 2004).

Ipconazole, applied at 0.1 kg a.i./ha, had a first-order half-life of 330 days in North Dakota sandy loam soil at 25°C in the dark. The only major degradation product was triazole. It reached a maximum concentration of 11.85 percent of applied at 31 days post-treatment and ranged from 5.55–9.23 percent from 59 and 365 days. The estimated half-life for triazole was 495 days. No minor degradation products were identified (USEPA 2004).

The DT50 for ipconazole in five aerobic soils was calculated to be 170–593 days under normal conditions depending on the type of soil. The DT50 for ipconazole in the anaerobic soil was calculated to be 779 days (APVMA 2010).

Ipconazole is hydrolytically stable in aqueous solution, with the half-life being considered to be greater than one year. Ipconazole is also not considered to be readily biodegradable in water. However, ipconazole degraded upon irradiation in water, with the half-life calculated to be 32.1 days at pH 5 and 25 ± 1°C. Given the slow metabolism, photolysis may be a significant degradation pathway for ipconazole (APVMA 2010).

In a dark water-sediment study conducted on two natural aerobic aquatic systems, ipconazole dissipated rapidly from the water phase and was found predominantly in the sediment phase of both systems. No major metabolites were detected in water or sediment. Ipconazole is not likely to be found in groundwater (EFSA 2013).

Water solubility: the cis-cis isomer = 9 mg/L and the cis-trans isomer = 5 mg/L. The octanol/water partition coefficients, Log(KOW), are cis-cis isomer = 4.6, and cis-trans isomer = 4.4. Henry’s Law constant = 3 x 10-5 Pa m3 mol-1. Partition coefficient = LogPow = 4.3.

APVMA (2010) discusses metabolites.

### Removal methods

Water treatment processes that remove particulate matter should reduce the concentration of ipconazole in water.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

EFSA (2013) discusses the analysis of ipconazole, and the metabolites triazole alanine, triazole acetic acid, and triazole pyruvic acid.

### Health considerations

It is unknown whether just one or both isomers that are present in technical grade ipconazole are biologically active, or the extent to which they differ in biological activity. The toxicity data were developed on tests performed with technical grade ipconazole.

Neither an acute nor chronic dietary RfD was established because the proposed registration is for a non-food use (USEPA 2004).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.015 mg/kg body weight, with a NOEL of 1.5 mg/kg bw based on a one-year dietary study in dogs, using a default 100-fold safety factor. No ARfD is required to be established, as ipconazole is not considered likely to present an acute hazard (including developmental toxicity) to humans.

The proposed Acceptable Daily Intake (ADI) is 0.015 mg/kg bw per day, based on the subchronic (one-year) NOAEL of 1.5 mg/kg bw per day in dogs, with an uncertainty factor (UF) of 100; the Acute Reference Dose (ARfD) and the Acceptable Operator Exposure Level (AOEL) are 0.015 mg/kg bw (per day) as well, but they are derived from the rat developmental toxicity NOAEL with an UF of 200 (the majority of the experts decided to have the same margin as with the ADI between the reference values and the teratogenic effects occurring at 10 mg/kg bw per day, therefore an increased UF was applied). The ADI for triazole alanine is 0.1 mg/kg bw per day. The ADI for triazole acetic acid is 0.02 mg/kg bw per day. The ARfD for triazole alanine is 0.1 mg/kg bw per day. The ARfD for triazole acetic acid is 0.06 mg/kg bw per day (EFSA 2013). See datasheet for triazole metabolites for latest ADI and ARfD.

Ipconazole belongs to the class of chemicals known as triazoles and several chemicals in this class have induced liver tumours in mice. The developmental toxicity LOAEL for ipconazole in rats is 30 mg/kg/day based on decreased fetal body weight and increased incidences of visceral and skeletal variations. The developmental toxicity NOAEL is 10 mg/kg/day. Ipconazole testing indicates it is not mutagenic (USEPA 2004).

Ipconazole did not show a potential for genotoxicity, or carcinogenicity. The chemical was neither a reproductive nor a developmental toxicant (APVMA 2010).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2010. *Public Release Summary on the Evaluation of the New Active Ipconazole in the Product Rancona C Seed Treatment*. APVMA Product Number 63309 [58 pp]. <http://apvma.gov.au/sites/default/files/publication/13836-prs-ipconazole.pdf>

EFSA. 2013. Conclusion on the peer review of the pesticide risk assessment of the active substance ipconazole. *EFSA Journal* 11(4): 3181 [76 pp]. https://www.efsa.europa.eu/en/efsajournal/pub/3181

USEPA. 2004. Ipconazole. *Pesticide Factsheet* [14 pp]. <https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/fs_PC-125618_01-Sep-04.pdf>

# Iprodione

CAS No. 36734-19-7. The IUPAC name for iprodione is 3-(3,5-dichlorophenyl)-N-isopropyl-2,4-dioxoimidazolidine-1-carboxamide. The CAS name is 3‑(3,5‑dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide. Has previously been called glycophene and promidione.

### Maximum Acceptable Value

Iprodione is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

In Japan the average annual environmental guideline for iprodione in public waters is 0.3 mg/L.

### Sources to water

Iprodione is a non-systemic [dicarboximide](http://en.wikipedia.org/wiki/Neonicotinoids) fungicide used to control a wide variety of crop diseases. It inhibits the germination of spores and the growth of the fungal mat (mycelium). NZFSA has often found iprodione in nectarines.

Iprodione appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is sometimes used in formulations with other fungicides such as thiabendazole and carbendazim (qv). The EC (2002) supported the use of iprodione for use on vines, fruits, vegetables, arable crops, ornamentals, turf and for seed treatment.

Iprodione was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the default MRL in strawberries, cucumbers, capsicums and courgettes. It has also been found in wine.

### Forms and fate in the environment

Half-life in aerobic soil is about 64 days, anaerobic soil 32 days, hydrolysis in water five days. A major breakdown product (and possible impurity) of health concern is 3,5‑dichloroaniline (qv). JMPR (2006) states that 3,5-dichloroaniline does not show toxicity that is qualitatively different from iprodione. The main breakdown product is [(dichloro-3,5 phenyl)-1 isopropyl carbamoyl-3]-2-acetic acid.

If released to soil, iprodione is expected to have moderate mobility based upon a Koc of 700. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 3.12 x 10-9 atm-cu m/mole. Iprodione is not expected to volatilise from dry soil surfaces based upon its vapour pressure. The US Department of Agric’s Pesticide Properties Database lists a soil half-life of 14 days for iprodione, however in acclimated soil, the half-life can be as low as two days; in non-acclimated soil, the half-life can be >35 days. If released into water, iprodione is expected to adsorb to suspended solids and sediment based upon the Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. An estimated BCF of 41 suggests the potential for bioconcentration in aquatic organisms is moderate. The high rate of hydrolysis however should be considered, especially when determining BCF. Under basic conditions, iprodione will rapidly hydrolyse decreasing the potential for bioconcentration. Based upon experimental measurements at 60°C and conversion to pseudo first-order rate constants at 25°C, the aqueous hydrolysis half-lifes of iprodione at respective pHs of 3, 5, 7, and 9 are 545.2, 37.4, 1.1, and 0.015 days (EAWAG accessed February 2015).

NPIC (1994) quotes for iprodione a soil half-life of 14 days, water solubility of 14 mg/L and a sorption coefficient (soil Koc) of 700. This resulted in a pesticide movement to groundwater rating of low.

EC (2002) requires particular attention to the potential for groundwater contamination when the active substance is applied at high use rates (in particular, use in turf) on acidic soils (pH below 6) under vulnerable climatic conditions.

EFSA (2013) states that the DT90 values of iprodione and its relevant soil metabolite (RP30228) are expected to range between 85–90 days.

In soil laboratory incubations under aerobic conditions in the dark, iprodione exhibited moderate to high persistence, forming the major metabolite RP35606 (maximum 25.5 percent AR after seven days) which exhibited low to moderate persistence, the metabolite RP30228, a constitutional isomer of iprodione (maximum 29.5 percent AR after 30 days) which exhibited moderate to medium persistence, the metabolite RP36221 (maximum 12.7 percent AR after 100 days), which exhibited high to very high persistence, and the metabolite RP 32596 (maximum 12.6 percent AR after 120 days), which exhibited moderate to high persistence. Degradation of iprodione was slower in acidic soils (EFSA 2016).

The potential for groundwater exposure by metabolite RP35606 (in acidic soils only), and by metabolite RP30181 is predicted to be high over a wide range of geoclimatic conditions represented by the Forum for the Co-ordination of Pesticide Fate Models and their Use (FOCUS) groundwater scenarios (EFSA 2016).

In laboratory incubations in dark aerobic natural sediment water systems, iprodione exhibited low persistence, forming metabolites RP35606 (maximum 73.3 percent AR in water but only maximum 4.0 percent in sediment), and metabolite RP30228 (maximum 10.3 percent in water and maximum 79.2 percent in sediment) (EFSA 2016).

Water solubility is about 12–13 mg/L. At pH 9 it is unstable.

### Typical concentrations in drinking-water

Many groundwater studies have been conducted (USEPA 1998), and iprodione has often been detected but at less than 0.0001 mg/L.

### Removal methods

There are no reports of removal of iprodione from water. However, it is expected that some of the newer advanced oxidation processes may be effective. EFSA (2016) considers this to be a data gap.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2016).

### Health considerations

Rats given dietary doses of approximately 60 mg/kg/day over 18 months suffered no ill effects. Dogs fed approximately 60 mg/kg/day over 18 months also showed no adverse effects. Beagle dogs fed dietary doses of about 2.3 mg/kg/day for one year showed liver and kidney weight increases. At doses starting at about 1.5 mg/kg/day, the dogs had decreased prostrate weights and changes within red blood cells (damage to the haaemoglobin molecules). Females also had slight decreases in uterus weights. No effects were noted below 0.5 mg/kg/day dose (EXTOXNET 1996).

Exposure guidelines in EXTOXNET (1993) are: NOEL 4.2 mg/kg (rat); ADI 0.3 mg/kg (human); RfD 0.042 mg/kg/day. EXTOXNET (1996) states ADI: 0.2 mg/kg/day, RfD 0.04: mg/kg/day.

USEPA (1998) established an acute RfD of 0.06 mg/kg/d, and a chronic RfD of 0.02 mg/kg/d, the latter based on a NOEL of 6.1 mg/kg/day from a rat combined chronic toxicity/carcinogenicity study based on histopathological lesions in the male reproductive system and effects on the adrenal glands in males at 12.4 and in females at 16.5 mg/kg/day (LOEL). The NOEL was adjusted with an uncertainty factor of 300. The oral RfD had earlier been 0.04 mg/kg/d (USEPA 1991). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for iprodione is 1.65 mg/L.

Iprodione has been reviewed by the FAO/WHO Joint Committee Meeting on Pesticide Residues (JMPR). The World Health Organization (WHO) established an acceptable daily intake (ADI) of 0.3 mg/kg/day in 1977. This ADI was revised to 0.2 mg/kg/day in 1992.

EC (2002) report the lowest relevant NOAEL to be 6.1 mg/kg bw/d (two-year rat study) from which they derived an ADI of 0.06 mg/kg/d. They considered an ARfD was unnecessary.

JMPR allocated an ADI of 0–0.06 mg/kg bw/d, based on an NOAEL of 6 mg/kg bw per day derived from a two-year study of carcinogenicity in rats and a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.04 mg/kg body weight, with a NOEL of 4 mg/kg bw based on a one-year dietary study in dogs. The NOEL is based on changes in organ weights and haematological parameters at 25 mg/kg bw/day. The ADI incorporates a safety factor of 100.

As at September 2008 the USEPA has classified iprodione as likely to be carcinogenic to humans, B2. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

The toxicological profile of iprodione was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.06 mg/kg bw per day. No ARfD was deemed necessary. In view of the formation of 3,5-dichloroaniline after the use of iprodione, EFSA is of the opinion that the toxicological relevance of 3,5-dichloroaniline needs to be further investigated and if necessary, specific toxicological reference values have to be derived (EFSA 2012 and 2013).

USEPA (2015) found that based on weight of evidence considerations there is no convincing evidence of an interaction with the thyroid pathway. Overall, based on the weight of the evidence there appears to be a potential for iprodione to alter steriodogenesis, which may affect the estrogen and androgen pathways in mammals and wildlife. However, mammalian EDSP Tier 2 testing is not recommended for iprodione since additional testing is not expected to impact EPA’s current regulatory point of departures and endpoints for human health risk assessments.

EFSA (2016) refers to a genotoxicity concern for the major residue metabolite RP30228. Since 2013 the ADI has been adjusted to 0.02 mg/kg/d, and an ARfD has been established at 0.06 mg/kg bw based on the LOAEL of 20 mg/kg bw per day for increased incidence of umbilical hernia observed in the developmental toxicity study in rabbits. An additional UF of 3 to the standard 100 considering the use of a LOAEL was applied. Metabolite 3,5-dichloroaniline (RP32596) is unlikely to be genotoxic; its ADI is 0.0005 mg/kg bw per day, based on the NOAEL of 1 mg/kg bw per day for anaemic changes observed in the 90-day study in rats, applying an UF of 2,000. The ARfD is 0.0075 mg/kg bw, based on the NOAEL of 7.5 mg/kg bw per day for haematological changes from the 28-day study in rats applying an UF of 1,000. Reference values of 3,5‑dichloroaniline are also applicable to metabolite M610F007. No conclusion could be reached regarding the genotoxic potential or toxicological profile of RP25040, RP37176 and RP 36112. Metabolites RP36221 and LS720942 are unlikely to be genotoxic. However, no conclusion was reached regarding their toxicological profile. No data on metabolite RP35606 or RP30181 predicted to occur in groundwater above 0.1 μg/L are available (data gap). The metabolites are considered relevant due to the proposed classification for parent compound by the peer review experts as carcinogenic and toxic for the development and reproduction leading to a critical area of concern.

### Derivation of Maximum Acceptable Value

No MAV.

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# Iprovalicarb

CAS No. 140923-17-7. The IUPAC name for iprovalicarb is isopropyl 2-methyl-1-{[(RS)-1-p-tolylethyl]carbamoyl}-(S)-propylcarbamate. The CAS name is 1-methylethyl [(1S)‑2‑methyl-1-[[[1-(4-methylphenyl)ethyl]amino]carbonyl]propyl]carbamate.

Iprovalicarb occurs as the diastereoisomers SR and SS; the ratio of the diastereoisomers is approximately 1:1.

### Maximum Acceptable Value

Iprovalicarb is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Iprovalicarb is a fairly new carbamate (amino acid amide carbamate or valinamide) systemic fungicide, often used to control grapevine downy mildew (Plasmopara viticola), and downy mildew or blight in tomatoes, potatoes, onions and other vegetables. It is a lipid synthesis inhibitor.

Iprovalicarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](https://eatsafe.nzfsa.govt.nz/web/public/acvm-register%20and%20select%20entire%20register)).

### Forms and fate in the environment

Significant residues are found in soil and water after 100 days, half-life ranging from 1.8 to 69 days depending on soil type. The major metabolites are iprovalicarb-carboxylic acid and p-methyl-phenethylamine, also called 2‑(4‑methylphenyl)ethanamine or PMPA, which has moderate to very high persistence, and has been determined to be toxicologically significant due to its moderate acute toxicity when administered orally to rats (EFSA 2015).

Although iprovalicarb is highly mobile in soil, no problems concerning groundwater contamination will be expected from iprovalicarb or iprovalicarb-carboxylic acid. Water solubility (unaffected by pH) is about 18 mg/L at 20°C (mixed isomers; the SR isomer is about twice as soluble as the SS isomer).

### Typical concentrations in drinking-water

The metabolite PMPA may occur in groundwater above 0.1 μg/L (EFSA 2015).

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2015).

### Health considerations

The lowest relevant NOAEL for short-term toxicity based on a 28-day oral study on dogs is 3 mg/kg/d. EC (2002) quote an ADI of 0.015 mg/kg on the basis of the liver toxicity observed in male dogs at 2.62 mg/kg bw per day where a NOAEL was not identified in the 53-week dog study. A standard uncertainty factor (UF) of 100 plus an additional UF of 2 was applied to take into account the lack of a NOAEL. An ARfD was not allocated due to low acute toxicity. These values were reaffirmed by EFSA (2011 and 2015).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0262 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for iprovalicarb is 0.183 mg/L (no acute one-day value available.)

In accordance with the USEPA Draft Guidelines for Carcinogen Risk Assessment (July, 1999) the Agency has classified iprovalicarb into the category “likely to be carcinogenic to humans”. Iprovalicarb is not mutagenic and unlikely to be genotoxic. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. EFSA (2015) states that iprovalicarb is proposed to be classified as carcinogenic category 2 but not classified or proposed to be classified as toxic for reproduction category 2.

No endocrine disruption potential was observed in the two-generation reproduction study, developmental toxicity studies, subchronic feeding studies, and chronic feeding studies.

### Derivation of Maximum Acceptable Value

No MAV.

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# Irgarol

CAS No. 28159-98-0. Irgarol is the trade name for 2-(tert-butylamino)-4-(cyclopropylamino)-6-(methylthio)-s-triazine. The IUPAC name for irgarol is N‑tert‑butyl-N’-cyclopropyl-6-(methylthio)-1,3,5-triazine-2,4-diamine. The USEPA calls it N‑cyclopropyl-N’-(1,1-dimethylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine. Also known as cybutryne, and various trade names.

Irgarol 1051 is an algicide intended for use in formulating antifouling paints for boats and vessels only. Irgarol 1071 is an algicide intended for use in the manufacture of aqueous and solvent coating compositions: paints, coatings, stucco, stains, and caulks for outdoor uses to inhibit or control the growth of algae on coating surfaces (PMEP 1996).

### Maximum Acceptable Value

Irgarol is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for irgarol in water (set by an approval under Part 5 of the HSNO Act) of 0.000024 mg/L (0.024 µg/L).

EPA established an environmental exposure limit of 0.000024 mg/L (0.024 µg/L) for irgarol in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Irgarol inhibits photosynthesis. It is used in long-life antifouling coatings for marine applications to prevent the growth of algae, and has comparatively low biological activity to fish, shellfish and humans. In antifouling paints, it is often combined with copper compounds, such as cuprous oxide, or copper thiocyanate (CAS No. 1111‑67‑7), where irgarol may comprise as little as 2 percent.

Irgarol does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It is also on the Timber Preservatives, Antisapstains and Antifouling Paints Transfer Notice.

In June 2013 EPA stated that antifouling paints containing irgarol will no longer be able to be manufactured in or imported into New Zealand as the approvals to do so have been declined. See EPA (2013).

Considering that use of cybutryne is restricted to commercial coastal and ocean-going vessels treated in a floating dock or marine lift (in the open air, on a hard standing area, enshrouded), no direct emissions to soil or groundwater are expected from the use of cybutryne in antifouling products. Predicted concentrations in soil and groundwater are therefore considered negligible (ECHA 2015).

### Forms and fate in the environment

Two main degradation processes for Irgarol 1051 were identified: microbial metabolism and photolysis. The speed of the degradation in the natural environment depends on various factors, the most important ones being temperature, the microbial activity of the environment (sediment and water) and presence of daylight. The half-life of the active substance and each major degradation metabolite was found to vary typically between one and three months. The metabolites are less biologically active than the parent irgarol.

PMEP (1996) states: Irgarol is stable. There was no hydrolysis in either fresh or salt water. EPA considered the aqueous photolysis to be stable with a half-life ranging from 35.9 to 84.8 days. Anaerobic and aerobic aquatic metabolism were considered stable. Adsorption/desorption studies on clay loams indicated half-lives of 502–548 days, and 820–956 days on sandy loam.

Irgarol has been found in water and sediment around marinas and in ponds (Mohr et al 2011).

See Hall et al (1999), Gardinali (2005) and ERMA for comments on environmental issues. Because of environmental issues, the use of irgarol on ship hulls (>25 m) has been banned in Denmark since 2003. Leaching from buildings is a major source to natural waters (Burkhardt et al 2008).

The water solubility of irgarol is 7 mg/L.

### Health considerations

No information available on the effects of oral intake by humans. PMEP (1996) states that Irgarol was not toxic in a 90-day rat feeding study, and did not cause teratogenic effects in a rat development toxicity study, or local systemic effects in a 21-day rat dermal exposure study. Irgarol was negative in a battery of genotoxicity tests.

ECHA (2015) reported that in repeated dose studies in rat with cybutryne, the predominant effects were reduced food consumption and body weight at higher doses. Neither genotoxic nor a carcinogenic potential was identified in a number of studies. A NOAEL of 2.7 mg/kg bw/day was derived, in which the effects in the gastrointestinal tract were considered local.

### Derivation of Maximum Acceptable Value

No MAV.

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# Isazofos

CAS No. 42509-80-8. The IUPAC name for isazofos is O-5-chloro-1-isopropyl-1H-1,2,4-triazol-3-yl O,O-diethyl phosphorothioate. The CAS name is O-[5-chloro-1-(1-methylethyl)-1H-1,2,4-triazol-3-yl] O,O-diethyl phosphorothioate. Isazophos-methyl has CAS No. 42509-83-1.

### Maximum Acceptable Value

Isazofos does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Isazofos is a triazole organothiophosphate insecticide and nematicide.

Isazofos appears on EPA’s 27 June 2013 list of organophosphate and carbamate (OPC) pesticides which no longer are able to be manufactured in or imported into New Zealand. There did not appear to be any current usage of the product in New Zealand.

### Forms and fate in the environment

If released to soil, isazofos is expected to have high to moderate mobility based upon Koc values ranging from 91.3 to 385. Volatilisation from moist soil surfaces is expected based upon a Henry’s Law constant of 5.21 x 10-7 atm-cu m/mole. Isazofos was reported to have a half-life in soil of 10 days in laboratory studies. Field half-lifes of 2.5 to 48.4 days have been reported. A half-life of 40 days at 25°C has been reported for photolysis of isazofos on soil (pH 5). If released into [water](https://pubchem.ncbi.nlm.nih.gov/compound/water), isazofos may be expected to adsorb to suspended solids and sediment based upon its Koc values. Volatilisation from [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) surfaces is expected based upon this compound’s Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 270 and 2,000 days, respectively. An estimated BCF of 170 suggests the potential for bioconcentration in aquatic organisms is high. Isazofos is hydrolysed more rapidly in alkali than in acids; half-lifes were calculated at 20°C as 85 days (pH 5), 48 days (pH 7), and 19 days (pH 9). A half-life of four days at 25°C has been reported for photolysis of isazofos in [water](https://pubchem.ncbi.nlm.nih.gov/compound/water) (pH 7.5).

The water solubility of isazofos is 69 mg/L at 20°C.

### Health considerations

No information.

### Derivation of Maximum Acceptable Value

No MAV..

### Bibliography

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# Isoproturon

CAS No. 34123-59-6. The IUPAC name for isoproturon is 3-(4-isopropylphenyl)-1,1-dimethylurea or 3-p-cumenyl-1,1-dimethylurea. The CAS name is N,N-dimethyl-N′-[4-(1-methylethyl)phenyl]urea. Occasionally seen written as IPU.

### Maximum Acceptable Value

Based on health considerations, the concentration of isoproturon in drinking-water should not exceed 0.01 mg/L.

### Sources to water

Isoproturon is a substituted urea (or phenylurea) used as a selective systemic post-emergence herbicide for the control of grass and broadleaf weeds in winter and spring wheat and barley.

Isoproturon appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 72.9 tonnes of isoproturon were used in New Zealand in 2004, at an application rate of 1,500 grams of active ingredient per hectare. As at 2007 its use is being phased out; every year IPU is identified by the UK’s Environment Agency as one of the top pesticides polluting water (*Pesticide News* March 2009).

JMPR (1990) states that the ortho and meta isomers may appear as impurities, up to 10 and 20 g/kg respectively. EFSA (2015) considers N-nitroso-dimethylamine is a potential relevant impurity at a maximum content of 0.2 mg/kg.

### Forms and fate in the environment

Isoproturon shows high mobility in soils, has a low tendency to [adsorb](http://www.marbef.org/wiki/Adsorption) to soils, and has been detected in surface and groundwater overseas. In anaerobic soil incubations isoproturon was essentially stable. It is quite persistent in water and hydrolyses slowly with a half-life of about 30 days. Due to its low affinity for organic matter it is not expected to have a high tendency towards [bioaccumulation](http://www.marbef.org/wiki/Bioaccumulation) or [biomagnification](http://www.marbef.org/wiki/Biomagnification). It undergoes photolysis, biodegradation and hydrolysis in soil with a half-life of up to 40 days. See EFSA (2011/2015) for a list of metabolites, some of which can occur in groundwater above 0.0001 mg/L.

The water solubility of isoproturon is 70 mg/L. Henry’s Law constant is 1.46 x 10–5 Pa m3 mol-1.

### Typical concentrations in drinking-water

No data are available on the concentration of isoproturon in New Zealand drinking-water supplies.

In Germany, concentrations between 0.0001 and 0.000125 mg/L (0.1 and 0.125 g/L) have been found in surface waters.

Levels above 0.0001 mg/L (0.1 g/L) have been found in drinking-waters in the UK, where it was the most heavily used pesticide in the late 1900s.

Isoproturon has been detected in surface water and groundwater, usually at concentrations below 0.0001 mg/L; levels above 0.0001 mg/L have occasionally been detected in drinking-water (WHO 2004/2017).

### Removal methods

No information on methods of removing isoproturon from water is available. However, chlorine has been reported to be effective in the break down of this family of pesticides. Slow sand filtration has no effect on the concentrations of these pesticides. WHO (2004/2011/2017) states that concentrations down to 0.0001 mg/L should be achievable using ozonation.

### Recommended analytical techniques

#### Some alternative methods

No alternative methods have been recommended for isoproturon because no methods meet the required criteria. However, the following information may be useful:

WHO (2003) states that isoproturon may be determined in water samples by separation with reverse-phase high-performance liquid chromatography and ultraviolet or electrochemical detection. Detection limits between 0.00001 and 0.0001 mg/L (10–100 ng/L) have been reported. High levels of phenoxyacidic herbicides may interfere with the determination of isoproturon.

### Health considerations

Isoproturon is absorbed readily and rapidly when given orally. Distribution is rapid, and no accumulation of isoproturon in any particular organ or tissue has been reported. Isoproturon is metabolised and excreted rapidly by the rat.

Isoproturon is of low acute oral toxicity and low to moderate toxicity following short-and long-term exposures in mammals. It does not cause skin and eye irritation or sensitisation after repeated skin exposure. It does not possess significant genotoxic activity, but it causes marked enzyme induction and liver enlargement. Isoproturon caused an increase in hepatocellular tumours in male and female rats, but this was apparent at doses which also caused liver toxicity. Isoproturon appears to be a tumour promoter, rather than a complete carcinogen.

Isoproturon has been in commercial use for a relatively short period, and so far no cases of human poisoning have been reported. Data on human health effects of isoproturon are limited to studies involving occupational exposures. One three-year study was carried out on a group of workers employed in various parts of the manufacturing process. Following urine and blood analysis, the authors reported no pathological abnormalities in the peripheral blood count or any indication of haemolytic anaemia.

EC (2002) quotes the short-term and long-term NOEALs to be 3 mg/kg/d from which an ADI of 0.015 mg/kg was derived; isoproturon is said to cause hepatocellular tumours and cholangiocarcinomas in rats. An ARfD was deemed unnecessary. EFSA (2011) reaffirmed these values. EFSA (2015) reaffirmed the ADI but agreed to set an ARfD based on haematological effects observed in short-term dog studies since the onset of these effects can be acute. The agreed ARfD is 0.1 mg/kg bw based on the NOAEL of 10 mg/kg bw per day for haematological effects observed at 38 mg/kg bw per day in the dog studies (ie, increased Heinz body formation at four weeks in the first 90‑day dog study and methaemoglobin formation at the end of the second 90‑day dog study). An uncertainty factor of 100 was applied.

### Derivation of Maximum Acceptable Value

As isoproturon is considered to be a tumour promoter rather than a complete carcinogen, a tolerable daily intake approach has been used for the derivation of the MAV. The no-observable-adverse-effect level used in the derivation of the MAV is from a study in dogs and a two-year feeding study in rats.

The MAV for isoproturon in drinking-water was derived as follows:

3 mg/kg body weight/day x 70 kg x 0.1 = 0.011 mg/L (rounded to 0.01 mg/L)

2 L/day x 1,000

where:

* no-observable-adverse-effect level = 3 mg/kg body weight per day a 90-day study in dogs and a two-year feeding study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 because there is evidence of non-genotoxic carcinogenicity in rats).

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# Isopyrazam

CAS No. 881685-58-1 (syn-isomer: 683777-13-1 and anti-isomer: 683777-14-2). The IUPAC name for isopyrazam is mixture of 2 syn-isomers: 3-(difluoromethyl)-1-methyl-N-[(1RS,4SR,9RS)-1,2,3,4-tetrahydro-9-isopropyl-1,4-methanonaphthalen-5-yl]pyrazole-4-carboxamide and 2 anti-isomers 3-(difluoromethyl)-1-methyl-N-[(1RS,4SR,9SR)-1,2,3,4-tetrahydro-9-isopropyl-1,4-methanonaphthalen-5-yl]pyrazole-4-carboxamide. The CAS name is 3-(difluoromethyl)-1-methyl-N-[1,2,3,4-tetrahydro-9-(1-methylethyl)-1,4-methanonaphthalen-5-yl]-1H-pyrazole-4-carboxamide.

The ratio of syn- to anti-isomers should be stated. Both are biologically active and the specification for technical isopyrazam covers the range of syn:anti-isomer content of 70 percent syn:30 percent anti to 100 percent syn.

### Maximum Acceptable Value

Isopyrazam does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Isopyrazam is a new broad spectrum amide or pyrazole or pyrazole carboxamide fungicide, used for the control of a wide range of fungal diseases in cereals, eg, barley, oats and wheat.

Isopyrazam appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

The soil half-life for seguris flexi (of which 13.1 percent is isopyrazam) is reported at 70 days, and 21 days in water (Syngenta Safety Data Sheet). The soil half-life for isopyrazam ranges from 90 to 760 days (EFSA 2012). EFSA (2013) states that soil studies demonstrated that isopyrazam is highly persistent in the soil; the maximum DT90f was up to 2,089 days.

Isopyrazam exhibits medium to very high persistence in soil under laboratory aerobic conditions with no change in the proportion of syn- and anti- isomer pairs. Two major soil metabolites CSCD460260 and CSCD465008 were identified to require further consideration with respect to groundwater contamination. Groundwater metabolites CSCD459488 and CSCD459489 were found relevant according to the guidance document on the EC assessment of groundwater metabolites, resulting in the identification of a critical area of concern as they exceeded 0.1 μg/L in the majority of the scenarios (EFSA 2012).

Water solubility of the isopyrazam isomers is between 0.5 and 1 mg/L. The metabolites are considerably more soluble (EFSA 2012).

JMPR (2011) reports: vapour pressure (syn-isomer) 2.4 x 10-7 Pa at 20°C (anti-isomer) 2.2 x 10-8 Pa. Henry’s Law constant (syn-isomer) = 1.9 x 10-4 Pa.m3/mol (anti-isomer) = 3.7 x 10-5 Pa.m3/mol. Water solubility (syn-isomer) = 1.05 mg/L (anti-isomer) = 0.55 mg/L. n-Octanol/water partition coefficient = log Pow = (syn-isomer) = 4.1 (anti-isomer) = 4.4. Hydrolysis: stable for 30 days at pH 5 to 9. Photolysis in natural water DT50 = 4.5 days.

### Removal methods

Because the main dissipation route of isopyrazam in aquatic systems is by partition to sediment, treatment processes that remove particulate matter should reduce the level of isopyrazam in water.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2012).

### Health considerations

Syngenta states that isopyrazam did not show mutagenic effects in animal experiments. Increased levels of liver and uterine tumours were observed at high doses in female rats. Animal testing did not show any effects on fertility. There was evidence of developmental toxicity (reduction of foetal weight) and embryolethality in rabbits.

Isopyrazam is reported to have low acute oral toxicity. The USEPA adopted an acute RfD of 0.3 mg/kg/d based on a NOAEL of 30 mg/kg/d and an uncertainty of 100. Chronic dietary (food only) risk assessments for parent isopyrazam plus metabolite CSCD459488 were performed for all population subgroups using a chronic reference dose (cRfD) of 0.055 mg/kg-bw/day, based upon a two-year study in rats with a no observed adverse effect level (NOAEL) of 5.5 mg/kg-bw/day and an uncertainty factor of 100X.

The JMPR 2005 meeting established an ADI of 0–0.06 mg/kg bw derived from the NOAEL of 5.5 mg/kg bw per day in the 104-week rat feeding study on the basis of decreased body weight gain in females and foci of eosinophilic hepatocytes and clinical chemistry changes (triglycerides, bilirubin) of equivocal toxicological significance in both sexes at 27.6 mg/kg bw per day. A safety factor of 100 was applied. The ADI is supported by the NOAEL of 9.9 mg/kg bw per day in the mouse 80-week feeding study, based on periportal hepatocellular hypertrophy in females at 500 ppm (equal to 56.2 mg/kg bw per day). The margin between the maximum ADI and the LOAEL at 232.8 mg/kg bw per day for uterine and liver tumours in female rats is approximately 3,900 (FAO 2005). This ADI (sum of isomers) was reaffirmed in JMPR (2011).

The JMPR 2005 meeting established an ARfD of 0.3 mg/kg bw derived from the NOAEL of 30 mg/kg bw in the rat acute neurotoxicity study, on the basis of nonspecific clinical signs of toxicity (weak appearance and decreased activity) at 250 mg/kg bw. A safety factor of 100 was applied. In a rat developmental toxicity study, the NOAEL of 20 mg/kg bw per day for maternal and developmental toxicity was based on reduced body weight gain in dams only on day 4 of treatment. The margin between the ARfD and the LOAEL at 500 mg/kg bw per day for teratogenic effects (microphthalmia) in rabbits is approximately 1,700 (FAO 2005). This ARfD (sum of isomers) was reaffirmed in JMPR (2011).

In accordance with the USEPA’ s Final Guidelines for Carcinogen Risk Assessment (March 2005), isopyrazam is classified “likely to be carcinogenic to humans”. This classification is based on the presence of thyroid follicular cell tumours in male rats, and liver and uterine tumours in female rats at doses that were adequate to evaluate the carcinogenic potential of isopyrazam. No treatment-related tumours were seen in mice. There is no mutagenic concern for isopyrazam. The JMPR meeting concluded that isopyrazam is unlikely to pose a carcinogenic risk to humans at dietary exposure levels (FAO 2005).

NZSFA has adopted a provisional ADI of 0.0385 mg/kg/d for the sum of isopyrazam isomers.

The FAO/WHO 2011 meeting established an acceptable daily intake (ADI) of  
0–0.06 mg/kg bw for isopyrazam, derived from the NOAEL of 5.5 mg/kg bw per day in the 104-week rat feeding study on the basis of decreased body weight gain in females and increased incidences of foci of eosinophilic hepatocytes and clinical chemistry changes (triglycerides, bilirubin) of equivocal toxicological significance in both sexes at 27.6 mg/kg bw per day. A safety factor of 100 was applied. The ADI is supported by the NOAEL of 9.9 mg/kg bw per day in the mouse 80-week feeding study, based on periportal hepatocellular hypertrophy in females at 56.2 mg/kg bw per day. The margin between the maximum ADI and the lowest-observed-adverse-effect level (LOAEL) at 232.8 mg/kg bw per day for uterine and liver tumours in female rats is approximately 3,900. The meeting also established an acute reference dose (ARfD) of 0.3 mg/kg bw, derived from the NOAEL of 30 mg/kg bw in the rat acute neurotoxicity study, on the basis of non-specific clinical signs of toxicity (weak appearance and decreased activity) at 250 mg/kg bw. A safety factor of 100 was applied. In a rat developmental toxicity study, the NOAEL of 20 mg/kg bw per day for maternal and developmental toxicity was based on reduced body weight gain in dams only on day 4 of treatment. The margin between the ARfD and the LOAEL at 500 mg/kg bw per day for teratogenic effects (microphthalmia) in rabbits is approximately 1,700. Values reaffirmed in 2017.

APVMA also adopted an ADI of 0.06 mg/kg/d and an ARfD of 0.3 mg/kg for Australia (<https://apvma.gov.au/>).

EFSA (2012 and 2013) states that the Acceptable Daily Intake (ADI) for isopyrazam is 0.03 mg/kg bw/day, based on the LOAEL of 5.5 mg/kg bw/day from the two-year rat study and applying an increased uncertainty factor (UF) of 200 considering the LOAEL instead of a NOAEL. The Acute Reference Dose (ARfD) is 0.2 mg/kg bw, based on the NOAEL of 20 mg/kg bw/day for decreased maternal body weight gain in rats in the first days of dosing, with an UF of 100 applied.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Isoxaben

CAS No. 82558-50-7. The IUPAC name for isoxaben is N-[3-(1-ethyl-1-methylpropyl)-1,2-oxazol-5-yl]-2,6-dimethoxybenzamide. The CAS name is N-[3-(1-ethyl-1-methylpropyl)-5-isoxazolyl]-2,6-dimethoxybenzamide. Was previously called benzamizole.

### Maximum Acceptable Value

Isoxaben does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Isoxaben is an amide, benzamide or oxazole herbicide, used to control broadleaf weeds pre-emergence in cool-season turf and winter cereals, by disrupting root and stem development in germinating seeds.

Isoxaben does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it is listed in Table 2 (Pesticides that are manufactured for export) of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides).

### Forms and fate in the environment

Based on a preliminary assessment of the fate data, isoxaben is expected to be moderately persistent and may be mobile. There is some indication that the mobility of isoxaben decreases with increasing soil clay content and soil cation exchange capacity. It may represent a groundwater concern when applied to certain soils and/or where high water tables are present (ie, less than one foot below grade) and high rainfall/irrigation occurs. Isoxaben does not appear to readily undergo aerobic and anaerobic degradation in soil. Primary routes of degradation appear to be aqueous photolysis, aerobic aqueous metabolism and anaerobic aqueous metabolism (USEPA 2007).

Isoxaben soil half-life has been reported at about four to eight months. Water solubility is about 1 to 2 mg/L.

NPIC (1994) quotes for isoxaben a soil half-life of 100 days, water solubility of 1 mg/L and a sorption coefficient (soil Koc) of 1,400. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Using the procedures for oncogenic effects, a value for isoxaben associated with a one-in-a-million increased lifetime cancer risk is 0.009 mg/L based on the mouse oncogenicity data. If it were necessary to develop a drinking-water standard for isoxaben or its degradate, isoxaben’s oncogenic potential would have to be considered and a standard less than 0.05 mg/L would be likely both at the federal and state levels (PMEP 1994).

The chronic dietary reference dose (RfD) is estimated to be 0.05 mg/kg, based on a combined chronic toxicity/carcinogenicity study in rats (USEPA 2007). The USEPA will revisit the cancer potency estimate based on the lack of a dose-response relationship.

IUPAC quotes an ADI of 0.05 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia for isoxaben is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Kasumin

CAS No. 19408-46-9. Kasumin is the commercial product containing 2 percent kasugamycin, as the hydrated hydrochloride, and 0.02 percent of the preservative 1,2‑benzisothiazolin-3-one (CAS No. 2634-33-5).

The IUPAC name for kasugamycin is 1L-1,3,4/2,5,6-1-deoxy-2,3,4,5,6-pentahydroxycyclohexyl 2-amino-2,3,4,6-tetradeoxy-4-(α-iminoglycino)-α-D-arabino-hexopyranoside, or [5-amino-2-methyl-6-(2,3,4,5,6-pentahydroxycyclohexyloxy)tetrahydropyran-3-yl]amino-α-iminoacetic acid.

The CAS name is 3-O-[2-amino-4-[(carboxyiminomethyl)amino]-2,3,4,6-tetradeoxy-α-D-arabino-hexopyranosyl]-D-chiro-inositol.

### Maximum Acceptable Value

Neither kasumin nor kasugamycin have a MAV in the DWSNZ, and are not mentioned in the WHO Guidelines.

### Sources to water

Kasumin is an aminoglycoside antibiotic fungicide and bactericide product. It has been in use since 1965 elsewhere, but approved for limited use in New Zealand only in October 2013 for control of Psa in kiwifruit. It has also been used to control fire blight in apples and pears.

Kasugamycin (CAS No. 6980-18-3) was originally isolated in 1965, from Streptomyces kasugaensis, a [Streptomyces](http://en.wikipedia.org/wiki/Streptomyces) strain found in [Japan](http://en.wikipedia.org/wiki/Japan). Kasugamycin inhibits proliferation of bacteria by tampering with their ability to make new [proteins](http://en.wikipedia.org/wiki/Protein).

### Forms and fate in the environment

Water solubility of kasugamycin hydrochloride hydrate is about 20 percent at pH 5 to 7, and 40 percent at pH 9. The Octanol/Water Partition Coefficient, Log [KOW], is <1.96 at 23°C and pH 5.

Kasugamycinic acid is a significant metabolite.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The EPA considered the overall risks to human health and the environment arising from the hazardous properties (effects on reproductive/developmental toxicity, target organ systemic toxicity, effects on soil-dwelling organisms and terrestrial invertebrates) and the use of Kasumin are non-negligible.

The absorption and metabolism of kasugamycin in rats was limited (less than 5 percent of the dose) and was not affected by sex, dose level, or duration of dosing. The parent compound was the major component identified in the urine, faeces, liver, kidney, and plasma.

Kasumin is not carcinogenic, mutagenic or teratogenic.

The chronic dietary RfD of kasugamycin is 0.113 mg/kg/d, based on a NOAEL of 11.3 mg/kg/d. Kasugamycin is “not likely to be carcinogenic to humans” (USEPA 2005). The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for kasugamycin is 0.70 mg/L (no acute one-day value available.)

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EPA. 2013. Kasumin 2L. *Decision and Application Summary*. <http://www.epa.govt.nz/search-databases/HSNO%20Application%20Register%20Documents/APP201581_APP201581_Application_summary.pdf>

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# Kresoxim-methyl

CAS No. 143390-89-0. The IUPAC name for kresoxim-methyl is methyl (E)‑methoxyimino[α-(o-tolyloxy)-o-tolyl]acetate. The CAS name is methyl (αE)‑α‑(methoxyimino)-2-[(2-methylphenoxy)methyl]benzeneacetate.

### Maximum Acceptable Value

Kresoxim-methyl does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Kresoxim-methyl is a systemic strobilurin fungicide. Strobilurins are based on naturally occurring antifungal compounds in certain wood-decaying mushrooms. On grapes, kresoxim-methyl controls powdery mildew, downy mildew and black rot. It also controls scab and powdery mildew on apples and pears.

Kresoxim-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Kresoxim-methyl breaks down rapidly in soil and water, with a half-life of less than one day in aerobic and anaerobic soils, and 1.2 days in aquatic environments and has a low potential to leach. BF 490-1, the major degradate, is expected to be more mobile than the parent compound and is expected to be more persistent. Therefore, it is believed that the impact of BF 490-1 on the environment is expected to be greater than the parent compound.

EFSA (2015) states that soil degradation field studies demonstrated that the degradation rate of kresoxim-methyl is rapid (DT90 less than one day), and the soil metabolite BF 490-1 DT90 was up to 284 days.

Water solubility about 2 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

As at September 2008 the USEPA has classified kresoxim-methyl as being likely to be carcinogenic to humans.

A carcinogenicity feeding study in rats was used to establish the reference dose: the RfD for kresoxim-methyl was established by the USEPA (1998) at 0.36 mg/kg/day. The NOEL for both sexes was 36 mg/kg/day for males and 48 mg/kg/day for females. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.36 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for kresoxim-methyl is 2.52 mg/L (no acute one-day value available.)

The EC (1998) established an ADI of 0.4 mg/kg bw based on a two-year study on rats.

The 1998 JMPR meeting estimated the ADI for humans to be 0–0.4 mg/kg body weight based on a two-year rat study of toxicity and carcinogenicity adopting a safety factor of 100. They decided that an estimate of acute reference dose (ARfD) was unnecessary (ICPS 1998; JMPR 2001). Reaffirmed in EFSA (2013 and 2015).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.4 mg/kg body weight, with a NOEL of 36 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 1998. *Review Report for the Active Substance Kresoxim-methyl*. European Commission, Directorate General for Agriculture. 7583/VI/97-Final [17 pp]. See: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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# Lindane

CAS No. 58-89-9. The IUPAC name for lindane is 1α,2α,3β,4α,5α,6β‑hexachlorocyclohexane. The CAS name is 1,2,3,4,5,6‑hexachlorocyclohexane.

In the production of hexachlorocyclohexane (HCH), a mixture of isomers is formed, of which only six are relatively stable. Lindane is the name given to (up to) 99 percent pure γ-hexachlorocyclohexane (γ-HCH or gamma-HCH). The commercial product consists mainly of the γ-isomer, small amounts of the α-and β-isomers, and a trace of the epsilon-isomer. The isomers are:

* alpha-lindane: CAS No. 319-84-6
* beta-lindane: CAS No. 319-85-7
* delta-lindane: CAS No. 319-86-8
* gamma-lindane: CAS No. 58-89-9
* ε-lindane: CAS No.6108-10-7.

According to IUPAC rules the designation “benzene hexachloride” is incorrect. Nevertheless, it is still widely used in some areas, especially in the form of its abbreviation BHC. Therefore, gamma-BHC sometimes appears as a synonym for gamma-HCH. Has also been called hexachlorane and OMS 17. Also, γ-lindane is considered to be incorrect usage.

Refer also to the datasheet for hexachlorocyclohexane.

### Maximum Acceptable Value

Based on health considerations, the concentration of lindane in drinking-water should not exceed 0.002 mg/L (2 g/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.0002 mg/L.

The 2004 version of the *Australian Drinking Water Guidelines* stated that lindane should not be detected in drinking water. If present in drinking water, lindane would not be a health concern unless the concentration exceeded 0.02 mg/L. If it is detected, remedial action should be taken to stop contamination. The limit of determination is 0.00005 mg/L (50 ng/L).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.01 mg/L; excursions above this level even for a relatively short period are of concern, as the health-based guideline is based on effects observed in a three-month dietary study.

α-Hexachlorocyclohexane, β-hexachlorocyclohexane and lindane were added to the Persistent Organic Pollutants (POP) Stockholm Convention list in May 2009 (ICS 2009).

Each of the four main isomers is a “priority pollutant” under the US Clean Water Act. Lindane appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>

In the past, the percentage of impurities in technical lindane varied according to the source. The isomers, alpha- and ß-HCH, were the major impurities. Lindane should be almost odourless; the characteristic smell of technical HCH is attributed to the impurities, particularly heptachlorocyclohexane.

### Sources to water

Lindane (the gamma isomer of hexachlorocyclohexane) may enter source waters as a result of its use as a broad spectrum organochlorine insecticide on fruit and vegetable crops, for seed treatment, and in forestry. It can also used as a therapeutic pesticide (eg, treatment of scabies and head lice, but not after 2015 in New Zealand) in humans and animals. Only the gamma isomer has insecticidal properties.

In surface waters, levels of 0.00001–0.0001 mg/L have been reported; 0.012 mg/L of lindane was detected in a sewage-contaminated river.

The total annual usage of lindane in New Zealand in the late 1980s was 1,500 kg, all of it in the South Island. Usage before that was probably much greater than this amount. Its registration was cancelled in 1989. Lindane does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It had previously been used in sheep dips.

### Forms and fate in the environment

Lindane can be degraded in soil with half-lifes ranging from 90 to 1,400 days. The recommended average half-life in soil is 400 days. It is also fairly resistant to hydrolysis and photolysis, with half-lifes measured in months (4 to 10 months depending on conditions). JMPR (2003) reports that in hydrolysis studies at pH 9, lindane was unstable, with half-lifes of 36.3 and 35.4 days at buffer concentrations of 0.05 and 0.10 M, respectively. After 30 days, 43–44 percent of lindane had been degraded, forming 7 percent 2,3,4,5,6-pentachlorocyclohexene and 4 percent trichlorobenzenes (1,2,4-trichlorobenzene and 1,2,3-trichlorobenzene), and 32–33 percent was unaccounted for.

In water, degradation is mostly by micro-organisms in the sediments. Bacteria and fungi metabolise lindane into tetra- and pentachlorocyclohexene.

If released to soil, lindane is expected to have low mobility based upon a mean Koc value of 1,080 from three soils. Volatilisation from moist soil surfaces may be an important fate process based upon a Henry’s Law constant of 5.14 x 10-6 atm-cu m/mole. Volatilisation half-lifes from a sandy soil and a peat soil ranged from 2.3 to 22.2 days. Half lifes were dependent on soil type and air humidity. Lindane was not biodegraded in aerobic soil suspensions during a three-week incubation period. Lindane is expected to biodegrade in soil under anaerobic conditions; 63.8 percent biodegraded in three weeks in soil suspensions, while in clay loam soil 60 percent biodegraded after 15 days. Metabolites gamma-2,3,4,5,6-pentachloro-1-cyclohexene, alpha-, beta-, and gamma-3,4,5,6-tetrachloro-1-cyclohexene and pentachlorobenzene were isolated from pure cultures studies of lindane in loamy sand. If released into water, lindane is expected to adsorb to suspended solids and sediment in the water column based upon experimental Koc values. In unsterilized natural water, <30 percent of lindane remained after 16 weeks, suggesting biodegradation may be important in natural waters. Volatilisation from water surfaces may be an important fate process based on its Henry’s Law constant. Following 24 hours’ incubation, 16.4 percent of lindane volatilised from tap water, 11.5 percent volatilised from tap water with suspended loam particles, and 5.5 percent volatilised from tap water with algal cells indicating that volatilisation from water may be mediated by adsorption to soil and biomaterials. BCFs ranging from 5.5 to 4,240 suggest bioconcentration in aquatic organisms is low to very high. Aquatic photolysis is also expected to be a slow process, with reported half-lifes in natural waters ranging from seven days at pH 9.2 to 74 days at pH 7.3. Hydrolysis data for the similar natural water samples at pH values 9.2, 7.8 and 7.3 were 92, 748 and 771 hours, respectively indicating that hydrolysis may be an important fate process. However temperature can mediate hydrolysis; other studies report hydrolysis half lifes of lindane in water ranging from 42 years at pH 8 and 5°C to four days at pH 9 and 25°C (EAWAG accessed February 2015).

The water solubility is fairly low, about 10–15 mg/L (IARC 2017 quotes 0.7 mg/L), and leaching to groundwater is rarely found overseas above 0.0001 mg/L. In surface waters lindane can be removed by evaporation.

NPIC (1994) quotes for lindane a soil half-life of 400 days, water solubility of 7 mg/L and a sorption coefficient (soil Koc) of 1,100. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

Lindane was not detected in 230 samples received from 212 New Zealand supplies between 1988 and 1992. The detection limit was approximately 0.00001 mg/L  
(0.01 g/L).

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of lindane (limit of detection = 0.0001 mg/L) (ESR 2001).

Lindane has been detected in both surface water and groundwater, usually at concentrations below 0.0001 mg/L, although concentrations as high as 0.012 mg/L have been measured in wastewater-contaminated rivers (WHO 2004).

Forty-two water utilities in the US reported detecting lindane in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00027 mg/L.

### Removal methods

Partial removal of lindane has been reported for slow sand filtration. The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of lindane in water. Also, isotherm adsorption data indicate that removal by adsorption on to granular activated carbon should be possible, perhaps down to 0.0001 mg/L (WHO 2017).

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (EPA 525).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

2. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 505).

3. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6630B).

### Health considerations

Following oral administration, absorption of lindane is almost complete. In humans, the lindane content seems to increase with age, but no correlation has been established with levels or duration of exposure. Higher levels of the b-isomer are found in >80 percent of postmortem human adipose tissue samples. Lindane crosses the placenta and can also be present in human milk. Metabolism of lindane in animals and humans is via dehydrochlorination, dechlorination, dehydrogenation and oxidation. The final metabolites are isomers of dichlorophenol, trichlorophenol and tetrachlorophenol.

The most commonly reported effects associated with oral or occupational exposure to lindane are neurophysiological and neuropsychological disorders and gastrointestinal disturbances.

Deaths of humans (usually children) have been reported following ingestion of lindane.

In a study conducted in an Indian pesticide factory where handlers were directly exposed to hexachlorocyclohexane for 7–30 years, 94 percent of the handlers and 69 percent of non-handlers reported paraesthesia of the face and extremities. Headache and giddiness occurred in over 70 percent of the handlers and 40 percent of the non-handlers, compared with 7 percent of the control group.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.003 mg/kg body weight, with a NOEL of 0.31 mg/kg bw based on a short-term (three-month) dietary study in rats. The NOEL is based on kidney tubule distension, nephritis, increased liver weight and centrilobular hypertrophy. The ADI incorporates a safety factor of 100.

JMPR (2003) reports an ADI of 0.005 mg/kg/d bw, and an acute RfD = 0.06 mg/kg bw. These values still hold as at 2015.

The oral reference dose or RfD for lindane (USEPA 2006/2009/2011) is 0.005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.2 mg/L. The oral RfD had earlier been 0.0003 mg/kg/d (USEPA 1988).

ATSDR quotes a minimal risk level (MRL) for γ-HCH (lindane) of:

* 0.003 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.00001 mg/kg/day for intermediate-duration oral exposure (15–364 days).

Lindane causes liver tumours in mice given very high doses, but there is no evidence that this is a result of tumour promotion. JMPR has concluded that there was no evidence of genotoxicity. The International Agency for Research on Cancer has classed lindane in Group 2B (possibly carcinogenic to humans). Further, in an epidemiological study designed to assess the potential association between breast cancer and exposure to chlorinated pesticides, no correlation with lindane was found.

As at September 2008 the USEPA considered there was suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential. Lindane appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. In addition, there is evidence that lindane may act as an endocrine disruptor (USEPA 2002).

Gamma-HCH (lindane) is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

IARC (2017) states that there is sufficient evidence in humans for the carcinogenicity of lindane. Lindane causes non-Hodgkin lymphoma. There is sufficient evidence in experimental animals for the carcinogenicity of lindane. The overall evaluation is that lindane is carcinogenic to humans (Group 1).

### Derivation of Maximum Acceptable Value

Due to the lack of evidence of the carcinogenicity of lindane to humans, a tolerable daily intake approach has been used for the derivation of the MAV of lindane in drinking-water. The no-observable-adverse-effect level used in the derivation is based on results of a liver and kidney toxicity/carcinogenicity short-term study in rats, in which an increased incidence of periacinar hepatocellular hypertrophy, increased liver and spleen weights, and increased mortality occurred at higher doses.

The MAV for lindane in drinking-water was derived as follows:

0.47 mg/kg body weight/day x 70 kg x 0.01 = 0.00165 mg/L (rounded to 0.002 mg/L)

2 L/day x 100

where:

* no-observable-adverse-effect level = 0.47 mg/kg body weight found in a two-year toxicity / carcinogenicity study in rats in which an increased incidence of periacinar hepatocellular hypertrophy, increased liver and spleen weights and increased mortality occurred at higher doses
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01
* uncertainty factor = 100 for inter and intra-species variation.

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# Linuron

CAS No. 330-55-2. The IUPAC name for linuron is 3-(3,4-dichlorophenyl)-1-methoxy-1-methylurea. The CAS name is N′-(3,4-dichlorophenyl)-N-methoxy-N-methylurea. Also called lorox.

### Maximum Acceptable Value

There is no MAV for linuron in the DWSNZ; WHO does not mention linuron in their Guidelines.

### Sources to water

Linuron and diuron (similar structures) are broadly applied phenylurea selective herbicides used to control annual grass and broadleaf weeds in vegetables, sweetcorn, linseed, and fruits.

Linuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 13.7 tonnes of linuron were used in New Zealand in 2004, at an application rate of 2,250 grams of active ingredient per hectare.

Linuron should not contain more than 20 mg/kg of 3,3′,4,4′-tetrachloroazobenzene (TCAB), or 2 mg/kg of 3,3′,4,4′-tetrachloroazoxybenzene (TCAOB). Free amine salts should not exceed 0.4 percent as dimethylamine hydrochlroride. EFSA (2016) considers tetrachlorobenzene (TCB), TCAB and TCAOB relevant impurities at a maximum content of 1 mg/kg, each.

### Forms and fate in the environment

Linuron is biologically degraded to 3,4-dichloroaniline (3,4-DCA) see datasheet, plus 1‑(3,4-dichlorophenyl)-3-methylurea, 1-(3,4,dichlorophenyl)urea, and 1‑(3,4‑dichlorophenyl)-3-methoxyurea. A high bioaccumulation of linuron and its metabolites is not to be expected owing to their low log Pow values of 3.2 and 2.68, respectively. The half-life in aerobic soil is about 16 days, and 28 days in anaerobic soil. Solubility is about 50 mg/L at pH 5, 65 mg/L at pH 7, and 75 mg/L at pH 9 (all at 25°C).

Linuron is completely, although slowly, degraded by direct photolysis in sterile, aqueous solution up to the formation of inorganic compounds (CO2). Under realistic use conditions, it is to be expected that photolytic degradation is considerably accelerated by sensitisers always present in natural bodies of surface water (EC 2002).

Fate and behaviour of linuron in dark water/sediment systems under aerobic conditions was investigated in a study with two systems. Linuron partitioned to the sediment to a limited extent (maximum 34.3 percent AR after seven days). Linuron exhibited moderate persistence in both systems (DT50 whole system = 20.1–28.8 days). Desmethoxy linuron and norlinuron were found above 5 percent AR in both water and sediment (desmethoxy linuron: maximum 19.5 percent AR in water and 54.6 percent AR in sediment; norlinuron: maximum 7.8 percent AR in water and 11 percent AR in sediment). The metabolite desmethyl linuron was found above 5 percent in the water phase and 3,4-DCA was found above 5 percent AR in sediment. Mineralisation was practically negligible (maximum 2.5 CO2 percent AR after 120 days, end of the study) and the unextractable residue in the sediment accounted for up to 52.6 percent AR after 120 days (end of the study) (EFSA 2016).

Linuron is considered to be not readily biodegradable (EFSA 2016).

NPIC (1994) quotes for linuron a soil half-life of 60 days, water solubility of 75 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

In surface soils with adequate organic matter, the combined processes of adsorption and microbial degradation would limit linuron’s potential to migrate to groundwater, however linuron is sufficiently persistent and may be mobile under certain environmental conditions, it therefore has the potential to impact groundwater quality.

In regions of intensive agriculture, linuron concentrations up to 1.1 and 2.8 mg/L have been detected in Canadian surface waters and groundwaters, respectively (Caux et al 1998).

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Linuron was detected in one well at a concentration of 0.043 µg/L, ie, 0.000043 mg/L.

### Removal methods

Structurally similar to diuron (qv).

### Analytical methods

#### Referee method

No MAV, so no need.

### Health considerations

IUPAC (2003) reports some effects of linuron and its metabolites on juvenile and adult rats. A loss of weight of sexual organs of the animals was observed within two weeks after daily doses of 100 or 200 mg/kg of rat. In short-term in vivo studies, linuron treatment reduced testosterone- and DHT-dependent tissue weights in the Hershberger assay (oral 100 mg/kg daily dose for seven days) and altered the expression of androgen-regulated ventral prostate genes (oral 54 days, 100 mg/kg daily dose). Linuron and some of its metabolites (eg, 3,4-DCA) probably act as competitive antagonists at the androgen receptor. Owing to the structural similarities between linuron and diuron and the common metabolite 3,4-DCA, an intrinsic endocrine potential may be expected.

The Reference Dose (RfD) is 0.008 mg/kg/day based on a one-year feeding study in dogs in which a No Observed Effect Level (NOEL) of 0.77 mg/kg/day was demonstrated. An uncertainty factor of 100 was used to account for inter-species extrapolation and intra-species variability (USEPA 1995). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0077 mg/kg/d, and an ARfD of 0.12 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for linuron is 3.96 mg/L.

The USEPA assessed the dietary risk posed by linuron. For the overall US population, chronic exposure from all existing linuron tolerances represents 2 percent of the Reference Dose (RfD), ie, the amount believed not to cause adverse effects if consumed daily over a 70-year lifetime. The two most highly exposed subgroups are non-nursing infants (less than one year old), whose exposure represents 6 percent of the RfD, and children aged one to six years, with exposures representing 4 percent of the RfD.

EC (2002) adopted an ADI of 0.003 mg/kg/d and an ARfD of 0.03 mg/kg.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1.25 mg/kg bw.

The USEPA re-registered linuron in 1995, stating linuron is a Group C carcinogen (ie, a possible human carcinogen for which there is limited animal evidence); it is still on their September 2008 list. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

The acceptable daily intake (ADI) set during the first review was 0.003 mg/kg bw per day by the European Commission in [2002](http://onlinelibrary.wiley.com/enhanced/doi/10.2903/j.efsa.2016.4518#efs24518-bib-0009). The majority of experts agreed to maintain the ADI, on the basis of the relevant long-term LOAEL of 1.3 mg/kg bw in the two-year study in rats based on decreased incidence of pituitary tumours and equivocal increase in Leydig cell adenoma indicative of hormonal disturbance at 1.3 mg/kg bw per day. In addition to the standard uncertainty factor (UF) of 100, an UF of 5 was applied to cover uncertainties regarding the lack of a clear NOAEL.

An acute reference dose (ARfD) of 0.03 mg/kg bw was set during the first review on the basis of a developmental toxicity study in rabbits. The experts agreed that an ARfD was needed for linuron. However, the basis for the ARfD could not be established as developmental end points from a rabbit developmental study that might be more critical (evaluated by Health Canada and USEPA) are still open leading to a data gap and issue that could not be finalised (EFSA 2016).

Linuron is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015). However, EFSA (2016) states that linuron is currently classified as carcinogenic category 2 and as toxic for reproduction category 1B, in accordance with the provisions of Regulation (EC) No 1272/2008.

USEPA (2015) found that overall, while some in vitro assays did indicate potential interaction with the estrogen pathway, these findings were not supported by the results of in vivo mammalian and wildlife studies, so in summary, for the estrogen pathway, the available data suggests that linuron does not interact with the estrogen pathway. In mammalian studies, linuron caused changes in testes and epididymal weights and histopathology in the testes and epididymides. There is convincing evidence of potential interaction of linuron with the thyroid pathway.

### Derivation of Maximum Acceptable Value

No MAV.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for linuron is 0.001 mg/L.

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# Lufenuron

CAS No. 103055-07-8. The IUPAC name for lufenuron is (RS)-1-[2,5-dichloro-4-(1,1,2,3,3,3-hexafluoropropoxy)phenyl]-3-(2,6-difluorobenzoyl)urea. The CAS name is N-[[[2,5-dichloro-4-(1,1,2,3,3,3-hexafluoropropoxy)phenyl]amino]carbonyl]-2,6-difluorobenzamide.

Lufenuron is a racemic mixture of two enantiomers. Lufenuron technical active ingredient is manufactured under non-stereo-specific conditions giving a racemate (R:S 50:50).

### Maximum Acceptable Value

Lufenuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Lufenuron is a chitin synthesis inhibiting benzoylurea insecticide. Lufenuron is the [active ingredient](http://en.wikipedia.org/wiki/Active_ingredient) in the [veterinary](http://en.wikipedia.org/wiki/Veterinary_medicine) [flea](http://en.wikipedia.org/wiki/Flea) control medication, Program. Lufenuron is also sold as a crop protection pesticide for use against [mites](http://en.wikipedia.org/wiki/Mites) and thrips. Lufenuron may be co-formulated with profenofos or fenoxycarb (EC 2009). It is also used in bait stations against pests such as fruit fly (EFSA 2017).

Lufenuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The EC (2009) stated that particular attention should be made due to the high persistency in the environment and the high risk for bioaccumulation and shall ensure that the use of lufenuron has no adverse long-term effects on non-target organisms. Hydrolysis occurs slowly at pH 9 and very slowly at pH 5 and 7. Photolysis occurs slowly (JMPR 2008).

Because it is toxic to zooplankton, lufenuron was included in a biocide ban proposed by the Swedish Chemicals Agency. The ban was approved by the European Parliament on 13 January 2009.

In aerobic soil metabolism studies lufenuron was degraded with half-lifes of 9–24 days in microbial active soil and 17–83 days in sterilised soil. 2,6-Difluorobenzamide which is a common soil metabolite to other active substances, eg, diflubenzuron, was investigated for its behaviour in soil; within 120 days it was completely degraded, leaving 2,6-difluoro-benzoic acid as its main degradate within the first two weeks. JMPR. 2015. Due to the very high log Kow, EFSA (2017) concluded that lufenuron can easily be adsorbed into the soil and not taken up by plants. According to the soil degradation studies evaluated in the framework of the peer review, period required for 90 percent dissipation (DT90) values of lufenuron range between 503 and 1,444 days.

The physical-chemical properties of lufenuron indicate low volatility and no accelerated photochemical degradation in water or soil. Water solubility about 0.05 mg/L. Partition coefficient = log POW = 5.12 (± 0.14) at 25°C.

### Removal methods

No information available.

### Analytical methods

#### Referee method

No MAV, so no need.

### Health considerations

JMPR (2008) states that lufenuron is an insecticide which has not been evaluated by the FAO/WHO JMPR or WHO/IPCS. Lufenuron is not classified as dangerous if swallowed, in contact with skin, or by inhalation, and is not irritating to skin or eyes. Lufenuron is classified as sensitising.

The Acceptable Daily Intake (ADI) adopted in Australia for lufenuron is 0.02 mg/kg body weight, with a NOEL of 2.1 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The EC (2009) derived an ADI of 0.015 mg/kg body weight, and based on the low toxicity of lufenuron; no ARfD was needed. These values were reaffirmed in EFSA (2017).

An ADI of 0–0.02 mg/kg bw was established on the basis of the NOAEL of 1.93 mg/kg bw per day for tonic-clonic seizures and findings in lungs, gastrointestinal tract, liver and urinary tract in the two-year dietary study in rats, using a safety factor of 100. The meeting concluded that it was not necessary to establish an ARfD for lufenuron in view of its low acute oral toxicity and the absence of developmental toxicity and any other toxicological effects that would be likely to be elicited by a single dose. The meeting concluded that lufenuron is not carcinogenic in mice or rats, and is unlikely to pose a carcinogenic risk to humans. It is unlikely to be genotoxic or teratogenic (JMPR 2015).

### Derivation of Maximum Acceptable Value

No MAV.

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# Malathion

CAS No. 121-75-5. The IUPAC name for malathion is diethyl (dimethoxyphosphinothioylthio)succinate, or S-1,2-bis(ethoxycarbonyl)ethyl O,O‑dimethyl phosphorodithioate. The CAS name is diethyl [(dimethoxyphosphinothioyl)thio]butanedioate.

It has also been called S-[1,2-di(ethoxycarbonyl)ethyl] dimethylphosphorothiolothionate, dicarbethoxyethyl O,O-dimethyl phosphorodithioate, carbophos, mercaptothion and diethyl(dimethoxyphosphinothioylthio)succinate. Maldison is a common trade name.

Some products may also contain captan or methoxychlor.

### Maximum Acceptable Value

WHO (2004/2011/2017) states that because malathion occurs at concentrations well below those at which toxic effects are observed, it is not considered necessary to derive a guideline value.

WHO (2017) derived a health-based value of 0.9 mg/L.

In DWSNZ 2005, the provisional MAV for malathion in drinking-water had been 1 mg/L.

The maximum acceptable concentration for malathion in Canada is 0.19 mg/L.

The USEPA (2006) established a lifetime health advisory of 0.1 mg/L for malathion, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity. USEPA (2009/2011) now show a lifetime health advisory of 0.5 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EFSA (2011) states that the enforcement residue definition is the sum of malathion and malaoxon (CAS No. 1634-78-2) expressed as malathion.

EC (2010) states that the active substance shall comply with the FAO specification with the exception of the level of the manufacturing impurity isomalathion which is of toxicological concern must not exceed 2 g/kg. Malaoxon, MeOOSPS-triester and MeOOOPs-triester impurities must not exceed respectively 1 g/kg, 15 g/kg and 5 g/kg as stated in the relevant FAO specification. Some formulations also contain gamma-cyhalothrin.

### Sources to water

Malathion, a broad spectrum non-systemic aliphatic organophosphate insecticide and acaricide, is commonly used to control mosquitos, and a variety of insects that attack fruits, vegetables, landscaping plants and shrubs. It can also be found in other pesticide products used indoors, on pets to control ticks and insects and to control human head and body lice.

Malathion appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), where malathion is the trade name and maldison the chemical name.

Malathion is manufactured as a technical-grade concentrate that is >90 percent pure malathion and contains approximately 5 percent of impurities consisting largely of reaction by-products and degradation products. As many as 14 impurities have been identified in technical-grade malathion. The identities of the impurities and their percent (w/w) in technical grade malathion were found to be as follows: S‑1,2‑ethyl‑O,S-dimethyl phosphorodithioate (isomalathion; 0.2 percent), S‑1,2‑bis(ethoxycarbonyl)-ethyl-O,O-dimethyl phosphorothioate (malaxon; 0.1 percent), diethylfumarate (DEF; 0.9 percent), O,S,S-trimethyl phosphorodithioate  
(0.003–1.2 percent), O,O,S-trimethyl phosphorothioate (0.04 percent), O,O,S-trimethyl phosphorodithioate (1.2 percent), O,O,O-trimethyl phosphorothioate (0.45 percent), diethylhydroxysuccinate (0.05 percent), ethyl nitrite (0.03 percent), diethyl mercaptosuccinate (0.15 percent), diethyl methylthiosuccinate (1.0 percent), O,O‑dimethylphosphorothioate (0.05 percent), diethyl ethylthiosuccinate (0.1 percent), and sulphuric acid (0.05 percent).

Malathion was detected in four of 949 stream samples in southern Ontario agricultural watersheds at concentrations of 0.0002–0.0018 mg/L.

### Forms and fate in the environment

Malathion is quite soluble in water (about 145 mg/L), creating the potential for it to move through the soil profile and into groundwater. However, because malathion binds moderately to soil, and degradation occurs rapidly in the environment, the potential for malathion movement into groundwater is generally not significant and leaching of the chemical into groundwater is usually not observed.

In surface waters, malathion degrades by hydrolysis and microbially mediated biodegradation. Hydrolysis is considered to be the predominant degradation process, and occurs more rapidly at alkaline pHs (half-life <1 week at pH 8), while the compound is stable to hydrolysis at acidic pHs (half-life 21 weeks at pH 6). Malathion appears to be relatively stable to direct aqueous photolysis, but may be transformed in the water by indirect photolysis. Adsorption to sediment and suspended particulate matter is not expected to be a significant factor in the fate of the compound in the environment. Under least favourable conditions, ie, low pH and low organic content, malathion may persist in water with a half-life of months or even years. However, under most conditions, the half-life appears to be roughly 7–14 days (WHO 2017).

Octanol-Water Partition Coefficient (log Kow): 2.36–2.89. Henry’s constant: a wide range of values has been reported (see NPIC) – IARC (2016) quotes 4.9 × 10−9 atm m3 mole–1 at 25°C. Soil Sorption Coefficient (Koc): 90–1,800 depending on soil type and environmental conditions.

The half-life of malathion in water was estimated as 1.65 days at pH 8.2 and 17.4 days at pH 6.0, whereas malathion remained stable in distilled water for three weeks. Applied at 1 to 6 pounds/acre in ponds for mosquito control, it was effective for 2.5 to six weeks. The breakdown products in water are mono- and di-carboxylic acids.

Reported half-lives in soil range from 1 to 17 days. The extractable residues of malathion in the soil decline rapidly due to volatilisation, binding to soil, uptake by plants, and metabolism by soil microbes. NPIC.

If released to soil, malathion is expected to have low mobility based upon Koc values of 1,175 to 1,800. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 4.9 x 10-9 atm-cu m/mole. Utilising the Japanese MITI test, 22 percent of the theoretical BOD was reached in four weeks indicating that biodegradation may be an important environmental fate process. If released into water, malathion is expected to adsorb to suspended solids and sediment based upon the Koc values. The half-life for malathion in Limon River water was reported as 9.73 to 10.87 days. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. Malathion did not bioconcentrate in the freshwater fish Pseudorasbora parva or in pinfish (Lagodon sp). Hydrolysis half-lifes in seawater/sediment systems at pH 7.3 to 7.7 are 2.0 days, and in freshwater at pH 7.4 and 20°C, 11 days. Photodegradation may compete with hydrolysis based on a study finding the first order photolysis rate of malathion in river water as 0.0013/minutes; this calculates to a half-life of 533 minutes (EAWAG accessed February 2015).

NPIC (1994) quotes for malathion a soil half-life of one day, water solubility of  
130–150 mg/L and a sorption coefficient (soil Koc) of 1,800. This resulted in a pesticide movement to groundwater rating of extremely low.

USGS (2006) give the following values: log Kow = 2.8; log Koc (where Koc is in mL/g) = 3.26; water solubility = 145 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -2.64 or 4.9 x 10-9 atm m3 mole-1 at 25°C; half-life in aerobic soil = <1 days; half-life in water = 6.3 days.

Malaoxon is the primary metabolite of malathion and, under certain conditions, is formed as an environmental breakdown product of malathion, making it available for direct human exposure (USEPA 2009); malaoxon is a more potent ChE inhibitor.

The formation of malaoxon can also occur via oxidation during water treatment process, up to 100 percent, and, following the treatment process, only concentrations of malaoxon exiting the plant. Once converted, malaoxon may remain stable in treated water long enough to be available at the tap for direct consumption. Recently received hydrolysis data indicates that malaoxon may remain stable for 72 hours, which is within delivery times for some supplies (USEPA 2009). Therefore malaoxon should also be tested.

If released to soil, malaoxon is expected to have very high mobility based upon an estimated Koc of 46. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 1.8 x 10-12 atm-cu m/mole. Malaoxon is not expected to volatilise from dry soil surfaces based upon its vapour pressure. If released into water, malaoxon is not expected to adsorb to suspended solids and sediment in water based upon the estimated Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 3.2 suggests the potential for bioconcentration in aquatic organisms is low (EAWAG accessed February 2015).

See EFSA (2011) for a list of other metabolites.

### Typical concentrations in drinking-water

Malathion was not detected in 179 samples from municipal and private water supplies from Prince Edward Island (1986), Nova Scotia (1986), Ontario (1971 to 1982, 1985) and Manitoba (1986) (detection limits ranged from 0.000001 to 0.0003 mg/L) (Health Canada 1986/89).

Malathion has been detected in surface water and drinking-water at concentrations below 0.002 mg/L (WHO 2004/2017).

Surface-water contamination is also relatively low. The California Department of Pesticide Regulation collects pesticide monitoring data: of the 12,941 measurements of malathion, 602 (4.7 percent) were “non-zero” and only 37 were >1 μg/L. Of the 1,064 measurements of malaoxon, only one was non-zero. From IARC (2016).

### Removal methods

Because malathion binds moderately to soil, treatment processes that remove particulate matter should reduce the concentration of malathion from turbid water. The weak soil adsorption suggests that treatment processes that remove particulate matter should be ineffective at reducing the concentration of malathion in water. Some of the newer advanced oxidation processes and activated carbon may be more effective.

### Analytical methods

#### Referee method

No MAV, so no need.

#### Some alternative methods

WHO (2004) states that malathion in water may be determined by extracting into dichloromethane, drying the extract, redissolving in hexane and analysing by gas–liquid chromatography, phosphorus mode. The detection limit is 0.0001 mg/L.

### Health considerations

Malathion is absorbed rapidly and effectively by practically all routes including the gastrointestinal tract, skin, mucous membranes, and lungs.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand for maldison is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw based on a two-year dietary study in rats. This NOEL is based on inhibition of red blood cell cholinesterase. The ADI incorporates a safety factor of 100. The ARfD is 1.5 mg/kg bw based on a NOEL of 15 mg/kg bw/day from an acute dietary study in humans. The ARfD incorporates a safety factor of 10.

The reference dose or RfD (USEPA 1992/2006) was 0.02 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006) was 0.8 mg/L. USEPA (2009/2011) now list 0.07 and 2 mg/L respectively. Malaoxon is considered to be 20 to 30 times more toxic than malathion (NPIC).

EC (2010) established an ADI of 0.03 mg/kg/d and an ARfD of 0.3 mg/kg. These values were reaffirmed by EFSA (2011 and 2014).

JMPR (2013/2016) quotes an ADI of 0.3 mg/kg/d, and an ARfD of 2 mg/kg bw for malathion. The 2016 meeting concluded that the metabolite malaoxon is approximately 30-fold more toxic than malathion. Both the ADI and ARfD are established for the sum of malathion and malaoxon (corrected for its potency), expressed as parent malathion. The other metabolites of malathion considered by the present meeting are less potent than the parent compound and therefore would be covered by the ADI and ARfD for malathion. The impurity isomalathion may need to be taken into consideration in the risk assessment depending on its concentration in food commodities.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.02 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.02 mg/kg/day for chronic-duration oral exposure (>364 days).

Malathion inhibited cholinesterase activity in mice, rats and human volunteers. It increased the incidence of liver adenomas in mice when administered in the diet. Most of the evidence indicates that malathion is not genotoxic, although some studies indicate that it can produce chromosomal aberrations and sister chromatid exchange in vitro. JMPR has concluded that malathion is not genotoxic.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for malathion since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

As at September 2008 the USEPA considered there was suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.

IARC (1983) stated that the available data provide no evidence that malathion and its metabolite malaoxon is likely to present a carcinogenic risk to humans, ie, Group 3. However, IARC (2016) states that there is limited evidence in humans for the carcinogenicity of malathion. Positive associations have been observed with non-Hodgkin lymphoma and cancer of the prostate. There is sufficient evidence in experimental animals for the carcinogenicity of malathion. The overall evaluation is that malathion is probably carcinogenic to humans (Group 2A).

### Derivation of Maximum Acceptable Value

WHO (2004) states that as the chemical occurs in drinking-water at concentrations much lower than the health-based value, the presence of malathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. Also, the intake of malathion from all sources is generally low and well below the ADI. For this reason, it is considered unnecessary to derive a guideline value for malathion in drinking-water.

In DWSNZ 2005, the PMAV for malathion in drinking-water had been derived as follows; WHO (2011) now calls this a health-based value, and WHO (2017) use this to derive their current health-based value:

29 mg/kg body weight/day x 70 kg x 0.1 = 1.015 mg/L (rounded to 1 mg/L)

2 L x 100

where:

* no-observable-adverse-effect level = 29 mg/kg body weight per day, based on a two-year study of toxicity and carcinogenicity in rats, and supported by a NOAEL of 25 mg/kg of body weight per day in a developmental toxicity study in rabbits
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult per day = 2 L
* uncertainty factor = 100.

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# Maleic hydrazide

CAS No. 123-33-1. The IUPAC name for maleic hydrazide is 6-hydroxy-2H-pyridazin-3-one or 1,2-dihydropyridazine-3,6-dione. The CAS name is 1,2-dihydro-3,6-pyridazinedione. May be sold as its choline, or potassium (commonest), or sodium salt.

Maleic hydrazide is often named as its two isomeric structures: 1,2-dihydro-3,6-pyridazinone and 6-hydroxy-2H-pyridazin-3-one (JMPR 2008).

### Maximum Acceptable Value

Maleic hydrazide does not have a MAV in the DWSNZ; maleic hydrazide is not mentioned in the WHO Guidelines.

The USEPA (2006) established a lifetime health advisory of 0.1 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity. USEPA (2009/2011) now quote a lifetime health advisory of 4 mg/L.

### Sources to water

Maleic hydrazide is a systemic plant growth regulator and herbicide, commonly used to control sprouting of potatoes and onions while in storage, or to grass and trees to limit their growth. Maleic hydrazide is approved in the UK for control of weeds in or near water.

Maleic hydrazide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

EC (2002) states that the product must not contain more than 1 mg/kg of free hydrazine expressed on the basis of the acid equivalent; hydrazine is toxic and carcinogenic.

Regarding the groundwater metabolite maleic acid, it is not considered a relevant impurity as it occurs naturally in corn, cacao, ginseng, sour cherries and alcoholic beverages such as beer and wine (EFSA 2016).

### Forms and fate in the environment

Maleic hydrazide does not break down in water after 61 days at pHs 3, 6 and 9; this suggests it could leach readily to groundwater. USEPA (1994) states that maleic hydrazide is rapidly metabolised in soil under aerobic conditions. Half-lifes of  
30–60 days were observed under anaerobic conditions and the product of metabolism is CO2.

Water solubility is high: about 4000 mg/L in acidic conditions, about 14 percent in neutral and alkaline conditions.

NPIC (1994) quotes for maleic hydrazide acid a soil half-life of 30 days, water solubility of 6000 mg/L and a sorption coefficient (soil Koc) of 250. This resulted in a pesticide movement to groundwater rating of moderate.

EFSA (2016) states that maleic hydrazide exhibited low persistence in soils (DT50  
0.2–3.9 days) and degraded to minor metabolites, CO2 and maleic acid (DT50  
0.3–0.6 days). Succinic and maleic acids have also been identified but are not considered relevant to groundwater. Maleic hydrazide may be considered to exhibit high to very high mobility in soil. Maleic hydrazide may be considered stable to aqueous hydrolysis under normal environmental conditions. Photolysis is slow. Maleic hydrazide is not readily biodegradable. In natural water systems maleic hydrazide can partition to the sediment but most of the product remains in the aqueous phase.

### Removal methods

No information available.

### Analytical methods

#### Referee method

No MAV, so no need.

#### Some alternative methods

See EFSA (2016).

### Health considerations

No carcinogenic effect was observed in adult mice and rats following oral or subcutaneous administration of maleic hydrazide. The significance of hepatomas obtained in newborn mice cannot be assessed because of the contamination of maleic hydrazide with hydrazine (IARC 1974).

In 1994, the USEPA concluded that maleic hydrazide appears to be genotoxic at high doses in some of the mutagenicity tests. Since maleic hydrazide is a uracil antimetabolite, and this is presumably its mechanism of action with respect to its plant growth/herbicidal properties, it might be expected that equivocal or positive results would be observed in some genotoxicity tests. When the totality of genotoxicity studies is considered together with the results of all the toxicological studies on maleic hydrazide and its potassium salt, including negative carcinogenicity studies in rats and mice, it was concluded that the potential human genotoxic hazard is negligible.

Technical grade maleic hydrazide contains hydrazine as a contaminant. Since hydrazine has been associated with tumour induction, the USEPA established and maintained an upper limit for hydrazine at 15 ppm in technical maleic hydrazide products in 1982. This was a level determined not to cause concern based on the calculations of lifetime carcinogenicity risks to humans. The carcinogenic potential of maleic hydrazide per se was classified into “Group E” – evidence of non-carcinogenicity for humans (USEPA 2005). IARC classified maleic hydrazide as Group 3: not classifiable as to human carcinogenicity.

Lowest relevant oral NOAEL/NOEL: one-year dog: 25 mg/kg bw/day; ADI 0.25 mg/kg bw; the weight of evidence suggests no genotoxic concern (EC 2002). An ARfD is not necessary as maleic hydrazide is not acutely toxic or toxic to reproduction. EFSA (2011/2016) reaffirmed these values. EFSA states that 3-pyridazinone is a metabolite.

JMPR (2008) quotes an ADI of 0–0.3 mg/kg/d based on decreased weight gain and clinical chemical changes in chronic testing on rats and dogs.

Twenty-five male and 50 female SPF Wistar rats were fed 0, 1 or 2 percent maleic hydrazide (MH) in their diet during the one-week premating period and the one-week mating period. At weaning, F1 offspring males and females were taken at random from the three experimental groups for the 28-month carcinogenicity study. The same levels of MH were administered in the diet. Group 1 consisted of 65 female and 65 male rats (2 percent); Group 2 consisted of 55 animals from each sex (1 percent); and Group 3 consisted of 55 control animals (diet only) from each sex. Observations included renal dysfunction. This resulted in the reference dose or RfD (USEPA 1992/2006/2009/2011) of 0.5 mg/kg/d; the Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 20 mg/L. The (brief) USEPA (1994) RfD of 0.25 mg/kg/d had been based on chronic feeding studies in rats and dogs and an uncertainty factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for maleic hydrazide is 5 mg/kg body weight, with a NOEL of 571 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

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# Mancozeb

CAS No. 8018-01-7, formerly 8065-67-5. The IUPAC name for mancozeb is manganese ethylenebis(dithiocarbamate) (polymeric) complex with zinc salt. The CAS name is [[2‑[(dithiocarboxy)amino]ethyl]carbamodithioato(2−)-κS,κS′]manganese mixture with [[2‑[(dithiocarboxy)amino]ethyl]carbamodithioato(2−)-κS,κS′]zinc.

It appears in New Zealand under a wide range of trade names.

### Maximum Acceptable Value

Mancozeb does not have a MAV in the DWSNZ; mancozeb is not mentioned in the WHO Guidelines.

Mancozeb degrades in the environment to ethylene thiourea (ETU), so it would be logical for guidelines for mancozeb to be based on the health effects of ETU – there is no MAV for ETU in the DWSNZ; WHO (2011) states that ETU is unlikely to occur in drinking-water so has been excluded from guideline value derivation.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.009 mg/L for ethylenethiourea (ETU); excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Mancozeb should not contain more than 0.5 percent of ethylenethiourea (ETU) – qv.

### Sources to water

Mancozeb is an ethylenebisdithiocarbamate (EBDC) compound, which includes the related active ingredients maneb (CAS No. 12427-38-2, not on ERMA’s list) and metiram, propineb, thiram, and ziram (see datasheets). Mancozeb is a polymeric dithiocarbamate broad spectrum fungicide complex with zinc (2.5 percent) and manganese (20 percent). Dithiocarbamates have a similar action to carbamate insecticides except they affect the nervous system through their main metabolite, carbon disulphide (CS2). It is used to protect many fruit, nut, and field crops from a wide spectrum of fungal diseases. CS2 is also found in crops belonging to Brassicaceae and Caricaceae families.

Mancozeb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 441.9 tonnes of mancozeb were used in New Zealand in 2004, at an application rate of 19,200 grams of active ingredient per hectare. Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007). Dithiocarbamates can act as a fumigant by rapidly breaking down into methylisothiocyanate (MITC). Mancozeb is approved as an ingredient in anti-fouling paints for use in New Zealand (EPA 2013).

### Forms and fate in the environment

Mancozeb, if applied to soil, will have a low mobility based on its high adsorption coefficient. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 5.9 x 10-4 Pa x m3/mole. It has low soil persistence with a reported half-life of 1 to seven days. The primary concern with mancozeb is its spontaneous degradation to ethylenethiourea (ETU, see datasheet) in the presence of water and oxygen. Ethylenethiourea has a persistence of 5 to 10 weeks. The solubility of mancozeb in water is about 5 to 15 mg/L. Its metabolites, carbon disulphide, ethylenethiourea and ethyleneurea, have the potential to be mobile in soils.

If it is released into water, mancozeb will tend to adsorb to sediment and suspended solids. Mancozeb degrades by hydrolysis in water with a half-life of 1 to two days in slightly acidic to slightly alkaline conditions.

NPIC (1994) quotes for mancozeb a soil half-life of 70 days, water solubility of 6 mg/L and a sorption coefficient (soil Koc) of 2,000. This resulted in a pesticide movement to groundwater rating of low.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of mancozeb (but not the metabolites) in water.

Ozone treatment and some newer advanced oxidation products appear to degrade mancozeb and ETU. Aeration should remove the carbon disulphide.

### Analytical methods

#### Referee method

No MAV, so no need. The conversion factor for recalculating CS2 to mancozeb is 1.78.

### Health considerations

In 1992 the USEPA concluded that the dietary risks of EBDCs exceeded the benefits for the following food/feed uses for which one or more of the EBDC pesticides were registered: apricots, carrots, celery, collards, mustard greens, nectarines, peaches, rhubarb, spinach, succulent beans, and turnips. Accordingly, the USEPA cancelled all mancozeb and other EBDC products registered on the above listed food/feed crops.

Mancozeb is a cholinesterase inhibitor and can therefore affect the nervous system.

A major toxicological concern with respect to mancozeb and other dithiocarbamates is its primary metabolite, ethylenethiourea, shown to cause thyroid and carcinogenic effects in test animals. Many studies dating back to 1980 show that mancozeb can cross the placental barrier and induce or increase tumour incidence. A recent study shows that mancozeb and its metabolites are capable of crossing the placental barrier and can produce DNA damage and initiate tumours in foetal cells.

Similar to other EBDCs and ethylenethiourea, the thyroid is the target organ for mancozeb. Thyroid effects were observed in multiple studies across species. Thyroid toxicity was manifested as alterations in thyroid hormones, increased thyroid weight, and microscopic thyroid lesions (mainly thyroid follicular cell hyperplasia), and thyroid tumours.

Acute, chronic, and cancer dietary (food only) risk from mancozeb, mancozeb-derived ethylenethiourea, and ethylenethiourea from all sources are low and below the USEPA’s level of concern. Acute, short-term, and chronic (non-cancer) aggregate risks are low and not of concern. Aggregate cancer risk estimates are within a negligible risk range.

The drinking-water exposure assessment for mancozeb addresses concentrations of ethylenethiourea only, since mancozeb is not expected to remain in drinking-water long enough to reach a location that would supply water for human consumption, whether from surface or groundwater sources. Estimated concentrations of ethylenethiourea, for both surface and groundwater sources of drinking-water, are low and not of concern.

As at September 2008 the USEPA has classified mancozeb in Group B: a probable human carcinogen. Mancozeb appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

The ADI is 0.03 mg/kg, and the RfD is 0.003 mg/kg/day (EXTOXNET 1996). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.13 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mancozeb is 4.29 mg/L.

The 1993 JMPR evaluated several dithiocarbamate fungicides for toxicology and residues when the meeting established an ADI of 0–0.03 mg/kg bw (group or in any combination) for ethylene-bis-dithiocarbamates (EBDCs: mancozeb, maneb, metiram and zineb) based on thyroid toxicity. For their metabolite ethylenethiourea (ETU), an ADI of 0–0.004 mg/kg bw has been allocated (JMPR 2012 and 2014). No ARfD value is quoted. The mancozeb residue is defined as total dithiocarbamates, determined as CS2, evolved during acid digestion and expressed as mg CS2/kg, for compliance with MRLs in plant and animal commodities.

The Acceptable Daily Intake (ADI) adopted in Australia is for mancozeb 0.006 mg/kg body weight, with a NOEL of 0.6 mg/kg bw based on a long-term (one-year) dietary study in dogs. The NOEL is based on decreased iodine uptake into thyroid tissue at doses of 2.4 mg/kg bw/day and above. The ADI incorporates a safety factor of 100. There is currently no ADI for ETU.

EC (2009) established an ADI of 0.05 mg/kg/d and an ARfD of 0.6 mg/kg/d. These values were reaffirmed by EFSA (2011).

The available human health and ecological effects data for mancozeb suggest possible endocrine effects (USEPA 2005).

### Derivation of Maximum Acceptable Value

No MAV.

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# Mandipropamid

CAS No. 374726-62-2. The IUPAC name for mandipropamid is (RS)-2-(4-chlorophenyl)-N-[3-methoxy-4-(prop-2-ynyloxy)phenethyl]-2-(prop-2-ynyloxy)acetamide. The CAS name is 4-chloro-N-[2-[3-methoxy-4-(2-propynyloxy)phenyl]ethyl]-α-(2-propynyloxy)benzeneacetamide.

Mandipropamid is a racemic mixture of a pair of enantiomers; it is produced and applied as a racemate with an isomer ratio of 1:1.

### Maximum Acceptable Value

Mandipropamid does not have a MAV in the DWSNZ; mandipropamid is not mentioned in the WHO Guidelines.

### Sources to water

Mandipropamid is a carboxylic acid amide or mandelamide fungicide commonly used to control downy mildew.

Mandipropamid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2010 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is used on onions and potatoes.

### Forms and fate in the environment

Mandipropamid is considered to be persistent in the environment based on its degradation in soil and water. The major route of dissipation is degradation under aerobic aquatic conditions. Mandipropamid degrades to several intermediary degradation products. The transformation products are ultimately degraded to non-extractable residues and carbon dioxide. Mandipropamid is moderately mobile and some of its metabolites are mobile to highly mobile in soils, and therefore have the potential to leach into groundwater. Mandipropamid can reach surface waters via spray drift and rainfall events that cause run-off.

Mandipropamid appears to be stable to hydrolysis in the environmental pH range of 5–9, but is susceptible to photolysis in soil and water. The environmental photolysis half-lifes of mandipropamid in pH 7, 25°C aqueous solutions was estimated as  
0.63–1.1 days. The soil photolysis half-lifes of mandipropamid was estimated as  
16.4–23.9 days. Based on its vapour pressure and Henry’s Law constant, volatilisation from water and soil are not expected to be important environmental fate processes.

The linear biodegradation half-life of mandipropamid in six European and one US soils ranged from approximately 26 to 103 days under aerobic conditions. Based on results from the supplemental study, under anaerobic conditions the rate of biodegradation appears to be much slower. Mandipropamid degraded with linear half-lifes of 151 days in a silt loam soil from Switzerland maintained under anaerobic conditions. The aerobic aquatic degradation half-lifes of mandipropamid were 17.8–18.5 days in two river water/silt loam sediment systems from England and Germany.

See JMPR (2008) for discussion on metabolites.

Water solubility is about 3–4 mg/L.

### Removal methods

No information available.

### Analytical methods

#### Referee method

No MAV, so no need.

### Health considerations

NZFSA (2008) quotes an Acceptable Daily Exposure (ADE) of 0.15 mg/kg bw/day. The PDE (food), a value set by the Environmental Risk Management Authority (ERMA), which represents the proportion of the acceptable daily exposure to a substance via the food route as relevant to the New Zealand population, is 0.10 mg/kg bw/day.

USEPA (2008) report a chronic RfD (and cPAD) of 0.05 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.05 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mandipropamid is 0.35 mg/L (no acute one-day value available.)

The JMPR 2008 Meeting established an actable daily intake (ADI) of 0–0.2 mg/kg bw based on the NOAEL of 15.2 mg/kg bw per day, identified on the basis of decreased body weight and kidney effects (increased severity of chronic progressive nephropathy and associated osteodystrophia fibrosa) at 61.3 mg/kg bw per day in the long-term dietary study in rats and using a safety factor of 100. The meeting noted that mandipropamid was not acutely toxic after short-term dosing, that there were no adverse findings in a study of acute neurotoxicity and that mandipropamid did not exhibit developmental toxicity. The meeting concluded that the establishment of an acute reference dose (ARfD) was unnecessary (FAO/WHO 2008). These values were reaffirmed in JMPR (2013).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5.0 mg/kg bw; an ARfD is not necessary.

EFSA (2011) quotes an ADI value 0.03 mg/kg/d. EFSA (2012 and 2013) quotes 0.15 mg/kg/d. Because of the low acute toxicity of the active substance, it is not necessary to establish an ARfD.

There was no evidence of neurotoxicity, mutagenicity or carcinogenicity after exposure to mandipropamid. Mandipropamid is classified as not likely to be a human carcinogen. In addition, there was no estrogen-, androgen-, and/or thyroid-mediated toxicity (USEPA 2008).

### Derivation of Maximum Acceptable Value

No MAV.

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# Marbofloxacin

CAS No. 115550-35-1. The chemical name is 9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido(3,2,1-ij)(4,2,1)benzoxadiazin-6 carboxylic acid.

### Maximum Acceptable Value

Marbofloxacin does not have a MAV in the DWSNZ; marbofloxacin is not mentioned in the WHO Guidelines.

### Sources to water

Marbofloxacin is a fluoroquinolone anti-inflammatory, antibacterial, antifungal and antibiotic agent, which acts by inhibition of DNA-gyrase. It is used on a range of animals including poultry, and lactating cows for the treatment of types of mastitis at a dose of about 2 mg/kg/d for five days. The main residue is unmetabolised marbofloxacin, with most excreted with urine. There is very little biotransformation.

Marbofloxacin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2010 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Marbofloxacin is described as being water soluble; presumably it can be found in shallow groundwater that urine can seep into.

### Removal methods

No information available.

### Analytical methods

#### Referee method

No MAV, so no need.

### Health considerations

In a 13-week study, dogs were orally dosed at 1, 4 or 40 mg/kg/d. Typical quinolone-induced changes in the articular cartilage (lameness) were observed at the higher doses. Testicular tubular atrophy and spermatic granuloma was observed at that dose too. The NOEL was 4 mg/kg/d. Applying a safety factor of 100 to the 13-week dog study NOEL, results in an ADI of 0.04 mg/kg/d.

Covering the possible effects on the bacterial flora in the human stomach results in an ADI of 0.0045 mg/kg/d, ie, about 0.3 mg/d. This ADI has been adopted in New Zealand, see Proposal to Set MRLs for Marbofloxacin (<http://www.nzfsa.govt.nz/consultation/mrl/page-08.htm>).

The Australian Government considered an ARfD is not necessary.

There was no evidence of teratogenicity at doses up to 80 mg/kg/d. Marbofloxacin is thought to be not carcinogenic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# MCPA

CAS No. 94-74-6. IUPAC name is 4-chloro-o-tolyloxyacetic acid. CAS name is (4-chloro-2-methylphenoxy)acetic acid. Also sold as the MCPA-thioethyl ester (CAS No. 25319-90-8), the dimethylamine salt (CAS No. 2039-46-5), and in a variety of other salts and esters, see JMPR (2012). All forms of MCPA dissociate in water to the acid (anion) form.

### Maximum Acceptable Value

Based on health considerations, the concentration of MCPA in drinking-water should not exceed 0.002 mg/L (2 g/L). This was based on the WHO (2011) guideline value.

WHO (2017) states that MCPA occurs in drinking-water or drinking-water sources at concentrations well below those of health concern so there is no reason for establishing a guideline value. Instead, they have derived a health-based value of 0.7 mg/L, and an acute health-based value of 20 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.04 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.03 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

JMPR (1994) states that free phenols should not exceed 10 g/kg (1 percent) measured as 4-chloro-2-methylphenol – see datasheet for 4-chloro-3-methylphenol in organic chemicals section for further information.

Health Canada established a maximum acceptable concentration for 2-methyl-4-chlorophenoxyacetic acid (MCPA) of 0.1 mg/L in 2010. Short-term exceedances above the guideline value are unlikely to have an impact on health, unless these exceedances are due to massive contamination or spills.

### Sources to water

MCPA may enter source waters as a result of its use as a systemic hormone-type selective chlorophenoxy or phenoxyacetic acid herbicide which is readily absorbed by leaves and roots. It is used for the post-emergence control of annual and perennial broadleaf weeds such as buttercup and thistles in cereals, grassland and turf. It is applied as various salts and esters. MCPA is commonly used in formulations alongside mecoprop and dicamba.

In the USA, MCPA was found at levels of 0.00004 to 0.00054 mg/L in four of 18 surface water samples analysed.

The total annual usage of MCPA in New Zealand in the late 1980s was 276,000 kg which was evenly split between the North and South Islands. MCPA appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 446.7 tonnes of MCPA were used in New Zealand in 2004, at an application rate of 2250 grams of active ingredient per hectare.

MCPA is usually applied along with other phenoxy herbicides, such as 2,4-D, 2,4-DB, mecoprop-p, and MCPB.

### Forms and fate in the environment

Based on its Koc range of 50 to 62, MCPA can be expected to leach readily in most soils (less so in soil rich in organic matter) so could contaminate groundwater. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon a Henry’s Law constant of 5.5 x 10-5 Pa.m3/mol at 25°C. In aerobic soil conditions it biodegrades with half-lifes ranging from 7 (neutral pH) to 60 days (acidic soil). The recommended average half-life in soil is 25 days.

If released into water, MCPA is not expected to adsorb to suspended solids and sediment based on its Koc. It does not volatilise from surface waters, but undergoes photolysis and biodegradation with half-lifes between 10 and 24 days. In the pH range of 5 to 9 it does not degrade in sterile aqueous solutions. MCPA is very persistent in anaerobic conditions.

The octanol-water partition coefficient at 25ºC = log Pow = 0.28 to 0.59 at pH 5; -0.81 to -0.71 at pH 7; -1.07 to -0.88 at pH 9. JMPR (2012).

The water solubility of MCPA is 2.6 percent (pH 5), 29 percent (pH 7), 32 percent (pH 9). The water solubility of MCPA-thioethyl ester is about 2.2 mg/L.

Based on its Henry’s Law constant (7.46 × 10-5 Pa·m³/mol), MCPA is not expected to volatilise from water or moist surfaces. Its vapour pressure also indicates a low potential to volatilise, and its dissociation constant indicates that it will dissociate rapidly at environmental pH (Health Canada 2010).

NPIC (1994) quotes for MCPA dimethylamine salt a soil half-life of 25 days, water solubility of 86.6 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of high. The MCPA ester has a soil half-life of 25 days, water solubility of 5 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

Metabolites are mostly minor, the most significant being 2-methyl-4-chlorophenol (EC 2008).

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, did not find any detectable concentrations of MCPA (limit of detection = 0.0001 mg/L) (ESR 2001).

MCPA is not frequently detected in drinking-water, it has been measured in surface water and groundwater at concentrations below 0.00054 and 0.0055 mg/L, respectively (WHO 2004).

MCPA has been found in a Canterbury groundwater at 0.061 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). MCPA occurred at 61 µg/L, ie, 0.061 mg/L.

In Alberta, MCPA was seldom detected (11 percent) in a treated water survey program during the period 1995–2003. MCPA was detected in 190 of a total of 1788 water samples collected for analysis throughout this period. MCPA was detected more at treatment facilities with surface water sources (13.7 percent) than at facilities with groundwater sources (2 percent); the maximum concentrations detected were 571 ng/L and 5 ng/L, respectively. The data showed no overall or seasonal trend over the nine years in detection frequency or concentration (Health Canada 2010). UF and RO have been shown to be effective.

### Removal methods

After 50 to 80 percent oxidation of MCPA (500 mg/L) by ozone, no degradation products are detectable, indicating that ozonation may provide a practical means of removing this pesticide. WHO (2011) states that a concentration as low as 0.0001 mg/L should be achievable using GAC, ozonation, or ozone/UV. The concentrations of organic compounds, such as pesticides, may be reduced through coagulation/ flocculation if they are hydrophobic or have low molecular weight acidic functional groups: the chemical properties of MCPA (moderately lipophilic; substituted acetic acid) may result in limited removal by conventional water treatment (Health Canada 2010). RO may be effective (WHO 2017).

### Recommended analytical techniques

#### Referee method

High Performance Liquid Chromatography with a Photoiodide Array Ultraviolet Detector (EPA 555).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6640B).

### Health considerations

The target organs for the MCPA ion are the kidney, liver and blood. Animal studies have shown that MCPA is absorbed readily from the gut of mice and detected in all organs tested. It is metabolised by the liver. In humans, 5 percent of the total dose was detected in the urine within 48 hours.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.004 mg/kg/d based on a NOAEL of 4.4 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.14 mg/L. The oral RfD had earlier been 0.0005 mg/kg/d (USEPA 1991).

EC (2008) revised their ADI from 0.013 to 0.05 mg/kg/d. The ARfD is 0.15 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1.1 mg/kg bw based on a two-year dietary rat study. The NOEL is based on evidence of mild liver effects (changes in clinical chemical parameters). The ADI incorporates a safety factor of 100.

FAO/WHO (2012) established an estimate of acceptable daily intake for humans of  
0–0.1 mg/kg bw, and an estimate of acute reference dose of 0.6 mg/kg bw. The 2012 JMPR established an ADI for MCPA of 0–0.1 mg/kg bw/day and an ARfD of 0.6 mg/kg bw.

Epidemiological investigations on MCPA have involved chlorophenoxyacetic weed killer producers and users, so exposure to this product generally is accompanied by exposure to 2,4-D, 2,4,5-T, mecoprop and dichlorprop. The International Agency for Research on Cancer (1986) carried out a comprehensive evaluation related to “professional exposure to chlorophenoxyacetic weed killers” which were considered to show “limited evidence” of carcinogenicity. IARC (1983) had stated that the available data are insufficient to evaluate the carcinogenicity to humans of MCPA alone (Group 2B).

As at September 2008, the USEPA has classified MCPA as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of a MAV for MCPA. The no-observable-adverse-effect level used in the derivation is based on liver and kidney toxicity observed in a one-year feeding study in dogs.

The MAV for MCPA in drinking-water was derived as follows:

0.15 mg/kg body weight/day x 70 kg x 0.1 = 0.002 mg/L (2 g/L)

2 L/day x 300

where:

* no-observable-adverse-effect level = 0.15 mg/kg body weight per day based on liver and kidney toxicity observed in a one-year feeding study in dogs
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 300; 100 for inter and intra-species variation and 3 for the inadequacy of the data base.

The WHO (2016/2017) health-based value of 0.7 mg/L was derived from the 0–0.1 mg/kg bw ADI for MCPA ion, based on an overall NOAEL of 12 mg/kg bw per day for changes in clinical chemistry parameters indicative of effects on the kidneys from four subchronic studies in rats and application of a safety factor of 100. The ADI was established for the sum of MCPA and its salts and esters, expressed as MCPA acid equivalents.

The WHO (2016/2017) acute health-based value of 20 mg/L was derived from the 0.6 mg/kg bw ARfD for MCPA ion, based on an overall NOAEL of 60 mg/kg bw for maternal and developmental toxicity in rats and application of a safety factor of 100. The ARfD was established for the sum of MCPA and its salts and esters, expressed as MCPA acid equivalents.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for MCPA is 0.003 mg/L.

Young et al (1996) report MCPA to have taste threshold of about 0.004 mg/L, but a much higher odour threshold (of about 0.46 mg/L).

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# MCPB

CAS No. 94-81-5. IUPAC name is 4-(4-chloro-o-tolyloxy)butyric acid. CAS name is 4‑(4‑chloro-2-methylphenoxy)butanoic acid. Also called 4(2-methyl-4-chlorophenoxy)butyric acid. The sodium salt has CAS No. 6062-26-6.

### Maximum Acceptable Value

WHO (2004) states that currently available toxicological data are insufficient to be used as the basis for a guideline value for MCPB in drinking-water. WHO (2011) states that MCPB is unlikely to occur in drinking-water.

In DWSNZ 2005, the provisional MAV for MCPB in drinking-water had been 0.03 mg/L (30 g/L).

### Sources to water

MCPB may enter source waters as a result of its use as a systemic hormone-type selective chlorophenoxy herbicide. MCPB is used as an herbicide for the control of broadleaf weeds in young and established pastures, clover seed crops, peas, linseed, and undersown cereals, usually applied during active growth of the weed. It is absorbed readily by leaves and roots and is used for the control of annual and perennial weeds in cereals, grassland and turf.

Surface water in the Netherlands has been found to contain a maximum concentration of 0.01 mg/L.

MCPB appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). The total annual usage of MCPB in New Zealand in the late 1980s was 35,500 kg, with the majority of this being in the South Island. ERMA notes that 173.7 tonnes of MCPB were used in New Zealand in 2004, at an application rate of 1,540 grams of active ingredient per hectare.

EC (2005) states that MCPB must not contain more than 30 g/kg free phenols measured as 4-chloro-2-methylphenol – see datasheet for 4-chloro-3-methylphenol in organic chemicals section for further information.

### Forms and fate in the environment

If released to soil, MCPB is expected to have low mobility based upon an estimated Koc value of 780. Volatilisation from moist soil surfaces will not be an important fate process. MCPB degrades in soil to form MCPA and 4-chloro-2-methylphenol. Its half-life in soil ranges from 6 to 14 days unless the soil micro-organisms are acclimatised to the herbicide, in which case its half-life can be less than one day.

If released into water, MCPB is expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilisation from water surfaces will not be an important environmental fate process. MCPB is stable to hydrolysis at pH 5 to 9, but photolysed in aqueous solutions under optimal light exposure conditions with half-lifes of approximately two to three days. Photolytic degradation in water produces five major products (EC 2005): o-cresol, 4-(4-hydroxy-o-tolyloxy)butyric acid, 2,4 dihydroxyphenyl formate, benzoic acid, and 2-hydroxyphenyl formate.

The water solubility of MCPB is 110 mg/L at pH 5, 4400 mg/L at pH 7, and 44 percent at pH 9.

NPIC (1994) quotes for MCPB sodium salt a soil half-life of 14 days, water solubility of 20 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

No data are available on the concentration of MCPB in New Zealand drinking-water supplies. It was undetected in 447 Canadian surfaces waters, but was found in Dutch surface waters at maximum concentrations ranging from 0.001 to 0.01 mg/L (1 to 10 g/L).

MCPB has been found in a groundwater at 0.0021 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). MCPB occurred at 2.1 µg/L, ie, 0.0021 mg/L.

### Removal methods

No specific information on methods of removing MCPB from water is available. Slow sand filtration can partially remove members of the chlorophenoxy acid pesticide family of which MCPB is a member. Ozone has shown varying degrees of effectiveness in oxidising the chlorophenoxy acids. GAC is likely to be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so no need.

#### Some alternative methods

1. Chlorophenoxy herbicides, including MCPB may be determined by a liquid-liquid extraction, chemical derivatisation, and analysis by gas chromatography with electron capture, electrolytic conductivity or mass spectrometry detection (Que Hee and Sutherland).

2. Alternatively, high-performance liquid chromatography with ultraviolet detection may be used for the quantitation. Detection limits range from 0.001 mg/L to 1 mg/L depending on the method of analysis. Interference may occur from impurities in the reagents or glassware used for extraction.

### Health considerations

In general, chlorophenoxy herbicides are absorbed rapidly from the gastrointestinal tract and evenly distributed throughout the body. Accumulation in human tissues is not expected and a steady-state level in the human body will be achieved within  
3–5 days of exposure. Elimination occurs primarily in the urine, mostly in the unchanged form. Biological half-lifes of chlorophenoxy herbicides in mammals range from 10 to 33 hours. Metabolic conversions occur only at high doses. The salt and ester forms are hydrolysed rapidly and follow the same pharmacokinetic pathways as the free acid forms.

EC (2005) established an ADI of 0.01 mg/kg/d, and an ARfD of 0.05 mg/kg/d.

The oral RfD for MCPB was calculated at 0.01 mg/kg/d (USEPA 1990). A chronic oral reference dose (RfD) of 0.015 mg/kg-day was set by the USEPA (2006) for MCPB, based on a NOAEL of 4.4 mg kg/day in a chronic toxicity study of MCPA in rats. Effects observed at the LOAEL were liver and kidney toxicity. The RfD was calculated by dividing the NOAEL by an uncertainty factor of 300 (10x for interspecies variability, 10x for intraspecies variability, and 3x database uncertainty to account for the lack of a developmental neurotoxicity study). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0044 mg/kg/d, and an ARfD of 0.20 mg/kg/d for MCPB acid. For MCPB sodium salt the values are 0.015 mg/kg/d and 0.20 mg/kg/d respectively. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for MCPB (both the acid and the sodium salt) is 2.0 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for MCPB is 0.01 mg/kg body weight, with a NOEL of 1.1 mg/kg bw.

Chlorophenoxy herbicides as a group, including 2,4-D and MCPA, have been classified by the International Agency for Research on Cancer in Group 2B (possibly carcinogenic to humans). However, based on the available data from studies on exposed populations and on animals, it is not possible to assess the carcinogenic potential of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects. There were no tumour effects observed in any MCPA or MCPB studies, and therefore the USEPA did not conduct a cancer assessment. Mutagenicity tests conducted with MCPB and MCPA were negative (USEPA 2006).

### Derivation of Maximum Acceptable Value

WHO (2004) had stated that the then currently available toxicological data were insufficient to be used as the basis for a guideline value for MCPB in drinking-water. Since then WHO (2011) considers that MCPB is unlikely to be found in drinking-water.

In DWSNZ 2005, the provisional MAV for MCPB in drinking-water had been derived as follows:

0.01 mg/kg body weight/day x 70 kg x 0.1 = 0.03 mg/L

2 L/day

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# Mecoprop

CAS No. 93-65-2, and 7085-19-0 for the racemic mixture. The IUPAC name for mecoprop is (RS)-2-(4-chloro-o-tolyloxy)propionic acid. The CAS name is 2-(4-chloro-2-methylphenoxy)propanoic acid Also called MCPP, or 2-(2-methyl-4-chlorophenoxy)propionic acid.

The (R)-isomer of this substance has the ISO common name [mecoprop-P](http://www.alanwood.net/pesticides/mecoprop-p.html); CAS No. 16484-77-8. The IUPAC name is (R)-2-(4-chloro-o-tolyloxy)propionic acid; the CAS name is (2R)-2-(4-chloro-2-methylphenoxy)propanoic acid. Also called MCPP-p.

### Maximum Acceptable Value

Based on health considerations, the concentration of mecoprop in drinking-water should not exceed 0.01 mg/L.

JMPR (1984) states that free phenols should not exceed 15 g/kg (1.5 percent) measured as 4-chloro-2-methylphenol – see datasheet for 4-chloro-3-methylphenol in organic chemicals section for further information.

### Sources to water

Mecoprop is a phenoxy-benzoic acid herbicide. It may enter source waters as a result of its use for the post-emergent residual control of broadleaved weeds in cereals, grassland and under fruit trees and vines, and the control of dock in pasture. It is commonly used in formulations alongside MCPA and dicamba.

Surface water in the Netherlands has been found to contain a maximum mecoprop concentration of 0.01 mg/L.

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The total annual usage of mecoprop in New Zealand in the late 1980s was 115,000 kg, mostly in the South Island. The highest usage was in the Ashburton County (33,000 kg). ERMA notes that 178.4 tonnes of mecoprop were used in New Zealand in 2004, at an application rate of 2,400 grams of active ingredient per hectare.

### Forms and fate in the environment

Available environmental fate data indicates that MCPP-p is generally non-persistent in soil, but may be persistent in certain (acidic) terrestrial environments. MCPP-p does not adsorb strongly to soils and, based on Koc values of 5 to 47, is likely to be mobile in terrestrial and aquatic environments. Volatilisation from moist soil is not expected because MCPP-p exists as an anion and anions do not volatilise. Mecoprop is degraded in soil to 4-chloro-2-methylphenol and o-cresol with half-lifes of 7 to 21 days.

EFSA (2017) states there is the potential for the active substance mecoprop-P to be present in shallow groundwater above the parametric drinking water limit of 0.1 μg/L.

Mecoprop is fairly persistent in water with half-lifes reported at more than three weeks. The primary routes of dissipation appear to be photodegradation in water, microbial-mediated degradation, and leaching. Its water solubility is 620 mg/L for the acid and much higher (500,000 to 920,000 mg/L) for the alkali and amine salts.

NPIC (1994) quotes for mecoprop dimethylamine salt (MCPP) a soil half-life of 21 days, water solubility of 66 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, did not find any detectable concentrations of mecoprop (limit of detection = 0.0001 mg/L) (ESR 2001).

Chlorophenoxy herbicides are not frequently found in drinking-water, but when detected, concentrations are usually no greater than a few micrograms per litre (WHO 2004).

Mecoprop has been found in five groundwaters, in Marlborough and Canterbury, ranging from 0.00051 to 0.42 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Mecoprop occurred at 2.4 to 3.2 µg/L, ie, up to 0.0032 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Mecoprop occurred at 420 µg/L, ie, 0.42 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Mecoprop occurred at 0.51 to 0.67 µg/L, ie, up to 0.00067 mg/L.

Mecoprop was found in one bore during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.0002 to 0.00016 mg/L. The bore was in the Canterbury region.

### Removal methods

No specific information on methods of removing mecoprop from water is available. However, slow sand filtration can partially remove members of the chlorophenoxy acid pesticide family of which mecoprop is a member. Ozone has shown varying degrees of effectiveness in oxidising the chlorophenoxy acids. WHO (2011/2017) states that a concentration of 0.0001 mg/L should be achievable using GAC or ozonation.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction/Gas Chromatography with Electron Capture Detector (EPA 525.2).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6640B, although not mentioned in the 2005 edition).

2. Liquid/Solid Extraction/Gas Chromatography with Electron Capture Detector (EPA 552.1).

### Health considerations

In general, chlorophenoxy herbicides are absorbed rapidly from the gastrointestinal tract and distributed evenly throughout the body. Accumulation in human tissues is not expected and a steady-state level in the human body will be achieved within  
3–5 days of exposure. Elimination occurs primarily in the urine, mostly in the unchanged form. Biological half-lifes of chlorophenoxy herbicides in mammals range from 10 to 33 hours. Metabolic conversions occur only at high doses. The salt and ester forms are hydrolysed rapidly and follow the same pharmacokinetic pathways as the free acid forms. Mecoprop readily crosses the placental barrier.

Effects of dietary administration of mecoprop in short-term and long-term studies include decreased relative kidney weight (rats and dogs), increased relative liver weight (rats), effects on blood parameters (rats and dogs) and depressed body weight gain (dogs) (WHO 2017). Symptoms described in case histories of humans suffering from acute poisonings by weedkiller solutions containing mecoprop include coma, fever, respiratory problems, myotonia (muscle stiffness), muscle cramps, skeletal muscle damage, electrocardiographic changes, decreased blood pressure, distended abdomen and rhabdomyolysis with renal failure.

EC (2003) established an ADI of 0.01 mg/kg/d for mecoprop and mecoprop-p, and stated that an ARfD was unnecessary. Reaffirmed by EFSA (2013). EFSA (2017) introduced an ARfD of 0.2 mg/kg bw per day based on the NOAEL of 20 mg/kg bw per day for the increased incidence of late resorption in the rabbit developmental study and applying an UF of 100.

The USEPA (2007) established a chronic dietary RfD for mecoprop of 0.04 mg/kg/d based on a NOAEL of 4.4 mg/kg/d and a UF of 100. The LOAEL = 46 mg/kg/day based on increased incidence of chronic nephropathy and increased absolute/relative kidney weights in females. The oral RfD had earlier been 0.001 mg/kg/d (USEPA 1990). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.04 mg/kg/d, and an ARfD of 1.75 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for MCPP-p is 17.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for mecoprop is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw, and the ARfD is 0.5 mg/kg bw. The Acceptable Daily Intake (ADI) adopted in Australia for mecoprop-p is 0.04 mg/kg body weight, with a NOEL of 4 mg/kg bw, and the ARfD is 0.5 mg/kg bw. The ARfD for mecoprop and mecoprop--p only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

There were no genotoxic concerns based on in-vitro and in-vivo studies on mecoprop and mecoprop-P (EC 2003).

As at September 2008 the USEPA considers mecoprop-p shows suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential.

Chlorophenoxy herbicides as a group, including 2,4-D and MCPA, have been classified by the International Agency for Research on Cancer in Group 2B (possibly carcinogenic to humans). However, based on the available data from studies on exposed populations and on animals, it is not possible to assess the carcinogenic potential of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects (WHO 2017).

### Derivation of Maximum Acceptable Value

Because it is not possible to assess the carcinogenic potential to humans of any specific chlorophenoxy herbicide, a tolerable daily intake approach has been used for the derivation of the MAV. The no-observable-adverse-effects level used in the derivation is based on increased kidney weight in 1- and two-year studies in rats.

The MAV for mecoprop in drinking-water was derived as follows:

1 mg/kg body weight/day x 70 kg x 0.1 = 0.0117 mg/L (rounded to 0.01 mg/L)

2 L/day x 300

where:

* no-observable-adverse-effect level = 1 mg/kg body weight per day based on increased kidney weight in 1- and two-year studies in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 300 (100 for inter and intra-species variation and 3 for limitations of the data base).

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WHO. 2017. *Guidelines for Drinking-water Quality: Fourth edition incorporating the first addendum*. Geneva: World Health Organization [631 pp]. [http://www.who.int/water\_sanitation\_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\INetCache\Content.Word\www.who.int\water_sanitation_health\publications\2011\dwq_guidelines\en\)

# Mefenpyr

CAS No. 135591-00-3. The IUPAC name for mefenpyr is (RS)-1-(2,4-dichlorophenyl)-5-methyl-2-pyrazoline-3,5-dicarboxylic acid. The CAS name is 1-(2,4-dichlorophenyl)-4,5-dihydro-5-methyl-1H-pyrazole-3,5-dicarboxylic acid. This is commonly used as the ester [mefenpyr-diethyl](http://www.alanwood.net/pesticides/derivatives/mefenpyr-diethyl.html), CAS No. 135590-91-9. Called herbicide safener HOE 107982 in the US.

### Maximum Acceptable Value

Mefenpyr is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Mefenpyr is a herbicide safener. Safeners, which are rapidly absorbed by crop plants, are added to herbicides to accelerate their degradation and prevent damage to the plants.

This substance does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is stated by ERMA to be a component of the herbicide Hussar, along with iodosulfuron-methyl (qv). Hussar is a herbicide commonly used on cereals to control grass weeds. Mefenpyr-diethyl is also added to fenoxaprop-p-ethyl (qv).

### Forms and fate in the environment

Water solubility of mefenpyr-diethyl is about 20 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

For chronic toxicity, the USEPA has established a reference dose (RfD) of 0.51 mg/kg/day. This RfD is based on a chronic feeding study in dogs with a NOEL of 51.4 mg/kg/day and an uncertainty factor of 100. An LOEL of 260 mg/kg/day is based on increased alkaline phosphatase and absolute/relative liver weights and grade 1 (minimal) intrahepatic cholestasis in the liver. The results from a two-generation reproduction study in the rat support the NOEL from the chronic feeding study in the dog with a NOEL of 57.3 mg/kg/day and an LOEL of 305.9 mg/kg/day based on decreased mean body weight and mean body weight gain in the parents and offspring. The acute RfD is 1 mg/kg bw/day (PMEP 1997).

The USEPA (1998) used a No Observable Effect Level (NOEL) of 100 mg/kg/day, based on increased preimplantation loss (indicative of initiation of dosing too early, which appeared after a single dose) at the Lowest Observable Effect Level (LOEL) of 250 mg/kg/day, from a developmental toxicity study in rabbits. Using an uncertainty factor of 100 for intra- and inter-species differences, the acute RfD for oral exposure was calculated to be 1 mg/kg/day. USEPA (2003) determined that there was no acute toxicological concern. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.51 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mefenpyr-diethyl is 3.57 mg/L (no acute one-day value available.)

The USEPA determined that there is no acute toxicological concern. No appropriate endpoint was identified from oral toxicity studies including the developmental toxicity studies in rats and rabbits. No short-term or intermediate-term dermal or systemic toxicity was observed up to 1,000 mg/kg/day and no development effects were observed in the developmental rat study at 1,000 mg/kg/day. For chronic dietary risk assessment the NOAEL of 57.3 mg/kg/day in a two–generation reproduction toxicity study was identified as an appropriate end point. Taking into account the UF of 100, the chronic RfD is 0.57 mg/kg/day (NOAEL 57.3/UF 100 = 0.57) (USEPA 2003). The chronic RfD is stated to be 0.51 mg/kg/day (USEPA 2008). The USEPA has determined that mefenpyr-diethyl is not likely to be a human carcinogen. This was based on weight-of-the evidence from negative rat and mouse carcinogenicity studies as well as negative mutagenicity studies.

The Acceptable Daily Intake (ADI) adopted in Australia for mefenpyr-diethyl is 0.03 mg/kg body weight, with a NOEL of 2.8 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

PMEP. 1997. Mefenpyr-Diethyl – Pesticide Tolerance 8/98. *Federal Register* 63(174): 48116–24. Rules and Regulations, 9 September. See: <http://pmep.cce.cornell.edu/profiles/miscpesticides/misc_E_N/mefenpyr_diethyl/mefdie_tol_0898.html>

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# Mepiquat chloride

CAS No. 24307-26-4. Both the IUPAC and CAS name for mepiquat chloride is 1,1‑dimethylpiperidinium chloride. Also called N,N-dimethylpiperidinium chloride.

### Maximum Acceptable Value

Mepiquat chloride is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Mepiquat chloride, a derivative of [mepiquat](http://www.alanwood.net/pesticides/mepiquat.html) (CAS No. 15302-91-7) is a tertiary amine plant growth regulator (by inhibiting the biosynthesis of gibberellic acid) which acts to reduce internode length, hasten maturity, and retard abscission – all of which increase yield potential. It is used in onions, garlic and leeks to inhibit sprouting. Mepiquat is used on cereals to reduce unwanted longitudinal shoot growth without lowering plant productivity.

Mepiquat chloride appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 14.9 tonnes of mepiquat chloride were used in New Zealand in 2004, at an application rate of 460 grams of active ingredient per hectare.

### Forms and fate in the environment

Mepiquat chloride is very soluble in water: about 50 percent. It has a half-life in aerobic soil and water of up to 20 days, and about a year in anaerobic soil. It is relatively non‑mobile in sandy loam, loam, and clay loam soils. Mepiquat chloride is cationic and binds strongly to clay minerals in soil. It is stable to photolysis and hydrolysis, but is degraded rapidly to CO2 by aerobic micro-organisms. Mepiquat chloride appears to be mobile in sandy soil.

EFSA (2013) states that soil studies demonstrated the degradation rate of mepiquat is moderate, the maximum DT90 was 95 days.

NPIC (1994) quotes for mepiquat chloride a soil half-life of 1,000 days, water solubility of 100 percent and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The USEPA Hazard Identification Assessment Review Committee (HIARC) established a reference dose (RfD) of 0.6 mg/kg/day for mepiquat chloride based on the NOEL from the one-year dog study (58.4 mg/kg/day) and an uncertainty factor of 100. This RfD has not yet been adopted by the USEPA’s *Integrated Risk Information System (IRIS)* which lists the RfD for this chemical as 0.03 mg/kg/day based on a NOEL (25 mg/kg/day) from a 90-day dog feeding study and an uncertainty factor of 1,000. This RfD was placed in the USEPA’s IRIS in August 1988 and is based on a subchronic study. By contrast, the RfD for mepiquat chloride established by USEPA’s HIARC is based on a more recently completed chronic study. Generally, chronic studies are preferable to subchronic studies for establishing RfD values. See PMEP. 2001. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.195 mg/kg/d, and an ARfD of 0.195 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mepiquat chloride is 1.95 mg/L.

The EC (2008) derived an ADI of 0.2 mg/kg/d and an ARfD of 0.3 mg/kg bw/day. Reaffirmed by EFSA (2013, 2015, 2018).

The Acceptable Daily Intake (ADI) adopted in Australia for mepiquat is 0.15 mg/kg body weight, with a NOEL of 15 mg/kg.

USEPA (1997) classified mepiquat chloride into Group E (evidence of non-carcinogenicity for humans).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2008. *Final Review Report for the Active Substance Mepiquat*. European Commission Health & Consumers Directorate-General. *SANCO*/106/08 – rev. 2 [7 pp]. See: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

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# Mesosulfuron-methyl

CAS No. 208465-21-8. Sometimes spelt without the hyphen. The IUPAC name for mesosulfuron is 2-[(4,6-dimethoxypyrimidin-2-ylcarbamoyl)sulfamoyl]-α-(methanesulfonamido)-p-toluic acid. The CAS name is 2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-4-[[(methylsulfonyl)amino]methyl]benzoic acid.

The core or parent substance, mesosulfuron, CAS No. is 400852-66-6.

### Maximum Acceptable Value

Mesosulfuron-methyl is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Mesosulfuron-methyl is a systemically active pyrimidinylsulfonylurea herbicide, commonly used on wheat.

Mesosulfuron-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Biotransformation is the major route of degradation of mesosulfuron in the environment, as evidenced by mineralisation (ie, formation of CO2) in aerobic soils and persistence varying with microbial population and temperature (USEPA 2004).

Mesosulfuron exhibits weak binding to soils. Mesosulfuron, like other sulfonylurea herbicides, will predominate in the water phase and not in sediments. It has the potential to leach to groundwater or reach surface water by run-off. Mesosulfuron has low potential to volatilise from soil or water or to bioaccumulate in fish (USEPA 2004).

Considering the widespread, potential use areas of variable soils, microbial population and activity, water bodies, climates/meteorology, and agricultural practices, high variability in persistence in soil and water-sediment systems is expected.

The half-life in soil field studies of mesosulfuron-methyl is reported (EC 2004) as 30 to 114 days. In water/sediment studies the half-life ranged from 20 to 70 days.

The potential for groundwater exposure from the representative uses by mesosulfuron-methyl above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all FOCUS groundwater scenarios, except in two winter wheat scenarios where the limit was exceeded.

Water solubility (20ºC) of mesosulfuron-methyl is about 7.2 mg/L at pH 5, 480 mg/L at pH 7, and 15,400 mg/L at pH 9 (EC 2004).

### Health considerations

Mesosulfuron-methyl has low acute oral, dermal, and inhalation toxicity (USEPA 2004). The chronic RfD was calculated at 1.55 mg/kg/d; there is no acute dietary endpoint of concern. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 1.55 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mesosulfuron methyl is 10.9 mg/L (no acute one-day value available.)

EC (2004) and EFSA (2012 and 2016) established an ADI for mesosulfuron-methyl of 1 mg/kg/d; no ARfD was required.

The Acceptable Daily Intake (ADI) adopted in Australia for mesosulfuron-methyl is 1 mg/kg body weight, with a NOEL of 100 mg/kg, and the ARfD is 2 mg/kg bw. In Jan 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

Mesosulfuron-methyl is classified by the USEPA as “not likely to be carcinogenic to humans”. There was no evidence of neurotoxicity in the acute, subchronic, or chronic toxicity studies.

### Derivation of Maximum Acceptable Value

No MAV.

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USEPA. 2004. Mesosulfuron-methyl*. Pesticide Factsheet* [10 pp]. <http://www.epa.gov/opprd001/factsheets/>

# Mesotrione

CAS No. 104206-82-8. The IUPAC name for mesotrione is 2-(4-mesyl-2-nitrobenzoyl)cyclohexane-1,3-dione. The CAS name is 2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione. Has been misspelt as mestotrione.

### Maximum Acceptable Value

Mesotrione is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

EPA established an environmental exposure limit of 0.0008 mg/L (0.8 µg/L) for mesotrione in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Mesotrione is a systemic benzoylcyclohexanedione or triketone herbicide, based on a compound from bottle brush plants identified as leptospermone. It is commonly used for annual broadleaf weed control in field corn and maize, both pre-emergence and post-emergence.

Mesotrione appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The manufacturing impurity 1-cyano-6-(methylsulfonyl)-7-nitro-9H-xanthen-9-one is considered to be of toxicological concern and must remain below 0.0002 percent (w/w) in the technical product (EC 2003). 1,2-Dichloroethane should be <1 g/kg dry weight (EFSA 2016). The product Callisto comprises 48 percent mesotrione and 14 percent ethylene glycol.

### Forms and fate in the environment

Mesotrione is not persistent in water and soil as indicated by the photolysis, aerobic and anaerobic soil metabolism and terrestrial field dissipation studies. Mesotrione degradates are mobile, thus they have the potential to reach groundwater and/or surface water. Mobility and persistence are of the greatest concern in cold climates with low pH soils. Mesotrione is not persistent but degradates to MNBA [4‑(methylsulfonyl)-2-nitrobenzoic acid], and AMBA [2-amino-4-(methylsulfonyl)benzoic acid] may be persistent under suboxic conditions such as subsoil and groundwater (USEPA 2001a).

The half-life in water and in soil studies is reported (EC 2003) as three to seven days; also it is unlikely that mesotrione, MNBA and AMBA will exceed 0.0001 mg/L in groundwater. AMBA was the only major metabolite found in the sediment water system; it attained a maximum about 10 percent of the active ingredient in the water phase and was always <10 percent in the sediment.

DT90field values of mesotrione are expected to range between 36–78 days; the major soil metabolites MNBA and AMBA were also demonstrated to be of low persistence (DT50lab values of 7.5 and 3.2 days, respectively) (EFSA 2015).

Water solubility of mesotrione is 160 mg/L in unbuffered water at 20°C and 2200 mg/L at pH 9 at 20°C (EC 2003).

JMPR (2014) reports: Henry’s Law constant = <5.1 × 10–7 Pa/m3/mol and the partition coefficient = n-octanol/ water at 20°C = log POW = 0.90 at pH 5 and <1.0 at pH 7 and 9. Hydrolysis in water at 25°C: less than l0 percent degradation of mesotrione (1 μg/mL) occurred during the test period of 30 days in the pH of 4–9 at both 25 and 50°C. The photolysis half-life in sterile aqueous buffer solutions at pH 7 at 25°C was 83.7 days at 37°56’ latitude local sunlight, or 92 days at 50°N. Metabolism of mesotrione applied to various soils at rates ranging from 0.165 to 0.85 kg ai/ha and kept under aerobic conditions in the dark at 25±1°C for 28 to 60 days was investigated: mesotrione degraded relatively fast, with DT50 values ranging from 4.5 to 32 days; metabolites are discussed too. In two water sediment systems experiments with mesotrione showed DT50 values from three to six days.

### Recommended analytical techniques

#### Some alternative methods

See EFSA (2016); LOQ of 0.05 μg/L.

### Health considerations

Mesotrione has a low acute toxicity via the oral, dermal, and inhalation routes, therefore a quantitative acute dietary exposure assessment is unnecessary (USEPA 2001).

In subchronic and chronic oral studies, ocular lesions, liver and kidney effects, and/or body weight decrements were the major adverse effects seen in the rat, mouse, and dog. Plasma tyrosine levels were increased in the rat, mouse and dog in the chronic and reproduction studies in which levels were measured. USEPA (2001) quotes a chronic RfD of 0.007 mg/kg/d and a chronic PAD of 0.0007 mg/kg/d, although USEPA (2003) reports this as 0.00007 mg/L. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.007 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mesotrione is 0.049 mg/L (no acute one-day value available.)

EC (2003) established an ADI for mesotrione of 0.01 mg/kg/d and an ARfD of 0.02 mg/kg/d. These values were affirmed by EFSA (2015, 2016).

EC (2003) states that the weight of evidence suggests no genotoxic concerns for mesotrione and no classification for carcinogenicity is necessary.

JMPR (2014) reports an ADI of 0.3 mg/kg bw, and that an ARfD is unnecessary.

The Acceptable Daily Intake (ADI) adopted in Australia for mesotrione is 0.5 mg/kg body weight, with a NOEL of 1.8 mg/kg bw (<https://apvma.gov.au/>). The ARfD is 0.1 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose.

Mesotrione was negative for carcinogenicity in feeding studies in rats and mice and was classified by the USEPA as ‘not likely’ to be a human carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Metalaxyl

CAS No. 57837-19-1. The IUPAC name for metalaxyl is methyl N-(methoxyacetyl)-N-(2,6-xylyl)-DL-alaninate. The CAS name is methyl N-(2,6-dimethylphenyl)-N-(methoxyacetyl)-DL-alaninate. Has been called mefenozam and mefenoxam.

The CAS No. for metalaxyl-M (the R-enantiomer) is 70630-17-0 The IUPAC name is methyl N-(methoxyacetyl)-N-(2,6-xylyl)-D-alaninate. The CAS name is methyl N‑(2,6‑dimethylphenyl)-N-(methoxyacetyl)-D-alaninate. Metalaxyl and metalaxyl-M are mixtures of the same enantiomers but at different ratios; metalaxyl is the racemic mixture of metalaxyl-M and its S-enantiomer.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of metalaxyl in drinking-water should not exceed 0.1 mg/L (100 μg/L).

Metalaxyl is not mentioned in WHO 2004 or 2011.

### Sources to water

Metalaxyl is a benzenoid, or phenylamide, restricted-use systemic fungicide for the control of phytophtora spear rot in asparagus, and for the control of oomycete pathogens on other vegetables and fruit. NZFSA has often found metalaxyl in cucumbers and grapes. It also has bactericidal properties and is used in wood preservative products.

Metalaxyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is available in a variety of formulations, many of which include other active ingredients such as mancozeb, thiabendazole, cymoxanil and fludioxonil. Trade names include: Apron Combi, Apron TZ, Max MZ, Phytospear, Ridomil Gold 2.5G, Ridomil Gold MZ, Speartek and Wakil XL. ERMA notes that 15.3 tonnes of metalaxyl were used in New Zealand in 2004, at an application rate of 1,250 grams of active ingredient per hectare.

Metalaxyl was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in cucumbers and asparagus. Metalaxyl was found in tomatoes above the applicable MRL in the 2013/14 FRSP programme (MPI Technical Paper No: 2016/11. <http://www.mpi.govt.nz/news-and-resources/publications>).

Metalaxyl-m (also written as metalaxyl-M), the biologically active enantiomer (R‑enantiomer) of the racemic compound metalaxyl, is also registered for use as a fungicide in New Zealand. Some trade names are Apron XL, Ridomil Gold EC, Ridomil WG.

EC (2010) states that metalaxyl products must not contain more than 1 g/kg of 2,6‑dimethylaniline.

### Forms and fate in the environment

Metalaxyl is very soluble in water: 7.1 g/L (7,100 mg/L) (Merck & Co 1996). Metalaxyl-m is very soluble in water: 2.6 percent (EC 2002/EFSA 2015). Henry’s Law constant (metalaxyl-M) is 3.5 x 10-5 Pa.m3/mol at 25°C.

Metalaxyl is moderately stable under normal environmental conditions. Most soil studies show a half-life of more than three weeks with many exceeding three months. However, the rate of degradation is strongly influenced by the properties of the soil, including its biological activity and the conditions of temperature, moisture and concentration of the residue, with recorded half-lifes in the range of 5 to 180 days. The main metabolite is N-(2,6-dimethylphenyl)-N-(methoxyacetyl)alanine (JMPR 2004). EFSA (2011/2014) includes a list of metabolites.

It is photolytically stable in water when exposed to sunlight, with a half-life of 400 days. Less than 10 percent of the material photolysed during the 28-day test period.

It is poorly sorbed by soils and highly soluble in water; these properties in combination with its long persistence pose a threat of contamination to groundwater. Monitoring data demonstrate that metalaxyl has the potential to reach groundwater (USEPA 1994).

In soil laboratory incubations under aerobic conditions in the dark, metalaxyl-M exhibited low to medium persistence, forming the major (>10 percent applied radioactivity (AR)) metabolite NOA409045 (maximum 72 percent AR) which exhibited low to high persistence. The metabolites CGA67868 (maximum 6 percent AR) and SYN546520 (maximum 4 percent AR, still increasing at study end) were assessed as needing consideration for groundwater exposure, they exhibited low persistence (20°C pF2 SFO DT50: 1.6–4.9 days) and moderate to high persistence (20°C pF2 SFO DT50:  
42–288 days) respectively. The potential for groundwater exposure from the representative uses by metalaxyl-M was concluded to be low. Maximum DT90 values in soil for metalaxyl and metalaxyl-M are 289 and 103 days respectively (EFSA 2015).

NPIC (1994) quotes for metalaxyl a soil half-life of 70 days, water solubility of 8,400 mg/L and a sorption coefficient (soil Koc) of 50. This resulted in a pesticide movement to groundwater rating of very high. Its GUS score is 3.33, indicating that it will leach to groundwater.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included metalaxyl, and typical concentrations in New Zealand drinking-waters are unknown.

Metalaxyl has been detected in groundwater (NB: not necessarily drinking-water supplies) in five US states at levels typically reaching up to 0.003 mg/L. In order to reduce the possibility of groundwater contamination, USEPA is requiring a groundwater label advisory for metalaxyl end-use products (USEPA 1994).

Metalaxyl has been found in groundwater in Taranaki at 0.0024 mg/L (MAF 2006).

Metalaxyl was found in four bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.00005 to 0.000085 mg/L. The bores were in the Waikato, Manawatu and Tasman regions.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Metalaxyl was found in 2 wells, from 0.013 to 0.096 µg/L, ie, up to 0.000096 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Metalaxyl was found in one sample, at 0.017 µg/L, ie, 0.000017 mg/L.

### Removal methods

Metalaxyl has been reported to be decomposed completely by UV light in the presence of a titanium dioxide catalyst in the laboratory (Topalov et al 1999). This system has not been implemented in full-scale water treatment.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of metalaxyl, although a guide to the efficiency of the process cannot be provided.

### Health considerations

Based on international studies, people may be exposed to residues of metalaxyl through the diet, but chronic dietary risk is minimal (USEPA 1994). Application and post-application risks to workers and others also are minimal because metalaxyl has no toxicological endpoints of concern. There is no information available regarding the greatest source of exposure to metalaxyl for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

Studies with rats and goats showed rapid metabolism and excretion via the urine and faeces. Metalaxyl is metabolised to a variety of products before excretion (EXTOXNET 1996).

#### Acute poisoning

Metalaxyl generally is of low acute toxicity but is a moderate eye irritant and has been placed in USEPA toxicity class III (EXTOXNET 1996).

The acute oral LD50 for rats is 669 mg/kg (RSocC 1987), which suggests a moderate acute oral toxicity when compared with other pesticides.

#### Chronic exposure

In a subchronic feeding study using rats, reduced food consumption and liver cell effects were noted at the highest dose tested. In a chronic toxicity study using beagle dogs, blood serum enzyme effects and increased liver weights were noted in the highest dose group. A study using rats resulted in liver effects (USEPA 1994). The liver is the primary target organ in animal systems (EXTOXNET 1996).

Although people may be exposed to residues of metalaxyl in many food commodities, USEPA describes the chronic dietary risk from all uses as minimal. Application and post-application risks to workers and others also are minimal because metalaxyl has no toxicological endpoints of concern.

The oral RfD was calculated at 0.06 mg/kg/d (USEPA 1995). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0741 mg/kg/d (for mefenoxam). The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for mefenoxam is 0.52 mg/L (no acute one-day value available.)

JMPR (2004) quotes an ADI of 0–0.08 mg/kg/d; an ARfD was considered unnecessary.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EC (2002/2010) established an ADI for metalaxyl and metalaxyl-M of 0.08 mg/kg/d and an ARfD of 0.5 mg/kg/d. EFSA (2011, 2013, 2014 and 2015) reaffirmed these values.

The International Agency for Research on Cancer (IARC) has not classified metalaxyl. The USEPA classified it as a Group E carcinogen; that is, a chemical that does not show evidence of carcinogenicity for humans (USEPA 1994); as at September 2008 the USEPA has classified metalaxyl in Group E: evidence of non-carcinogenicity for humans.

USEPA (2015) found that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for metalaxyl since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways in mammals.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for metalaxyl in drinking-water, as follows:

3 mg/kg body weight per day x 70 kg x 0.1 = 0.105 mg/L (rounded to 0.1 mg/L)

2 L x 100

where:

* no observable adverse effect level = 3 mg/kg body weight per day.
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Metaldehyde

CAS No. 108-62-3. The IUPAC name for metaldehyde is r-2,c-4,c-6,c-8-tetramethyl-1,3,5,7-tetroxocane, or 2,4,6,8-tetramethyl-1,3,5,7-tetraoxacyclooctane. The CAS name is 2,4,6,8-tetramethyl-1,3,5,7-tetraoxacyclooctane. The technical grade contains some higher oligomers in addition to the tetramer (cyclic tetramer of acetaldehyde). The tetramer is (C2H4O)4. Also called metacetaldehyde.

The homopolymer is (C2H4O)n, CAS No. 9002-91-9.

### Maximum Acceptable Value

Metaldehyde does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; minor excursions above this level would need to occur over a significant period, as the health-based guideline is based on moderate- to long-term effects.

### Sources to water

Metaldehyde, a tetramer of acetaldehyde, is a molluscicide, commonly appearing in slug and snail bait, which go under many trade names. It breaks down in the pest’s body to acetaldehyde (see datasheet), affecting the nervous system, killing the pest. Metaldehyde appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

It is also used in camping, as a tablet to preheat portable stoves.

### Forms and fate in the environment

Metaldehyde is highly mobile in soils, and is generally stable to abiotic degradation mechanisms such as hydrolysis and photolysis. Metaldehyde is primarily dissipated from soils through biodegradation under aerobic conditions, with a half-life of approximately two months. Under anaerobic conditions, the half-life of metaldehyde is much higher (>200 days). Its low vapour pressure and Henry’s Law constant indicate that volatilisation from soils and water surfaces will not be an important transport process. In addition, the results of a laboratory volatility study suggest that volatilisation losses from soil surfaces will be minor.

EFSA (2014) states that soil degradation studies show that DT90 values of metaldehyde are expected to range between 8 to 22 days.

Water solubility is about 200 to 220 mg/L.

NPIC (1994) quotes for metaldehyde a soil half-life of 10 days, water solubility of 230 mg/L and a sorption coefficient (soil Koc) of 240. This resulted in a pesticide movement to groundwater rating of low.

Acetaldehyde is the primary degradation product of metaldehyde. Acetaldehyde is a relatively short-lived metabolite in the environment, and is readily oxidised to acetic acid and ultimately to carbon dioxide and water.

### Typical concentrations in drinking-water

Metaldehyde is used extensively in the UK, not always with due care, resulting in it being found in 2007 in the Bristol water supply, but <0.0001 mg/L. Other UK water supplies have subsequently detected it too.

DWI (2016) states that England continues to experience detections (65) of metaldehyde, a pesticide used to control slugs which, after application, can be washed into water sources by rain. It is difficult to remove both by catchment management and water treatment.

### Removal methods

No information available. The weak soil adsorption and high solubility suggest that treatment processes that remove particulate matter should be ineffective at reducing the concentration of metaldehyde in water. However, some newer advanced oxidation processes may be effective.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In studies reported in IPCS (1996), metaldehyde showed no increased incidence of tumour formation, no increased incidence of malformations was observed in reproduction studies, and no mutagenic effect was observed in several strains of Salmonella typhimurium, with or without metabolic activation.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.005 mg/kg body weight, with a NOEL of 5 mg/kg bw based on a rat study and applying a safety factor of 1,000. The NOEL was based on neurological effects.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.01 mg/kg/d, and an ARfD of 0.075 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for metaldehyde is 0.75 mg/L.

EFSA (2014) quotes an ADI of 0.02 mg/kg/d and an ARfD of 0.3 mg/kg bw.

As at September 2008 the USEPA considers that there is suggestive evidence of carcinogenic potential.

### Derivation of Maximum Acceptable Value

No MAV for metaldehyde.

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# Metamitron

CAS No. 41394-05-2. The IUPAC name for metamitron is 4-amino-4,5-dihydro-3-methyl-6-phenyl-1,2,4-triazin-5-one or 4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4H)-one. The CAS name is 4-amino-3-methyl-6-phenyl-1,2,4-triazin-5(4H)-one.

### Maximum Acceptable Value

Metamitron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Metamitron is a selective, systemic, post-emergence triazinone herbicide, absorbed mainly by roots and translocated. It inhibits photosynthesis.

Metamitron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of metamitron depends on the conditions; in aerobic soils it is between 2 and 45 days. Desamino metamitron is the significant metabolite; it exhibits medium to high mobility in soil. The metabolites 3-methyl-6-phenyl-1,2,4,5-tetrazine and 2‑methyl-5-phenyl-1,3,4-oxadiazole have been detected in soil and water systems.

Hydrolysis was considered to play a minor role in water, but photodegradation may be a significant route of degradation of metamitron in aquatic systems particularly close to the surface of natural water bodies where indirect photolysis may be significant due to the presence of photosensitisers. In natural sediment water systems metamitron exhibited moderate persistence (total system DT50 10.8–11.4 days) degrading to the major metabolite desamino-metamitron. The potential for groundwater exposure was concluded to be low (EFSA 2008).

Water solubility is about 1,700 mg/L.

### Typical concentrations in drinking-water

No information available.

### Removal methods

No information available.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

EFSA (2008) set the acceptable daily intake (ADI) at 0.03 mg/kg bw/d based on a NOAEL of 3 mg/kg bw/d obtained in a two-year dog study applying a safety factor of 100. The Acute Reference Dose (ARfD) was set at 0.1 mg/kg bw based on a maternal NOAEL of 10 mg/kg bw/d obtained in a rat developmental study that was supported by NOAELs obtained in single dose pharmacologic and functional studies in rats.

EC (2009) and IUPAC quote an ADI of 0.03 mg/kg bw, and an ARfD of 0.1 mg/kg/d.

APVMA adopted an ADI of 0.03 mg/kg/d for Australia (<https://apvma.gov.au/>). The ARfD is 0.1 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

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# Metam sodium

CAS No. 137-42-8. The IUPAC name for metam sodium is sodium methyldithiocarbamate. The CAS name is sodium methylcarbamodithioate. Metam sodium, a derivative of metam (CAS No. 144-54-7) is spelt with or without a hyphen. Also known as metham-sodium. The potassium salt is manufactured too, CAS No. 137‑41-7.

### Maximum Acceptable Value

Metam sodium does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.001 mg/L for methyl isothiocyanate or MITC (because metham degrades rapidly to methyl isothiocyanate). See methyl isothiocyanate datasheet. Excursions above 0.001 mg/L even for a short period are of concern because the health-based guideline is based on short-term effects.

A relevant impurity is DMTU: N,N’-dimethylthiourea (EFSA 2011).

### Sources to water

Metam sodium is a dithiocarbamate fungicide, herbicide, bactericide and nematicide. Metam sodium appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007).

Metam sodium is the most widely used soil fumigant, and the third most widely used pesticide in US agriculture, and use is increasing as metam sodium replaces the ozone-depleting fumigant methyl bromide; half of its use is in potato production, with tomatoes being an important use too. It is also used for sewer root control (often in conjunction with dichlobenil, qv). Metam sodium acts as a fumigant by rapidly breaking down into methylisothiocyanate (MITC). Metam sodium also breaks down into methyl isocyanate, carbon disulphide, and hydrogen sulphide.

### Forms and fate in the environment

The half-life metam in aerobic and anaerobic soils is up to one day; MITC up to three days. Metam sodium and methylisothiocyanate are very readily soluble in water (0.7 percent and 0.9 percent respectively) and have low absorption into soil, thus these compounds can potentially leach into shallow groundwater and leaky aquifers. However, in normal circumstances, they are more likely to volatilise.

Hydrolysis of metam in buffered aqueous solutions (pH 5, 7 and 9) at 25°C was investigated; hydrolysis is relatively fast at any pH, being slightly faster at the more acidic ones (pH 5: DT50 = 1.9 d; pH 7 DT50 = 2.2 d; pH 9 DT50 = 4.5 d).

NPIC (1994) quotes for metham (metam) sodium salt a soil half-life of seven days, water solubility of 96 percent and a sorption coefficient (soil Koc) of 6. This resulted in a pesticide movement to groundwater rating of moderate.

DMTU may be considered to have very low persistence in soil (half-life <1 day), and is not considered to threaten groundwater (EFSA 2011).

### Typical concentrations in drinking-water

No information available.

### Removal methods

No information available. The weak soil adsorption and high water solubility suggest that treatment processes that remove particulate matter should be ineffective at reducing the concentration of metam sodium and methylisothiocyanate in water. Activated carbon treatment may be effective.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Methylisothiocyanate is the most likely form to be ingested in food or water, and is more toxic than the parent compound. The dog appears to be the most sensitive species to MITC. In subchronic studies, the lowest NOEL of about 0.04 mg/kg/d was established in a three-month dog study (gavage). This was based on decreased testes weight and increased liver effects at 0.4 mg/kg/d.

Metam sodium has an acceptable daily intake (ADI) of 0.001 mg/kg body weight based on a dog study using a safety factor of 100, and an acute reference dose (ARfD) of 0.1 mg/kg body weight based on a rat study and a safety factor of 100 (USEPA 2009).

EFSA (2011 and 2019) reports that for metam the Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 0.001 mg/kg bw/day, based on the one-year dog study NOAEL with a Safety Factor (SF) 100; the Acute Reference Dose (ARfD) is 0.1 mg/kg bw based on an overall rat developmental toxicity NOAEL and supported by rabbit developmental study (SF 100). The ADI and AOEL for MITC are 0.004 mg/kg bw/day based on the one-year and 90-day studies in dog, respectively; the ARfD is 0.03 mg/kg bw based on a NOAEL for rat maternal toxicity with SF 100.

No Acceptable Daily Intake (ADI) has been adopted in Australia for metham. The ADI for methylisothiocyanate is 0.0004 mg/kg body weight, with a NOEL of 0.04 mg/kg bw from a three-month study in dogs. In this study there were decreased testis weights, increased pancreas weights, and abnormal liver histology at the highest dose tested, 2 mg/kg bw/day. The ADI incorporates a safety factor of 100 and was established in 2004.

As at September 2008 metam sodium and methylisothiocyanate have been classified by the USEPA in Group B: probable human carcinogens, and are suspected endocrine disruptors. Metham sodium appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Metam natrium is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

No MAV.

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# Methabenzthiazuron

CAS No. 18691-97-9. IUPAC name for methabenzthiazuron is 1-(1,3-benzothiazol-2-yl)-1,3-dimethylurea or 1-benzothiazol-2-yl-1,3-dimethylurea. The CAS name is N‑2‑benzothiazolyl-N,N′-dimethylurea. Sometimes called methibenzuron or MTT.

### Maximum Acceptable Value

Methabenzthiazuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Methabenzthiazuron is a selective post-emergence benzothiazole herbicide, or [urea herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#urea_herbicides), commonly used for the control of a spectrum of broad-leaved weeds and grasses in cereals, legumes, maize, garlic and onions. It is used in combination with other herbicides in vineyards and orchards.

Methabenzthiazuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). As at 2009, methabenzthiazuron is registered for use in Victoria on grapes, lucerne, pasture and potatoes. It is not registered for use in the US or the UK.

On the basis of a recommendation from the Standing Committee on the Food Chain and Animal Health, the European Commission decided on 25 April 2006 not to add methabenzthiazuron to the list of authorised active substances (Annex I) under Directive 91/414/EEC on the marketing of plant health products. The Commission Decision (C(2006)1653) implies the withdrawal of all temporary authorisations granted to herbicides containing this active ingredient.

### Forms and fate in the environment

Methabenzthiazuron degrades slowly in soils – studies have shown that more than 40 percent of the parent compound was found as soil-bound residues 111 days after application to a loess soil. The half-life in soils has been measured at 135 days, and  
90–180 days in water. This persistence is probably the reason for its restrictive use overseas.

Methabenzthiazuron is non-volatile. The aqueous half life is about 12 months and photolysis is slow, so methabenzthiazuron is very persistent in water.

Water solubility is about 60 mg/L. The octanol-water partition coefficient at pH 7, 20oC, log P, is 2.64.

### Typical concentrations in drinking-water

No information available.

### Removal methods

No information available. However, the strong soil adsorption suggests that treatment processes that remove particulate matter may be effective at reducing the concentration of methabenzthiazuron in water.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Methabenzthiazuron is considered to be non-mutagenic and is not a recognised or suspect carcinogen.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.004 mg/kg body weight, with a NOEL of 7.5 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Methamidophos

CAS No. 10265-92-6. IUPAC name is (RS)-(O,S-dimethyl phosphoramidothioate). CAS name is O,S-dimethyl phosphoramidothioate.

### Maximum Acceptable Value

WHO (2004) and (2011) states that methamidophos is unlikely to occur in drinking-water so a guideline value is unnecessary.

The USEPA concluded on 22 September 2009 that methamidophos is known or anticipated to occur in PWSs and may require regulation. Therefore they added methamidophos to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

Methamidophos appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

### Sources to water

Methamidophos is a highly active, broad spectrum, systemic, residual organophosphate insecticide/acaricide/avicide, used commonly on vegetables and fruit.

Methamidophos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). Formulations containing methamidophos have been registered for use in New Zealand since 1973. Four products containing methamidophos are currently (2009) registered for agricultural use in New Zealand: Tamaron, Monitor, Metafort 60SL and Methafos 600. ERMA notes that 18 tonnes of methamidophos were used in New Zealand in 2004, at an application rate of 900 grams of active ingredient per hectare. After 1 July 2023 methamidophos will no longer able to be manufactured in or imported into New Zealand (<http://www.mpi.govt.nz/news-and-resources/publications>).

Methamidophos should not contain more than 90 g/kg of O,O-dimethyl phosphoramidothioate, 80 g/kg of N-methylamidate, 20 g/kg of O,O,S-trimethyl phosphoramidothioate and 70 g/kg of trimethylphosphite: (CH3O)3P=S.

Acephate, which is currently included in pesticide formulations in New Zealand, degrades to methamidophos.

Methamidophos was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in tomatoes, celery, cucumbers, capsicums and in spinach. Methamidophos was found above its MRL in tomatoes in the FRSP 2013/14 programme. MPI Technical Paper: 2016/11.

### Forms and fate in the environment

Degradation of methamidophos in soils and natural waters has been found to be fairly rapid. The final degradation product is usually phosphoric acid. In aerobic soils, the half-life of methamidophos is as follows: 1.9 days in silt, 4.8 days in loam, 6.1 days in sand, and 10–12 days in sandy loam; the principal mechanism of degradation appears to be microbial metabolism.. It may be more persistent in anaerobic aquatic environments. JMPR (2003) reports the half-life for degradation of methamidophos in two water-sediment systems was estimated to be four and six days.

Methamidophos is degraded relatively rapidly in soils. Within one week, the residue dropped to 10 percent of the level measured on the day of application (IPCS HSG 1993).

If released to soil, methamidophos is expected to have very high mobility based upon a Koc of 5. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 8.7 x 10-10 atm-cu m/mole. Volatilisation from dry soil surfaces is not expected, based on its vapour pressure. Average half-lifes in soil under aerobic and anaerobic conditions are 4 and 7.5 days, respectively. If released into water, methamidophos is not expected to adsorb to suspended solids and sediment based upon the Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 3.1 suggests the potential for bioconcentration in aquatic organisms is low. Half-lifes for the hydrolysis of methamidiophos at 22°C and pH 4, 7, and 9 have been reported to be 1.8 years, 120 hours, and 70 hours, respectively. Photolysis rates in water and soil are 0.0079 and 0.210 per day; corresponding to half-lifes of 87 and 3.3 days, respectively (EAWAG accessed February 2015).

The half-life of the chemical in water is 309 days at pH 5.0, 27 days at pH 7.0, and three days at pH 9.0. Methamidophos will break down in the presence of sunlight, and has a half-life of 90 days in water at pH 5 when there is sunlight. It is very soluble in water, at least 20 percent.

NPIC (1994) quotes for methamidophos a soil half-life of six days, water solubility of 100 percent and a sorption coefficient (soil Koc) of 5. This resulted in a pesticide movement to groundwater rating of moderate.

See JMPR (2003) for information on metabolites.

### Typical concentrations in drinking-water

No information available.

### Removal methods

The weak soil adsorption and high water solubility suggest that treatment processes that remove particulate matter should be ineffective at reducing the concentration of methamidophos in water. Trials with strong oxidants and/or activated carbon may prove promising.

### Recommended analytical techniques

#### Referee method

A referee method cannot be selected for methamidophos because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

Methamidophos is a potent acetylcholinesterase inhibitor.

Methamidophos is absorbed rapidly through the stomach, lungs and skin. It is eliminated primarily in the urine. Methamidophos is highly toxic via oral, dermal and inhalation routes of exposure. The oral doses of methamidophos that resulted in the mortality of half of the test organisms (LD50 values) are 21 and 16 mg/kg body weight for male and female rats respectively, 30–50 mg/kg body weight in guinea pigs, and 10–30 mg/kg body weight in rabbits.

The primary target of organophosphate compounds is the nervous system. Some liver damage has been observed in rabbits. Reduced sperm count and reduced sperm viability have been observed in humans.

The 2002 JMPR established an ADI and acute RfD for methamidophos of  
0–0.004 mg/kg bw and 0.01 mg/kg bw, respectively.

WHO has set an Acceptable Daily Intake (ADI) value for methamidophos of 0.004 mg/kg body weight.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0003 mg/kg body weight, with a NOEL of 0.03 mg/kg bw, and the ARfD is 0.003 mg/kg bw.

The ADI for New Zealand is 0.0001 mg/kg/d.

The USEPA (2006) established a PAD (population adjusted dose) of 0.0001 mg/kg/d based on a eight-week subchronic oral toxicity cholinesterase rat study where the NOAEL was 0.03 mg/kg/d. The oral RfD had earlier been 0.00005 mg/kg/d (USEPA 1991). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0003 mg/kg/d, and an ARfD of 0.003 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for methamidophos is 0.03 mg/L.

Methamidophos residues have been found in New Zealand lettuce and capsicums at greater than the maximum residue limit (MRL), refer NZFSA: <http://www.nzfsa.govt.nz/science/research-projects/food-residues-surveillance-programme/>.

Methamidophos has tested positive for genotoxicity, or ability to induce changes in chromosomes, in some tests and negative in others. It may be weakly mutagenic.

As at September 2008, the USEPA has classified methamidophos as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

There are limited and insufficient data on methamidophos on which to propose a MAV for drinking-water.

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# Methiocarb

CAS No. 2032-65-7. The IUPAC name for methiocarb is 4-methylthio-3,5-xylyl methylcarbamate. The CAS name is 3,5-dimethyl-4-(methylthio)phenyl methylcarbamate. Can also be called mercaptodimethur.

### Maximum Acceptable Value

Methiocarb does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, because the health-based guideline is based on long-term effects.

### Sources to water

Methiocarb, a carbamate, is used as an acaricide, bird repellent, insecticide and molluscicide; it occurs in some snail baits.

Methiocarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Methiocarb was found above its default MRL in celery in an extensive study of New Zealand foods (NZFSA 2007) and again in December 2009.

### Forms and fate in the environment

Methiocarb is degraded by soil bacteria. The half-life in aerobic and anaerobic soil is 64 days. Methiocarb breaks down in plants and animals by carbamate ester cleavage and oxidation to sulfoxides and sulfones.

Methiocarb sorbs strongly to soils, and has low mobility based on an estimated Koc of 660. Volatilisation from moist soil surfaces is not expected to be an important fate process based on a Henry’s Law constant of 1.20 x 10-04 Pa m3/mole at 20°C. The photolysis half-life of methiocarb in 3 different soils was shown to range from four to nine days. The main metabolites (methiocarb sulfoxide and the corresponding phenol) are highly mobile in soils, although methiocarb sulfoxide is unstable with respect to hydrolysis. Sulfone metabolites are likely to share these properties, but this has not been specifically tested.

Water solubility is about 30 mg/L.

NPIC (1994) quotes for methiocarb (mercaptodimethur) a soil half-life of 30 days, water solubility of 24 mg/L and a sorption coefficient (soil Koc) of 3000. This resulted in a pesticide movement to groundwater rating of very low.

Methiocarb exhibited medium to low mobility in soil. Methiocarb sulfoxide (M01) exhibited very high soil mobility, methiocarb sulfoxide phenol (M04) exhibited very high to high mobility, whilst methiocarb sulfone phenol (M05) and methiocarb methoxy sulfone (M10) both exhibited high to medium soil mobility. It was concluded that the adsorption of all these compounds was not pH dependent. The potential for groundwater exposure from the representative uses by methiocarb and its metabolites: methiocarb sulfoxide (M01), methiocarb sulfoxide phenol (M04), methiocarb sulfone phenol (M05) and methiocarb methoxy sulfone (M10) above the parametric drinking water limit of 0.1 μg/L was concluded to be low in geoclimatic situations that are represented by all eight FOCUS groundwater scenarios defined for the cultivation of maize. Neither methiocarb nor any of its degradation products that trigger assessment (methiocarb sulfoxide (M01), methiocarb phenol (M03), methiocarb sulfoxide phenol (M04) and methiocarb methoxy sulfone (M10)) would be expected to be present at significant concentrations in water bodies (ie, above 0.1 μg/L) where drinking water would be abstracted (ie, the same situation that is predicted for groundwater), provided that a minimum drilling depth of 3 cm for the maize seed be specified (EFSA 2018).

### Typical concentrations in drinking-water

The USEPA factsheet notes that methiocarb appears to be moderately persistent and relatively immobile in soil, and is not likely to contaminate groundwater. However, methiocarb was a common contaminant of groundwaters in Spain, particularly during the summer months but also into the winter in some wells. Concentrations detected ranged up to about 0.0004 mg/L. Investigations at one well found that methiocarb was accompanied by roughly equal amounts of its sulfone, thought to arise by microbial oxidation in the unsaturated soil layer. Separate investigations found this hydrophilic metabolite to be unstable under simulated aquifer conditions, suggesting that its detection in groundwater reflects continuous loading from the overlying soil. Methiocarb has also been detected in Nebraska groundwater, at concentrations below 0.0005 mg/L. Samples from two US water supplies have been found to contain 0.0005 mg/L methiocarb.

### Removal methods

Because methiocarb sorbs strongly to soils, treatment processes that remove particulate matter may reduce the concentration of methiocarb and some of its metabolites in water. Some newer advanced oxidation processes may also be effective.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Methiocarb is a highly toxic inhibitor of cholinesterase, an essential nervous system enzyme.

USEPA (1994) established a RfD of 0.005 mg/kg/d based on a NOEL of 1.5 mg/kg/d for tremors and muscle weakness in a long-term feeding study in dogs.

JMPR (in IPCS 1998) adopted an ADI of 0.02 mg/kg bw/day, based on a revised NOEL of 1.5 mg/kg bw/day from a two-year dog study and a safety factor of 100, and an ARfD of 0.02 mg/kg/d. Because of concerns about the major metabolites, JMPR requires residues to be reported as “the sum of methiocarb, methiocarb sulfoxide and methiocarb sulfone, expressed as methiocarb”.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw from a two-year dietary study in dogs. The NOEL is based on reduced plasma cholinesterase activity. The ADI incorporates a safety factor of 100. An ARfD of 0.03 mg/kg bw/day has been determined (APVMA 2005), based on two developmental toxicity studies in rats and rabbits with a safety factor of 100 being applied to the No Observable Effect Level (NOEL). In December 2017 APVMA adjusted the ARfD for methiocarb to 0.005 mg/kg based on a developmental rat study – a NOAEL of 0.5 mg/kg bw/d was based on clinical signs (muscle fasciculations) at the next higher dose (<https://apvma.gov.au/>).

EC (2006) established an ADI and ARfD of 0.013 mg/kg/d.

The agreed acceptable daily intake (ADI) and the acceptable operator exposure level (AOEL) are 0.00025 mg/kg bw per day, on the basis of the relevant short‐term NOAEL of 0.25 mg/kg bw in the 90‐day study in dogs based on reduced body weight gain in males and females at 1.3 mg/kg bw per day. The agreed acute reference dose (ARfD) and acute acceptable operator exposure level (AAOEL) are 0.00050 mg/kg bw based on the NOAEL of 0.5 mg/kg bw per day for clinical signs indicative of cholinergic inhibition observed at 1.5 mg/kg bw per day in the developmental toxicity study in rats. In addition to the standard uncertainty factor (UF) of 100, an additional UF of 10 was applied for the derivation of all reference values, in order to cover the lack of developmental neurotoxicity and the likely higher sensitivity to AChE inhibition of pups compared to adults (EFSA 2018).

As at September 2008 the USEPA has classified methiocarb in Group D: not classifiable as to human carcinogenicity.

### Derivation of Maximum Acceptable Value

No MAV.

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# Methomyl

CAS No. 16752-77-5. IUPAC name is S-methyl (EZ)‑N‑(methylcarbamoyloxy)thioacetimidate. CAS name is methyl N‑[[(methylamino)carbonyl]oxy]ethanimidothioate.

### Maximum Acceptable Value

WHO 2004) and (2011) states that methomyl is unlikely to occur in drinking-water so a guideline value is unnecessary.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.2 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; excursions above this level even for a relatively short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Methomyl, an oxime carbamate, was introduced in 1966 as a broad spectrum insecticide. It is also used as an acaricide to control ticks and spiders. It is used for foliar treatment of vegetable, grape, fruit and field crops, cotton, commercial ornamentals, and in and around poultry houses and dairies. It is also used as a fly bait. Methomyl is particularly effective against organophosphorus resistant pests.

Methomyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The USEPA (1998) has determined that methomyl is a degradate of thiodicarb (qv).

Because of its high solubility in water (58,000 mg/L) and its soil half-life (33 days), methomyl may have potential for groundwater contamination.

Trace impurities in the technical product include S-methyl-N-hydroxy-thioacetimidate (0.2 percent), and 3-dimethylurea (0.4 percent) (IPCS HSG 1995).

### Forms and fate in the environment

Methomyl is very mobile in sandy loam and silty clay loam soils, but only slight leaching was observed in a silt loam and in a sandy soil. Adsorption of methomyl to soil particles is weak to moderate. Despite that, because of its high solubility in water (58,000 mg/L), methomyl may have potential for groundwater contamination.

Methomyl is degraded rapidly by soil microbes. The dissipation half-life for methomyl in soil is reportedly three to six weeks. However, one month after methomyl treatment, test soil had traces of the insecticide and some of its breakdown by-products, or metabolites. Methomyl residues are not expected to be found in treated soil after the growing season in which it is applied.

Under aerobic conditions, methomyl has a soil half-life of 30–45 days and degrades predominately to carbon dioxide. It is relatively stable to hydrolysis under neutral and acidic conditions. Under basic conditions (ie, high pH) , it degrades with a half-life of 30 days. Under anaerobic conditions, acetonitrile is the major metabolite in the early stages of degradation, but carbon dioxide is the end product, with total conversion within eight days.

Methomyl is stable in sterile distilled water at pH values of 5–7 but decomposes increasingly with higher pH and temperature levels. Its half-life in water at pH 9 is 30 days.

Aqueous solutions of methomyl have been reported to decompose more rapidly on aeration, in sunlight, or in alkaline media. One study indicated a half-life of six days for the insecticide in water. In one experiment the hydrolysis half-lifes of methomyl in solutions at pHs of 6.0, 7.0 and 8.0 were 54, 38, and 20 weeks respectively. In pure water, the hydrolysis half-life has been estimated to be 262 days. Methomyl is unlikely to bioconcentrate in aquatic systems.

The estimated aqueous half-life for the insecticide is six days in surface water and over 25 weeks in groundwater.

NPIC (1994) quotes for methomyl a soil half-life of 30 days, water solubility of 58,000 mg/L and a sorption coefficient (soil Koc) of 72. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

Methomyl has been detected at very low levels, 0.009 mg/L and 0.0012 mg/L respectively, in groundwater in New York and New Jersey.

Twenty-five water utilities in the US reported detecting methomyl in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0021 mg/L.

### Removal methods

No information available. The weak soil adsorption suggests that treatment processes that remove particulate matter should be ineffective at reducing the concentration of methomyl in water. Activated carbon treatment, assisted by aeration, may be reduce the concentration sufficiently.

### Recommended analytical techniques

#### Referee method

A referee method cannot be selected for methomyl because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for methomyl for the above reason. However, the following method is recommended:

Reverse phase HPLC using a fluorescence detector (EPA 531.2; APHA 6610B which is in the supplement, pages S-1 to S-9).

### Health considerations

Methomyl is a highly toxic inhibitor of cholinesterase, an essential nervous system enzyme.

Carbamates, the class of active ingredients in which methomyl is included, are absorbed quickly from the skin, lungs and gastrointestinal tract and are broken down and transformed in the liver. Although they do not appear to accumulate in any particular body tissue, they do alter many other enzyme systems besides the cholinesterases. Carbamates generally are excreted rapidly and do not accumulate in mammalian tissue.

The LD50 for methomyl in rats is 12–48 mg/kg, in mice it is 10 mg/kg, and in guinea pigs it is 15 mg/kg.

In a 24-month study with rats fed doses of 0, 2.5, 5 or 20 mg/kg, the NOEL was 20 mg/kg. At 20 mg/kg, red blood cell counts and haemoglobin levels were reduced significantly in female rats. Based on a 5 mg/kg NOEL in a two-year feeding study with dogs, and utilising a 100-fold safety margin, the USEPA (1991) established a reference dose or RfD for methomyl of 0.025 mg/kg of body weight/day.

JMPR (2008) reports an ADI and ARfD of 0.02 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight from a human acute (capsule) study, with a NOAEL of 0.1 mg/kg bw based on significant and dose related RBC AChE inhibition at the next higher dose. APVMA established an ARfD in 2007 of 0.02 mg/kg (<https://apvma.gov.au/>).

The reference dose or RfD (USEPA 2006/2009/2011) is still 0.025 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.9 mg/L.

EC (2009) established an ADI and ARfD of 0.0025 mg/L. EFSA (2015) reaffirmed these values.

EFSA (2015) states that the metabolite methomyl-oxime does not share the mode of action of the parent compound because it does not induce acetyl-cholinesterase inhibition. It has also been demonstrated that this metabolite has no toxicological relevance.

Acetamide, a suspected oncogen, is a minor metabolite of methomyl. As at September 2008 the USEPA has classified methomyl in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

There are limited and insufficient data on methomyl on which to propose a MAV in drinking-water.

The USEPA has established a lifetime Health Advisory level of 200 ppb (0.2 mg/L) for methomyl. Water containing methomyl at or below this level is acceptable for drinking every day over the course of one’s lifetime and does not pose any health risk.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for methomyl since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

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# Methoprene

CAS No. 40596-69-8. The IUPAC name for methoprene is isopropyl (E,E)-(RS)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate. The CAS name is 1-methylethyl (2E,4E)‑11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate. Has also been called isopropyl (2E, 4E)-11-methoxy-3,7,11-trimethyl-2,4-dodecadienoate.

Methoprene is a racemic mixture of R and S enantiomers.

S-methoprene (CAS No. 65733-16-6) is the biologically active enantiomer in the racemic compound methoprene. In recent years it has become possible to manufacture S-methoprene on an industrial scale and to register products based on the active S‑enantiomer only. Since, S-methoprene constitutes 50 percent of methoprene, investigations into the metabolism and fate of methoprene can legitimately be accepted as supporting metabolism and fate requirements of S-methoprene (JMPR 2005).

### Maximum Acceptable Value

The WHO Guidelines 3rd addendum (2008) and WHO (2011/2017) state that a guideline value is not considered appropriate for pesticides used for vector control in drinking-water.

The recommended dosage of methoprene in potable water in containers should not exceed 1 mg/L (WHO 2011).

### Sources to water

Methoprene is a stable juvenile hormone analogue that interferes with metamorphosis in insects (larvacide). There is no equivalent process in mammals. Formulations for use as a vector control agent in drinking-water sources, particularly to control dengue fever, are specified by WHO. It is also used as an ingredient in flea collars.

Methoprene appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). MAF Biosecurity uses s-methoprene for the eradication of unwanted mosquito species. This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Extensive studies have shown that methoprene breaks down rapidly in the environment. Methoprene is of low persistence in the soil environment; reported field half-lifes are up to 10 days. In soil, microbial degradation is rapid, mainly to CO2, and appears to be the major route of its disappearance from soil. Methoprene also readily undergoes degradation by sunlight with a half-life <1 day, but >4 weeks in the dark. It undergoes demethylation, hydrolysis and oxidative cleavage in microbes, insects and plants and is rapidly metabolised in fish, birds and mammals.

In water, it would be expected to adsorb to suspended solids. Studies have demonstrated half-lifes in pond water of about 30 and 40 hours at initial concentrations of 0.001 mg/L and 0.01 mg/L, respectively. See JMPR (2005) for information about metabolites.

Water solubility of methoprene is about 1.4 mg/L. Water solubility of S-methoprene is about 0.5 mg/L.

### Typical concentrations in drinking-water

Although exposure of the public through either food or drinking-water is negligible, there is a potential for direct exposure when it is applied directly to drinking-water storage containers.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See WHO (2008) for further information.

### Health considerations

Methoprene is practically nontoxic when ingested or inhaled and slightly toxic by dermal absorption. As the LD50 for racemic methoprene given orally was >2,000 mg/kg of body weight, with no toxic signs seen at this dose and no signs indicative of acute toxicity seen in studies with repeated oral doses (including studies of teratogenicity), JMPR concluded that allocation of an acute reference dose (ARfD) was unnecessary.

No methoprene-related effects were observed in two-year feeding trials with rats given doses of 250 mg/kg/day. The ADI for methoprene, determined by JMPR in 2001 (FAO/WHO 2002), is 0–0.05 mg/kg of body weight. Young animals do not appear to be significantly more sensitive than adults, and exposure from food is considered to be low. EXTOXNET quotes an ADI of 0.1 mg/kg/d.

JMPR (2005) reports an ADI for racemic methoprene of 0.09 mg/kg/d bw (based on a NOAEL of 8.6 mg/kg bw in a 90-day study in dogs, corrected for product purity. JMPR made the conservative assumption that, in the absence of any information to the contrary, all the toxicity of the racemate was due to the S enantiomer. On this basis, JMPR established an ADI for (S)-methoprene of 0–0.05 mg/kg body weight, equal to one half the ADI for the racemate (which is a 1:1 mixture of the R and S enantiomers) (WHO 2011/2017).

Based on its review and evaluation of the available information, the USEPA concluded that there is a reasonable certainty that no harm will result to the general population, and to infants and children from aggregate exposure to residues of methoprene (USEPA 2003).

The Acceptable Daily Intake (ADI) adopted in Australia for methoprene is 0.4 mg/kg body weight, with a NOEL of 35 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The maximum dosage in drinking-water of 1 mg/L would be equivalent to approximately 66 percent of the upper limit of the ADI (0.033 mg/kg body weight) for a 60 kg adult drinking two litres of water per day. The exposure for a 10 kg child drinking one litre of water would be approximately 0.1 mg/kg body weight, and for a 5 kg bottle-fed infant, the exposure would be approximately 0.15 mg/kg body weight, compared with the upper limit of the ADI of 0.05 mg/kg body weight. However, the low solubility and the high log octanol–water partition coefficient of methoprene indicate that it is unlikely to remain in solution at the maximum recommended applied dose, and the actual levels of exposure are likely to be much lower than those calculated. Exposure from food is considered to be low. Consideration should be given to using alternative sources of water for small children and bottle-fed infants for a period after an application of methoprene, where this is practical. However, exceeding the ADI will not necessarily result in adverse effects (WHO 2017).

### Derivation of Maximum Acceptable Value

WHO (2008) states that it is not appropriate to set a formal guideline value for methoprene used as a vector control agent in drinking-water. Where methoprene is used for vector control in potable water, this will involve less than lifetime exposure. The maximum dosage in drinking-water of 1 mg/L would be equivalent to approximately 66 percent of the ADI (0.033 mg/kg of body weight) for a 60-kg adult drinking two litres of water per day. The exposure for a 10-kg child drinking one litre of water would be approximately 0.1 mg/kg of body weight, and for a 5-kg bottle-fed infant, the exposure would be approximately 0.15 mg/kg of body weight, compared with the ADI of 0–0.05 mg/kg of body weight. However, the low solubility and the high log Kow of methoprene indicate that it is unlikely to remain in solution at the maximum recommended applied dose, and the actual levels of exposure are likely to be much lower than those calculated.

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# Methoxychlor

CAS No. 72-43-5. The IUPAC name for methoxychlor is 1,1,1-trichloro-2,2-bis(4-methoxyphenyl)ethane. The CAS name is 1,1′-(2,2,2-trichloroethylidene)bis[4-methoxybenzene]. Other names include methoxy-DDT and DMDT. Has also been called dianisyl trichloroethane, 1,1-bis(para-methoxyphenyl)-2,2,2-trichloroethane and 2,2‑bis(para-methoxyphenyl)-1,1,1-trichloroethane.

### Maximum Acceptable Value

Based on health considerations, the concentration of methoxychlor in drinking-water should not exceed 0.02 mg/L.

The maximum contaminant level (MCL) and the lifetime health advisory (USEPA 2006/2009/2011) is 0.04 mg/L.

The maximum acceptable concentration in Canada is 0.9 mg/L.

### Sources to water

Methoxychlor may enter source waters as a result of its application as an insecticide used to protect vegetables, fruit trees, fodder cereals, and animals against a variety of pests.

Technical methoxychlor contains about 88–90 percent of the p,p’-isomer together with more than 50 structurally related contaminants, including 1,1,1,2-tetrachloro-2-p-(4-methoxyphenyl)ethane, o,p’-dimethoxydiphenyltrichloroethane, o,o’‑dimethoxydiphenyltrichloroethane, 1,1-bis(4-methoxyphenyl)-2,2-dichloroethene (DMDE) and o,p’-dimethoxydiphenyldichloroethene, and up to 2.5 g/kg chloral hydrate. See ATSDR (2002) for the others.

Methoxychlor does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 or 2016 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. USEPA (2004) failed to reregister methoxychlor.

### Forms and fate in the environment

Methoxychlor is chemically similar to DDT but, being more biodegradable, much less liable to accumulate in body tissues and environment. Methoxychlor may be biodegraded anaerobically with half-lifes ranging from one week to two months, or aerobically with half-lifes of greater than three months. The recommended average half-life in soil is four months.

The main route of disappearance from the water phase is volatilisation with a half-life in water of about 46 days. The water solubility of methoxychlor is 0.02–0.1 mg/L and the sorption coefficient is 80,000 mL/g. It binds tightly to soils and sediments and is unlikely to leach to groundwater. There is some potential for the accumulation of the parent compound and its metabolites in surface water sediments.

NPIC (1994) quotes for methoxychlor a soil half-life of 120 days, water solubility of 0.1 mg/L and a sorption coefficient (soil Koc) of 80,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of methoxychlor (limit of detection = 0.0002 mg/L) (ESR 2001).

It is detected occasionally in drinking-water, at concentrations as high as 0.3 mg/L in rural areas (WHO 2004).

Forty-three water utilities in the US reported detecting methoxychlor in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0011 mg/L.

### Removal methods

No information on methods of removing methoxychlor from water is available. However, isotherm adsorption data indicate that removal by adsorption on to granular activated carbon should be possible; concentrations as low as 0.0001 mg/L should be achievable using GAC (WHO 2004/2011/2017).

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (EPA 525).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6630B).

2. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

3. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 505).

### Health considerations

Although methoxychlor is absorbed from the gastrointestinal tract, it does not accumulate in mammalian tissue. Body stores built up under continuous exposure are cleared within a few weeks after cessation of exposure. It is metabolised to formaldehyde and phenolic metabolites and excreted in faeces.

The main effects of single high exposures to methoxychlor are disturbances of glycogen metabolism and fatty degeneration of the organs. The main effect observed after long-term exposure tests on animals was growth retardation.

In humans, a single dose of 2 mg/kg body weight was without effect on liver, testicles and small intestine. Doses of up to 2 mg/kg body weight per day administered orally to men and women over a period of four to six weeks and six to eight weeks were without effect on body weight and several biochemical parameters. Tissue damage did not occur. The menstrual cycle and the volume of ejaculation were not affected, although a shortening of the neck of the spermatozoa was observed in the first study.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of 0.005 mg/kg/day for intermediate-duration oral exposure (15–364 days) to methoxychlor.

The reference dose or RfD (USEPA 1991/2006/2009/2011) is 0.005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.2 mg/L.

The Tolerable Daily Intake (TDI) adopted in Australia is 0.1 mg/kg body weight.

The International Agency for Research on Cancer placed methoxychlor in Group 3 in 1979 and confirmed this in 1987. Although subsequent data suggest a carcinogenic potential for liver and testis in mice, which may be caused by the hormonal activity of proestrogenic metabolites of methoxychlor and thus may have a threshold, the study was inadequate because only one dose was used and because this may have been above the maximum tolerated dose. The database for studies on long-term, short-term and reproductive toxicity is inadequate. A teratology study in rabbits reported a systemic NOAEL of 5 mg/kg body weight per day, which is lower than the LOAELs and NOAELs from other studies. This NOAEL was therefore selected for use in the derivation of a TDI. The genotoxic potential of methoxychlor appears to be negligible. Methoxychlor may be a tumour promoter (WHO 2017).

### Derivation of Maximum Acceptable Value

As the genotoxic potential of methoxychlor appears to be negligible, a tolerable daily intake approach was used for the derivation of the MAV for methoxychlor in drinking-water. The data base for studies on long-term, short-term and reproductive toxicity of methoxychlor is inadequate. Therefore the no-observable-adverse-effect level used for the derivation of the MAV is based on a teratology study in rabbits.

The MAV for methoxychlor in drinking-water was derived as follows:

5 mg/kg body weight/day x 70 kg x 0.1 = 0.0175 mg/L (rounded to 0.02 mg/L)

2 L/day x 1,000

where:

* no observable adverse effect level = 5 mg/kg body weight per day based a teratology study in rabbits
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for concern for threshold carcinogenicity and the limited data base).

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# Methoxyfenozide

CAS No. 161050-58-4. The IUPAC name for methoxyfenozide is N-tert-butyl-N′-(3-methoxy-o-toluoyl)-3,5-xylohydrazide. The CAS name is 3-methoxy-2-methylbenzoic acid 2-(3,5-dimethylbenzoyl)-2-(1,1-dimethylethyl)hydrazide. Tebufenozide (qv) is described as a parent chemical.

### Maximum Acceptable Value

Methoxyfenozide does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 4 µg/L (0.004 mg/L) for methoxyfenozide in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Methoxyfenozide is a diacylhydrazine (a substituted dibenzoylhydrazine) insecticide that operates as a moulting hormone agonist. Methoxyfenozide has been reported to have been used as an insecticide on kiwifruit in Northland. NZFSA often finds methoxyfenozide in grapes.

Methoxyfenozide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Form and fate in the environment

The soil half-life is reported to approach or even exceed two years (aerobic and anaerobic), but with low to moderate mobility; methoxyfenozide is still the main residue, other degradates being <5 percent. Methoxyfenozide is fairly stable to photolysis with half-lifes of 173 days (soil photolysis) and 77 days (aqueous photolysis). Hydrolysis studies at pH 5, 7, and 9 in the dark at 25°C showed methoxyfenozide was stable at all three pH values.

Methoxyfenozide has properties and characteristics associated with chemicals detected in groundwater. The use of this chemical in areas where soils are permeable, particularly where the water table is shallow, may result in groundwater contamination (PMEP 2003). Water solubility is about 3 mg/L.

The potential for groundwater exposure from the representative field uses by methoxyfenozide and metabolite RH-131154 (M08) was above the parametric drinking water limit of 0.1 μg/L in the majority (methoxyfenozide) or all (RH-131154 (M08)) the geoclimatic situations that are represented by FOCUS groundwater scenarios (EFSA 2017).

### Removal methods

Once adsorbed to the soil, methoxyfenozide is tightly bound so should be removed in water treatment processes that remove particulate matter.

### Recommended analytical techniques

#### Some alternative methods

Methoxyfenozide residue in soil and drinking and surface water can be monitored by HPLC–MS/MS with LOQs of 0.01 mg/kg and 0.05 μg/L, respectively (EFSA 2017).

### Health considerations

The acute health risks from exposure to methoxyfenozide are minimal due to its low mammalian toxicity.

DPR (2003) found the submitted toxicology studies sufficient to satisfy the data requirements of the Birth Defects Prevention Act (SB 950). No adverse effects were observed. At this time, methoxyfenozide has not been prioritised by DPR for risk assessment.

The ADI is 0–0.1 mg/kg bw/day. The JMPR meeting concluded that the long-term dietary intake of residues of methoxyfenozide is unlikely to present a public health concern (FAO 2003).

Methoxyfenozide caused some toxicity in chronic animal feeding studies. In a chronic feeding/oncogenicity study in rats, methoxyfenozide caused haematological effects (decrease in red blood cell counts and haemoglobin concentrations) in males and females, liver toxicity (increase in liver weights in males and periportal hepatocellular hypertrophy in males and females), histopathological changes in the thyroid of males and increased adrenal gland weights in males and females. These toxicity effects occurred at dose levels of 411 and 491 mg/kg body weight per day for males and females, respectively; the respective no-observed-effect levels (NOELs) were 10.2 and 11.9 mg/kg/day. The USEPA Office of Pesticide Programs established a reference dose (RfD) of 0.10 mg/kg/day based on a NOEL of 10.2 mg/kg/day in the chronic feeding/oncogenicity study in rats and an uncertainty factor of 100. This same value was used as a Chronic Population Adjusted Dose (cPAD) for evaluating dietary risks. The RfD has not yet been adopted by the USEPA’s *Integrated Risk Information System (IRIS)*. Methoxyfenozide did not cause oncogenic effects in either rat or mouse chronic feeding studies. This active ingredient was negative in a number of genotoxicity studies. The USEPA classified methoxyfenozide as “not likely” to be carcinogenic to humans (PMEP 2003, USEPA 2003). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.102 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for methoxyfenozide is 0.71 mg/L (no acute one-day value available.)

EC (2004) established an ADI of 0.1 mg/kg/d and an ARfD of 0.2 mg/kg/d (EFSA 2012 and 2014).

EFSA (2017) reaffirmed the ADI, but report a new ARfD of 0.1 mg/kg bw based on the NOAEL of 9.8 mg/kg bw per day for haemolytic anaemia observed at 106 mg/kg bw per day in the one-year dog study.

The Acceptable Daily Intake (ADI) adopted in Australia for methoxyfenozide is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg; an ARfD is not necessary.

JMPR (2009 and 2012) reports an ADI of 0–0.1 mg/kg bw and an acute reference dose of 0.9 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# 1-Methylcyclopropene

CAS No. 3100-04-7. The IUPAC and CAS name is 1-methylcyclopropene; it has sometimes been spelt 1-methyl cyclopropene and occasionally called MCP or 1-MCP.

### Maximum Acceptable Value

1-Methylcyclopropene does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

1-Methylcyclopropene, a gas, is an ethylene plant growth regulator, and it is used commercially in enclosed spaces to slow down the ripening of fruit (such as apples) and to help maintain the freshness of cut flowers. The product consists of a homogeneous mixture of 1-methylcyclopropene at a concentration of 3.3 percent together with related manufacturing impurities, in the form of a complex (encapsulated) with alpha-cyclodextrin, together with any other necessary co‑formulants. The impurities 3-chloro-2-methylpropene and 1-chloro-2-methylpropene are to be <0.05 percent (FAO 2010).

1-Methylcyclopropene appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Form and fate in the environment

There are no expected risks to the environment because 1-MCP is approved for use only in indoor spaces, and is quickly diluted when released to open air. Toxicity tests show that 1-MCP is not expected to be harmful to living organisms or the environment.

EFSA (2018) found that no reliable hydrolytic experimental degradation data were available. However, the study submitted to address the biodegradability of 1‑methylcyclopropene showed that the active substance is stable to hydrolysis. 1‑Methylcyclopropene is considered not to be readily biodegradable. No information on the fate and behaviour of 1-methylcyclopropene in the water/sediment system was available.

Water solubility is about 140 mg/L.

### Typical concentrations in drinking-water

1-Methylcyclopropene is not expected to reach natural water systems.

The potential for groundwater exposure from the representative uses by 1‑methylcyclopropene above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by all nine FOCUS groundwater scenarios (EFSA 2018).

### Recommended analytical techniques

#### Referee method

See FAO (2010).

### Health considerations

Based on studies with laboratory animals, no adverse effects are expected to humans who are exposed to end products that contain 1-MCP, although eye irritation may occur if a user does not follow label directions. 1-MCP as a gas is not toxic to test animals. Human exposure is expected to be minimal because 1-MCP is approved only for use indoors.

Being a gas, very few oral studies have been conducted. 1-MCP was not tested in chronic (long-term) and carcinogenicity studies in the rat and mouse, because there is no potential for chronic, lifetime exposure of man. The 90-day inhalation study in rats raised no alarms for potential effects upon chronic lifetime exposure. There is also no evidence for carcinogenicity or genotoxicity for 1-MCP predicted by structure activity analysis.

The EC (2005) reports an acceptable daily intake (ADI) of 0.0009 mg/kg, and an acute reference dose (ARfD) of 0.07 mg/kg/d. These values were reaffirmed by EFSA (2014) These were based on inhalation studies.

These were revised by EFSA (2018): the ADI is now 0.02 mg/kg bw per day based on the rat two-generation study and the dog 90-day study, applying an UF of 100, with an additional factor of 2 for subchronic to chronic/lifetime extrapolation. The ArfD is 0.12 mg/kg bw based on effects observed during the first week of administration in the 90-day dog study, with the application of an uncertainty factor of 100.

### Derivation of Maximum Acceptable Value

No MAV.

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# Methylene bisthiocyanate

CAS No. 6317-18-6. Also called the methylene ester of thiocyanic acid or methylene dithiocyanate, or MBT. Can be spelt methylene bis(thiocyanate).

### Maximum Acceptable Value

Methylene bisthiocyanate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Methylene bis(thiocyanate) is used as a microbiocide/microbiostat, fungicide/fungistat, algicide, and disinfectant. End-use products are formulated as a soluble concentrate/liquid, a ready-to-use liquid, and a soluble concentrate/solid. Methylene bis(thiocyanate) is employed in water cooling systems, paint manufacturing, metalworking cutting fluids, pulp and paper mills, oil drilling/mud packing fluids, leather processing, wood pressure treatments (forest products), wood protection treatments to buildings/products, and latex paints (in-can) as a non-oxidising biocide. The chemical is applied by applicator rolls; brush; chemical pump; dip tank; drip-feed device; metering pump; paintbrush; roller; sprayer; sprinkler can; or from a tank (USEPA 1997).

Methylene bisthiocyanate does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …). In one product it is mixed with chlorothalonil. It is a component of Resene’s Woodsman Wood Oil Stain (<http://www.resene.co.nz/archspec/msds/Woodsman.pdf>).

### Form and fate in the environment

Laboratory experiments conducted to assess the potential for leaching from wood show extensive leaching after a period of 30 days. Photolysis of methylene bis(thiocyanate) on wood surfaces is unlikely to occur. In actual outdoor wood treatment situations, methylene bis(thiocyanate) products are applied with a sealant/water repellent which inhibits the leaching process. Most applications are residential, and involve little environmental exposure.

Methylene bis(thiocyanate) is susceptible to hydrolysis at higher pHs (eg, >7.5), but stable at lower pHs. The major hydrolysate observed is the thiocyanate ion (SCN-), which seems to be persistent once it is formed. Cyanide is a metabolite of methylene bis(thiocyanate), and both cyanide and formaldehyde are potential degradates. The thiocyanate ion may degrade to cyanide, but degradation data are lacking that would indicate whether this occurs in the working environment and, if so, under what conditions (USEPA 1997). Formic acid and mercaptomethylenethiocyanate also form.

Water solubility is about 0.2 percent. Methylene bis(thiocyanate) has a very low potential to leach into groundwater or to run off into surface water under typical use conditions. MBT is deactivated by high concentrations of ferric iron.

### Typical concentrations in drinking-water

The USEPA (1997) does not anticipate groundwater contamination from the pesticidal uses of methylene bis(thiocyanate).

### Removal methods

No information available.

### Health considerations

Methylene bis(thiocyanate) appears to have at least two modes of toxicity. At high doses, the release of cyanide may be more rapid than the conversion of cyanide to thiocyanate by rhodanese; thus, cyanide toxicity is observed. Since methylene bis(thiocyanate) has no food or feed uses, dietary risk is not expected.

In developmental toxicity studies for methylene bis(thiocyanate), developmental effects did not occur at any dose level, including doses which resulted in maternal toxicity.

Overall, the toxic effects of methylene bis(thiocyanate) were consistent with those of an irritant chemical administered by gavage. There was also some indication that the release of cyanide may result in acute toxicity at the higher dose levels used in these studies. The no-observed-adverse-effect level (NOAEL) for forestomach lesions in the 13-week studies was 4 mg/kg for male rats and 2 mg/kg for female rats and male and female mice (NTP 1993).

In a subchronic oral 13-week study (gavage) using rats, the NOEL was 1 mg/kg/day. In a chronic oral 2 year study (gavage) using dogs, the NOEL was 0.5 mg/kg/day. The USEPA OPP/RfD Peer Review Committee established the RfD for methylene bis(thiocyanate) at 0.005 mg/kg/day; an uncertainty factor (UF) of 100 was used (USEPA 1997).

In 13-week oral studies, there were effects on the nasal cavity, windpipe and (fore)stomach of rats and mice. The blood and sperm of rats were also affected. There was no evidence of mutagenicity in a limited Ames bacterial test, or of chromosomal damage in rats treated orally.

The USEPA considers methylene bis(thiocyanate) is a Group D carcinogen, ie, not classifiable as to human carcinogenicity.

### Derivation of Maximum Acceptable Value

No MAV.

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# Methyl isothiocyanate

CAS No. 556-61-6. The IUPAC name is methyl isothiocyanate. The CAS name is isothiocyanatomethane. Also spelt methylisothiocyanate, and often referred to as MITC.

### Maximum Acceptable Value

Methyl isothiocyanate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.001 mg/L for methyl isothiocyanate; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

### Sources to water

Methyl isothiocyanate has been used as a soil fumigant for control of nematodes.

The US manufacturer cancelled all food uses of Vorlex in 1994 due to the cost of reregistration. Vorlex contains the active ingredients methylisothiocyanate (usually about 80 percent) and 1,3-dichloropropene (qv). This will eliminate the use of Vorlex on food crops including greenhouse and field soil fumigation of fruits, vegetables, field crops, ornamentals, nursery stock, and seed beds. The registration of MITC on wood products, and 1,3-dichloropropene (1,3-D) on food products will continue (PMEP).

Neither methyl isothiocyanate nor vorlex is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides or Chemicals or Timber Preservatives, Antisapstains, and Antifouling Paints) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals).

However, methyl isothiocyanate is the major breakdown product (and effective agent) of the dithiocarbamates, eg, dazomet, mancozeb, metam sodium, propineb, zineb and ziram (all have individual datasheets).

### Form and fate in the environment

See dazomet, mancozeb, metam sodium, propineb, zineb and ziram datasheets. Also see methyl isocyanate (in organics section).

Water solubility is about 7,600 mg/L.

NPIC (1994) quotes for methyl isothiocyanate a soil half-life of seven days, water solubility of 7,600 mg/L and a sorption coefficient (soil Koc) of 6. This resulted in a pesticide movement to groundwater rating of moderate.

### Removal methods

No information available. The high water solubility suggests that treatment processes that remove particulate matter should be ineffective at reducing the concentration of methyl isothiocyanate in water. Activated carbon treatment may be effective.

### Recommended analytical techniques

#### Referee method

A referee method cannot be selected because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

See dazomet, mancozeb, metam sodium, propineb, zineb and ziram datasheets.

PMEP reports a six-month feeding trial in 1984 where rats tolerated 30 mg/kg daily.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0004 mg/kg body weight, with a NOEL of 0.04 mg/kg bw from a three-month study in dogs. In this study there were decreased testis weights, increased pancreas weights, and abnormal liver histology at the highest dose tested, 2 mg/kg bw/day. The ADI incorporates a safety factor of 100. The ARfD is 0.0005 mg/kg bw based on a NOEL of 0.1 mg/kg bw/day from an acute oral dosing study in dogs. At the next highest dose tested of 0.5 mg/kg bw/day and above, haemorrhagic lesions in liver and kidneys were seen at necropsy. The ARfD incorporates a safety factor of 200 and was established in 2004.

### Derivation of Maximum Acceptable Value

No MAV.

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Refer also to dazomet, mancozeb, metam sodium, propineb, zineb and ziram datasheets for further information.

# Methyl parathion

CAS No. 298-00-0. The IUPAC and CAS name is O,O-dimethyl O‑4‑nitrophenylphosphorothioate. Sometimes written as methyl-parathion. Also called parathion-methyl and metafos. The analogous diethyl ester has the ISO common name [parathion](http://www.alanwood.net/pesticides/parathion.html) (qv).

### Maximum Acceptable Value

WHO (2004, 2011 and 2017) states that because the health-based value is much higher than concentrations likely to be found in drinking-water, the establishment of a guideline value is not deemed necessary.

WHO (2017) includes a health-based value of 0.009 mg/L.

In the 2005 DWSNZ, the provisional MAV for methyl parathion in drinking-water had been 0.01 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0007 mg/L for parathion-methyl; excursions above the health-based guideline, even for a short period, could be of concern.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.001 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

Methyl-parathion (soluble liquid formulations exceeding 600 g/L active ingredient) appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

Methyl parathion should not contain more than 2 percent of free p-nitrophenol.

### Sources to water

Methyl parathion is a non-systemic organophosphate insecticide and acaricide, used by contact and stomach action to control many biting or sucking insect pests of grain, vegetables, fruit and ornamentals. 4-Nitrophenol is an insecticide and a break-down product of methyl parathion which does not adsorb to soil particles so may contaminate groundwater. The technical grade is about 80 percent methyl parathion. About 16–17 percent is usually xylene and 5 percent comprise inert compounds.

Formulations containing methyl-parathion were first registered for use in New Zealand since 1961. One substance, Folidol M50, was previously registered as late as 2004. This product is no longer registered for agricultural use. No products containing methyl-parathion are currently (2008) registered for agricultural use in New Zealand. Methyl parathion does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). Despite that, ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008 lists “emulsifiable concentrate containing 600 g/litre parathion-methyl”.

It is also listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It appears as parathion methyl.

Concentrations in natural waters of agricultural areas in the USA ranged up to 0.0005 mg/L, with highest levels in summer.

### Form and fate in the environment

Methyl parathion partitions mainly to air and soil in the environment. Solubility in water is about 50–60 mg/L. There is virtually no movement through soil so it is not likely to leach to groundwater. By far the most important route for the environmental degradation of methyl parathion is microbial degradation. In most situations, methyl parathion adsorbs to soil particles and degrades rapidly; it is therefore unlikely to contaminate groundwater. Soil retention is greatly influenced by soil type; sandy soil can lose residues of the compound more rapidly than loams. Methyl parathion is rapidly hydrolysed in alkaline media at a rate 4.3 times greater than parathion.

Half-lifes of methyl parathion in water are in the order of weeks to months. Concentrations of methyl parathion in natural waters of agricultural areas in the USA ranged up to 0.0005 mg/L, with highest levels in summer. In water, methyl parathion is subject to photolysis, with a half-life of eight days during the summer and 38 days in winter.

When it is applied as an insecticide, methyl parathion breaks down within several months, primarily by photolysis and biodegradation. The rate of degradation increases with temperature and with exposure to sunlight. Its biodegradation half-life in soil is 10 days to two months. Degradation was faster in flooded soils than in non-flooded soils. Mineralisation may occur, especially in moist soils. Some volatilisation of applied methyl parathion may occur. The degradation product 4-nitrophenol is usually utilised and transformed to undetectable metabolites by the micro-organisms. Methyl paraoxon is another degradate (USEPA 2006). Methyl paraoxon is less stable than the parent and is formed by oxidative degradation in the presence of UV radiation.

NPIC (1994) quotes for methyl parathion a soil half-life of five days, water solubility of 60 mg/L and a sorption coefficient (soil Koc) of 5,100. This resulted in a pesticide movement to groundwater rating of very low.

USGS (2006) give the following values: log Kow = 3.0; log Koc (where Koc is in mL/g) = 3.7; water solubility = 25 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -1.68; half-life in aerobic soil = 3.3 days; half-life in water = 41 days.

### Typical concentrations in drinking-water

Methyl parathion has been detected rarely in groundwater outside of areas where it is used. It has been detected in the groundwater of Mississippi at 8 ppb (0.008 mg/L).

### Removal methods

No information available. In situations where methyl-parathion is attracted to soil particles, treatment processes that remove particulate matter should be effective at reducing its concentration; activated carbon should enhance the process. Chlorine at typical water treatment doses breaks down methyl-parathion. Other oxidation processes show promise.

### Recommended analytical techniques

#### Referee method

A referee method cannot be selected for methyl parathion because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for methyl parathion for the above reason. However, the following information may be useful:

Suitable analytical methods for the breakdown product 4-nitrophenol involve:

1. liquid/liquid extraction followed by gas chromatography using an electron capture detector (EPA 515.3)

2. liquid/liquid extraction followed by gas chromatography/mass spectrometry (APHA 6410B).

### Health considerations

The general population can come into contact with methyl parathion via air, water or food. The organophosphate insecticides are cholinesterase inhibitors. They are highly toxic by all routes of exposure.

The oral LD50 for methyl parathion in rats is 18 to 50 mg/kg, in mice is 14.5 to 19.5 mg/kg, in rabbits is 420 mg/kg, in guinea pigs is 1,270 mg/kg, and in dogs is 90 mg/kg.

Studies with human volunteers found that 1 to 22 mg/person/day have no effect on cholinesterase activity. In a four-week study of volunteers given 22, 24, 26, 28 or 30 mg/person/day, mild cholinesterase inhibition appeared in some individuals in the 24, 26 and 28 mg dosage groups. In the 30 mg/person/day (about 0.43 mg/kg/day) group, red blood cholinesterase activity was depressed by 37 percent. When methyl parathion was fed to dogs for 12 weeks, a dietary level of 1.25 mg/kg soon caused a significant depression of red blood cell and plasma cholinesterase. A dietary level of 0.125 mg/kg produced no effects.

Methyl parathion is absorbed rapidly into the bloodstream through all normal routes of exposure. Following administration of a single oral dose, the highest concentration of methyl parathion in body tissues occurred within one to two hours. Metabolism occurs in the liver, eventually to phenols which can be detected in the urine. Methyl parathion does not accumulate in the body. It is almost completely excreted through the kidneys (urine) within 24 hours.

JMPR (2003) quotes an ADI of 0–0.003 mg/kg bw, and an acute RfD of 0.03 mg/kg bw/day.

The Acceptable Daily Intake (ADI) adopted in Australia for parathion-methyl is 0.0002 mg/kg body weight, with a NOEL of 0.02 mg/kg bw, from long-term (one-year and two-year) dietary studies in rats. The NOEL is based on time- and dose-dependent neuro-pathological effects in the form of neuronal degeneration and abnormal gait. The ADI incorporates a safety factor of 100. The ARfD is 0.03 mg/kg bw based on the aforementioned NOEL of 0.3 mg/kg bw/day for erythrocyte cholinesterase inhibition in a 30-day dietary study in humans. The ARfD incorporates a safety factor of 10.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.0002 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.007 mg/L. The oral RfD had earlier been 0.00025 mg/kg/d (USEPA (1991) – this value has probably been rounded down.

Methyl parathion is a possible human teratogen. As at September 2008, the USEPA has classified methyl parathion as “not likely to be carcinogenic to humans”. IARC (1983) stated that the available data provide no evidence that methyl parathion is likely to present a carcinogenic risk to humans, ie, Group 3.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.0007 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.0003 mg/kg/day for chronic-duration oral exposure (>364 days).

### Derivation of Maximum Acceptable Value

WHO (2004) states that because the health-based value is much higher than methyl parathion concentrations likely to be found in drinking-water, the presence of methyl parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a numerical guideline value for methyl parathion is not deemed necessary.

In DWSNZ 2005, the provisional MAV of 0.01 mg/L had been derived as follows. WHO (2011) now calls this a health-based value, and WHO (2017) uses this approach for the current health-based value:

A NOAEL of 0.3 mg/kg of body weight per day was derived from the combined results of several studies conducted in humans, based on the depression of erythrocyte and plasma cholinesterase activities. Methyl parathion decreased cholinesterase activities in long-term studies in mice and rats, but did not induce carcinogenic effects. Methyl parathion was mutagenic in bacteria, but there was no evidence of genotoxicity in a limited range of studies in mammalian systems.

A health-based value of 0.009 mg/L (0.01 mg/L for 70 kg body weight) can be calculated for methyl parathion on the basis of an ADI of 0.003 mg/kg of body weight, based on a NOAEL of 0.25 mg/kg of body weight per day in a two-year study in rats for retinal degeneration, sciatic nerve demyelination, reduced body weight, anaemia and decreased brain acetylcholinesterase activity, using an uncertainty factor of 100. Since the toxicological end-points seen in animals were other than acetylcholinesterase inhibition, it was considered more appropriate to use these data rather than the NOAEL derived for cholinesterase inhibition in humans.

Intake of methyl parathion from all sources is generally low and well below the ADI. As the health-based value is much higher than methyl parathion concentrations likely to be found in drinking-water, the presence of methyl parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a guideline value for methyl parathion is not deemed necessary (WHO 2011/2017).

The USEPA (1990) has established a Lifetime Health Advisory (LHA) level of 0.06 mg/L for 4-nitrophenol, a breakdown product of methyl parathion, in drinking water. This means that EPA believes that water containing 4-nitrophenol at or below this level is acceptable for drinking every day over the course of one’s lifetime, and does not pose any health concerns. However, consumption of 4-nitrophenol at high levels well above the LHA level over a long period of time has been shown to cause adverse health effects, including damage to the liver, respiratory stress, and inflammation of the stomach in animal studies.

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# Metiram

CAS No. 9006-42-2. The IUPAC name for metiram is zinc ammoniate ethylenebis(dithiocarbamate) – poly(ethylenethiuram disulfide).

### Maximum Acceptable Value

Metiram does not have a MAV in the DWSNZ; metiram is not mentioned in the WHO Guidelines. Metiram degrades in the environment to ethylene thiourea (ETU), so it would be logical for guidelines for metiram to be based on the health effects of ETU – there is no MAV for ETU in the DWSNZ; WHO (2011) states that ETU is unlikely to occur in drinking-water so has been excluded from guideline value derivation.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.009 mg/L for ethylenethiourea (ETU); excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EC (2005) states that the manufacturing impurity ETU (ethylene thiourea) is considered to be of toxicological concern and must not exceed 0.5 percent of the active substance.

### Sources to water

Metiram is a ethylenebisdithiocarbamate (EBDC) compound, which includes the related active ingredients maneb and mancozeb. Metiram is a non-systemic polymeric dithiocarbamate fungicide commonly used on apples and grapes. Dithiocarbamates have a similar action to carbamate insecticides except they affect the nervous system through their main metabolite, carbon disulfide.

JMPR (1995) states that metiram pure active ingredient is inaccessible. In the manufacturing process ethylenediamine is reacted with carbon disulfide in ammonia solution to form an ammonium ethylenebis(dithiocarbamate). This intermediate is further reacted with zinc chloride and then with hydrogen peroxide to produce a polymeric precipitate. The gel-like filter cake consists of about 65 percent water, 30 percent metiram and 5 percent impurities which stabilise the structure of the polymer and optimise the fungicidal activity of the end product.

Metiram is effective against a broad spectrum of fungi and is used to protect fruits, vegetables, field crops, and ornamentals from foliar diseases and during storage, or transport. Metiram is a cholinesterase inhibitor.

Metiram appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 15 tonnes of metiram were used in New Zealand in 2004, at an application rate of 4500 grams of active ingredient per hectare. Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007).

### Forms and fate in the environment

Metiram is probably similar in its environmental fate to closely related compounds such as maneb and mancozeb. They are of low persistence and are strongly bound to most soils. This property, and their low water solubilities, indicate that they probably do not pose a significant risk to groundwater. They are unstable in the presence of atmospheric moisture and oxygen and are rapidly degraded in biological systems to ethylenethiourea and other metabolites. These products are of moderate persistence and more mobile, and therefore may pose more risk to groundwater.

Major metabolites include carbimid, EBIS, TDIT, hydantoin, ETU and EU (EC 2005); apart from ETU these have short half-lifes.

Water solubility of metiram is about 2 mg/L.

NPIC (1994) quotes for metiram a soil half-life of 20 days, water solubility of 0.1 mg/L and a sorption coefficient (soil Koc) of 500,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Removal methods

Ozone treatment and some newer advanced oxidation products appear to degrade metiram and ETU. Aeration should remove the carbon disulphide.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Metiram is a practically non-toxic compound, included in USEPA toxicity class IV.

When rats were fed metiram at dietary doses of 50 mg/kg/day five days a week for two weeks, no symptoms of illness were produced. Adverse effects occurred at 500 mg/kg/day . No ill-effect was observed in dogs that received 45 mg/kg daily of the fungicide for 90 days, or 7.5 mg/kg daily for almost two years. When metiram was fed to rats at dietary doses of 0.25, 1, 4, or 16 mg/kg/day, the only effect observed was muscle atrophy in rats receiving 16 mg/kg/day.

The major toxicological concern in situations of chronic exposure to metiram, however, is ethylenethiourea, a contaminant (can be up to 2 percent) and a breakdown product of metiram that has been shown to cause birth defects and cancer in experimental animals. Refer to the ethylenethiourea datasheet for further information.

As at September 2008 the USEPA has classified metiram in Group B: a probable human carcinogen. Metiram appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. However, EC (2005) reports that there is No evidence of oncogenic potential in rats and mice.

No data were available regarding the target organs of metiram. It is likely that its target organs will be similar to those affected by closely related compounds such as maneb and mancozeb. Those compounds exert their principal effects on the thyroid.

EXTOXNET quotes an ADI of 0.03 mg/kg. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0004 mg/kg/d, and an ARfD of 0.01 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for metiram is 0.33 mg/L.

In 1993, the JMPR estimated a dithiocarbamate group ADI of 0–0.03 mg/kg bw for mancozeb, maneb, metiram and zineb based on thyroid toxicity. For their metabolite ethylenethiourea (ETU), an ADI of 0–0.004 mg/kg bw has been allocated (JMPR 2012). No ARfD value is quoted.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a LOEL of 5 mg/kg bw from a short-term (26-week) gavage study in monkeys and 250‑fold safety factor. The LOEL is based on decreased thyroxine levels at the lowest dose tested of 5 mg/kg bw/day and above. Decreased serum triiodothyronine levels, and partially reversible thyroid enlargement and hyperplasia were seen at doses of 15 and 75 mg/kg bw/day, following a 15-week recovery period. A no-observed-effect level (NOEL) was not demonstrated in this study. The ADI incorporates a safety factor of 200. There is currently no ADI for ETU.

EC (2005) adopted an ADI of 0.03 mg/kg/d; an ARfD (acute reference dose) for metiram was not necessary, the ETU ARfD of 0.05 mg/kg/d is more relevant.

The USEPA (2005) has not set limits for metiram in drinking-water because metiram is not expected to remain in drinking water long enough to reach a location that would supply water for human consumption, whether from surface or groundwater sources. The USEPA has restricted the use of metiram to just tomatoes and potatoes. Estimated concentrations of ethylenethiourea, for both surface and ground water sources of drinking-water, are low and not of concern.

### Derivation of Maximum Acceptable Value

No MAV.

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# Metofluthrin

CAS No. 240494-70-6. The IUPAC name for metofluthrin is 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (1RS,3RS;1RS,3SR)-2,2-dimethyl-3-[(EZ)-prop-1-enyl]cyclopropanecarboxylate, or 2,3,5,6-tetrafluoro-4-(methoxymethyl)benzyl (1RS)‑cis-trans-2,2-dimethyl-3-[(EZ)-prop-1-enyl]cyclopropanecarboxylate. The CAS name is [2,3,5,6-tetrafluoro-4-(methoxymethyl)phenyl]methyl 2,2-dimethyl-3-(1-propen-1-yl)cyclopropanecarboxylate.

The common name metofluthrin refers to an unspecified mixture of all eight possible isomers. Z- and E-isomers exist. The main isomer (at least 80 percent of the mixture) has its own ISO common name: [epsilon-metofluthrin](http://www.alanwood.net/pesticides/epsilon-metofluthrin.html), CAS No. 240494-71-7.

### Maximum Acceptable Value

Metofluthrin does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Metofluthrin is a pyrethroid ester insecticide.

Metofluthrin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2016 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is approved as a portable mosquito repellent for use outdoors.

### Forms and fate in the environment

The water solubility of metofluthrin is 0.5 to 0.7 mg/L. The octanol/water partition coefficient, logPow (25°C) = 5. Henry’s Law Constant (20°C) = 1.5 x 10-5 atm m3/mol (Z‑isomer) and 1.1 x 10-5 atm m3/mol (E-isomer). Metofluthrin is stable to hydrolysis, and has a photolysis half-life of six days (USEPA 2004).

If released to soil, metofluthrin is expected to have no mobility based upon an estimated Koc of 33,000. Volatilisation from moist soil surfaces is expected to be an important fate process based upon an estimated Henry’s Law constant of 9.5 x 10-6 atm-cu m/mole. However, adsorption to soil is expected to attenuate volatilisation. Metofluthrin is biodegraded aerobically with half-lifes of 1 to eight days in sandy loam. If released into water, metofluthrin is expected to adsorb to suspended solids and sediment based on the estimated Koc. Volatilisation from water surfaces is expected to be an important fate process based on its estimated Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 7.5 and 60 days, respectively. However, volatilisation from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. The estimated volatilisation half-life from a model pond is 31 years if adsorption is considered. An estimated BCF of 51 suggests the potential for bioconcentration in aquatic organisms is moderate, provided the compound is not metabolised by the organism. Hydrolysis is expected to be an important environmental fate process since this compound contains functional groups that hydrolyse under environmental conditions (NIH, accessed June 2016).

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of metofluthrin in water.

### Health considerations

Metofluthrin, like other pyrethroids, is neurotoxic in rats, rabbits, and dogs; both sexes were equally sensitive to metofluthrin.

The incidental oral short-term (1–30 days) NOAEL = 15 mg/kg/d, based on maternal neurotoxicity in the rat developmental study. Metofluthrin is likely to be a human carcinogen based on female rat liver combined adenoma and carcinoma tumour rates (USEPA 2004).

CIRCABC (2010) identified a medium term oral NOAEL of 10 mg/kg/d from a one-year study in dogs, and 8 mg/kg/d from a two-year study in rats for long-term.

### Derivation of Maximum Acceptable Value

No MAV.

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# Metolachlor

CAS No. 51218-45-2. The IUPAC name for metolachlor is 2-chloro-N-(6-ethyl-o-tolyl)-N-[(1RS)-2-methoxy-1-methylethyl]acetamide, or (aRS,1RS)-2-chloro-6′-ethyl-N-(2-methoxy-1-methylethyl)acet-o-toluidide. The CAS name is 2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl)acetamide. Has also been called 2-chloro-6’-ethyl-N-(2-methoxy-1-methylethyl) acet-o-toluidine.

The (S)-stereoisomer of this substance has the ISO common name [S-metolachlor](http://www.alanwood.net/pesticides/s-metolachlor.html); CAS No. 87392-12-9. IUPAC: [S-metolachlor](http://www.alanwood.net/pesticides/s-metolachlor.html) is a mixture of 80–100 percent of 2-chloro-N-(6-ethyl-o-tolyl)-N-[(1S)-2-methoxy-1-methylethyl]acetamide and 20–0 percent 2-chloro-N-(6-ethyl-o-tolyl)-N-[(1R)-2-methoxy-1-methylethyl]acetamide.

It is often applied in combination with broadleaf herbicides.

### Maximum Acceptable Value

Based on health considerations, the concentration of metolachlor in drinking-water should not exceed 0.01 mg/L.

The maximum acceptable concentration for metolachlor in Canada is 0.05 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.3 mg/L for metolachlor and for metolachlor-S; minor excursions above this level would need to occur over a relatively long period to be a health concern, as the health-based guideline is based on medium-term effects.

The USEPA concluded on 22 September 2009 that metolachlor is known or anticipated to occur in PWSs and may require regulation. Therefore they added metolachlor to their CCL 3 (Drinking Water Contaminant Candidate List 3). They added the degradation products metolachlor ethanesulfonic acid (metolachlor ESA – CAS No. 171118-09-5) and metolachlor oxanilic acid (metolachlor OA – CAS No. 152019-73-3) as well (USEPA 2009a).

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.7 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

Metolachlor should not contain more than 1 g/kg of 6-ethyl-o-toluidine, 2 g/kg of 6‑ethyl-N-(2-methoxy-1-methylethyl)-o-toluidine, and 15 g/kg of 2-chloro-6-ethylaceto-o-toluidine.

### Sources to water

Metolachlor, a chloroacetamide or chloracetanilide, may enter source waters as a result of its use as a selective herbicide for pre-emergence and incorporated pre-plant weed control in a variety of crops.

The total annual usage of metolachlor in New Zealand in the late 1980s was 19,000 kg with the majority of use in the North Island. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Metolachlor appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Metolachlor was found in 2091 of 4161 surface water samples and in 13 of 596 groundwater samples in the USA in 1988. The 85th percentile of all non-zero samples was 0.012 mg/L in surface water and 0.00025 mg/L in groundwater.

### Forms and fate in the environment

Metolachlor photodegrades slowly in water exposed to sunlight. Its hydrolysis half-life is greater than 200 days in water.

It can be lost from the soil through biodegradation, photodegradation and volatilisation. The half-life for metolachlor in soil ranges from 15 to 130 days with the recommended average soil half-life being 90 days. Metolachlor can leach beyond the root zone in detectable amounts although little leaching occurs in soils with high organic content. Leaching is also inhibited by high clay content of the soil. A predominant degradate is carbinol. It is fairly mobile and under certain conditions can contaminate groundwater, but it is mostly found in surface water.

The water solubility of metolachlor is 530 mg/L, the sorption coefficient is 200 mL/g, its vapour pressure at 20°C is 1.7 x10-3 Pa, and reported log octanol-water partition coefficients range from 3.04 to 4.72, indicating that metolachlor has some potential for bioaccumulation. It is fairly mobile and under certain conditions can contaminate groundwater, but it is mostly found in surface water.

NPIC (1994) quotes for metolachlor a soil half-life of 90 days, water solubility of 530 mg/L and a sorption coefficient (soil Koc) of 200. This resulted in a pesticide movement to groundwater rating of high. Its GUS score is 4.63, indicating that it will leach to groundwater.

USGS (2006) give the following values: log Kow = 3.13; log Koc (where Koc is in mL/g) = 2.26; water solubility = 430 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -2.63; half-life in aerobic soil = 26 days; half-life in water = 410 days.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of metolachlor (limit of detection = 0.0001 mg/L) (ESR 2001).

Metolachlor has been detected in surface water and groundwater at concentrations that can exceed 0.01 mg/L (WHO 2004).

Metolachlor has been found 5 times in groundwaters in the Auckland, Waikato and Gisborne areas, ranging from 0.000036 to 0.0045 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Metolachlor occurred at 0.1 µg/L, ie, at 0.0001 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Metolachlor occurred at 0.21 µg/L, ie, 0.00021 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Metolachlor occurred at 0.036 to 0.056 µg/L, ie, up to 0.000056 mg/L.

Metolachlor was found in two bore waters during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.000058 to 0.0001 mg/L. The bores were in the Auckland region.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Metolachlor was found in two wells, from 0.047 to 0.091 µg/L, ie, up to 0.000091 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Metolachlor was found in two samples, at 0.027 and 0.057 µg/L, ie, up to 0.000057 mg/L.

During a survey in southern Ontario conducted in 1985, 15 percent of 351 private wells suspected of being contaminated with alachlor had detectable metolachlor concentrations (detection limit 0.0001 mg/L). Metolachlor was detected in 125 of 917 samples from municipal and private water supplies in the Atlantic region (1985 to 1986), Quebec (1984 to 1985), Ontario (1979 to 1986) and Alberta (1986) (detection limits ranged from 0.0001 to 0.001 µg/L). The maximum concentration of metolachlor in a water supply was 1.80 mg/L, obtained from a site in Ontario (Health Canada 1986/90).

115 water utilities in the US reported detecting metolachlor in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.019 mg/L.

### Removal methods

Adsorption on to activated carbon appears to be the most promising technique for removal of metolachlor from drinking-waters, but more actual data are still required to determine its effectiveness. Health Canada (1986/90) stated that treatment with granular activated carbon is reported to be 99.5 percent effective in the removal of metolachlor from wastewater with an initial average concentration of 16.4 mg/L. WHO (2011/2017) states that a concentration as low as 0.0001 mg/L should be achievable using GAC. Coagulation/filtration reduce the concentration; ozone and chlorine can break down some of the metolachlor.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector (EPA 507).

#### Some alternative methods

No alternative methods have been recommended for metolachlor because no methods meet the required criteria. See WHO (2003) for further information.

### Health considerations

Metolachlor is absorbed and excreted readily in the rat. It is metabolised via dechlorination, O-methylation, N-dealkylation, and side-chain oxidation. No unchanged chemical was isolated.

S-metolachlor is moderately acutely toxic (USEPA Toxicity Category III) by the oral and dermal route. Signs of metolachlor intoxication in humans include abdominal cramps, anaemia, ataxia (loss of coordination), dark urine, methaemoglobinaemia, cyanosis, hypothermia, collapse, convulsions, diarrhoea jaundice, weakness, nausea, shock, sweating, vomiting, central nervous system depression, dizziness, dyspenea, liver damage, nephritis, cardiovascular failure, dermatitis, sensitisation, eye and mucous membrane irritation, corneal opacity and reproductive effects.

In a one-year study in beagle dogs, administration of metolachlor resulted in decreased kidney weight at the two highest dose levels. In two-year studies with rodents fed metolachlor in the diet, the only toxicological effects observed in albino mice were decreased body weight gain and decreased survival in females at the highest dose level, whereas rats showed decreased body weight gain and food consumption at the highest dose level (WHO 2017).

EFSA (2002) quotes an ADI of 0.1 mg/kg bw/d; an ARfD was not deemed necessary.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.08 mg/kg body weight, with a NOEL of 7.5 mg/kg bw from a medium-term (six-month) dietary study in dogs. The NOEL is based on decreased bodyweight gain. The ADI incorporates a safety factor of 100.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.1 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 3.5 mg/L. In the chronic dog study that supports S-metolachlor, the only adverse effect was decreased body weight gain in females at 33 mg/kg/day; the NOAEL was 10 mg/kg/day (USEPA 2003). The oral RfD had earlier been 0.15 mg/kg/d (USEPA 1994).

Metolachlor does not induce gene mutations in bacterial or mammalian cells. There is no evidence from available studies that metolachlor is carcinogenic in mice. In rats, an increase in liver tumours in females and a few nasal tumours in males have been observed. As at September 2008 the USEPA has classified metolachlor in Group C: a possible human carcinogen. S-metolachlor was not embryotoxic or teratogenic in rat or rabbit tests at maternally toxic doses (USEPA 2003).

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV of metolachlor in drinking-water. Long-term toxicity data are available in dogs and rodents. The lowest-observable-adverse-effect level used in the derivation is based on an apparent decrease in kidney weight at the two highest dose levels in a one-year dog study.

The MAV for metolachlor in drinking-water was derived as follows:

3.5 mg/kg body weight/day x 70 kg x 0.1 = 0.0123 mg/L (rounded to 0.01 mg/L)

2 L/day x 1,000

where:

* lowest observable adverse effect level = 3.5 mg/kg body weight per day based on an apparent decrease in kidney weight observed in a chronic dog study
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for concern regarding carcinogenicity).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health-based value (exposure greater than 10 percent of a lifetime) for metolachlor is 0.3 mg/L; the acute limit (one day exposure) is 0.4 mg/L. The chronic health-based value for metolachlor ESA and metolachlor OXA are both 0.8 mg/L.

USEPA (2015) found that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for metolachlor since additional testing is not expected to impact EPA’s current regulatory point of departures and endpoints for human health risk assessments.

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# Metrafenone

CAS No. 220899-03-6. The IUPAC name for metrafenone is 3′-bromo-2,3,4,6′-tetramethoxy-2′,6-dimethylbenzophenone. The CAS name is (3-bromo-6-methoxy-2-methylphenyl)(2,3,4-trimethoxy-6-methylphenyl)methanone.

### Maximum Acceptable Value

Metrafenone does not have a MAV in the DWSNZ and is not mentioned in the WHO Guidelines.

### Sources to water

Metrafenone is an aryl phenyl ketone (or benzophenone) fungicide with protectant and curative properties intended for the control of powdery mildew produced by Uncinula necator in all commercial varieties of grape vines.

Metrafenone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Non-compliant levels were found on leafy vegetables in the 2015–2016 MPI Food Residues Surveillance Programme (<http://www.mpi.govt.nz/food-safety/food-monitoring-and-surveillance/food-residues-survey-programme/>).

### Forms and fate in the environment

Soil degradation studies demonstrated that the degradation rate of metrafenone is slow as the maximum DT90field exceeded one year. Several metabolites are listed in EFSA (2013).

There do not appear to be any metabolites of health concern, and residues are not expected in drinking-water.

JMPR (2014) reports: Henry’s Law constant = KH = 0.132 Pa.m³ mol–1 (20°C). Water solubility is about 0.5 mg/L over a pH range of 5 to 9. The n-octanol/water partition coefficient = Log Kow = 4.3 (pH 4.0, 25°C). Metrafenone is stable to hydrolysis in the dark after incubation for five days at 50°C in pH 4, pH 7, pH 9 buffers. Extensive degradation in natural water after irradiation by simulated sunlight (15 days, pH 7, 22°C): DT50 : 2.6 days, DT90 : 8.5 days). Metrafenone degraded slowly in the loamy sand, sandy loam and clay loam soils incubated for up to 210 days under aerobic laboratory conditions at 10°C and 20°C. About 66–69 percent AR was still present as the parent compound at the end of the 20°C study and about 82 percent AR remaining as metrafenone at the end of the 10°C study. Calculated half-lifes (first order kinetics) ranged from 182–365 days.

### Health considerations

EC (2006) adopted an ADI of 0.25 mg/kg/d for metrafenone. Based on the toxicological characteristics of metrafenone setting an ARfD is not needed. These values were confirmed in EFSA (2011, 2013 and 2015).

There was evidence of increased incidences of tumours in the two-year rat and 78‑week mouse studies. The USEPA (2006) classified metrafenone as “suggestive evidence of carcinogenicity”, and concluded that human risk to liver tumourigenesis would not be expected at exposure levels that do not cause tumours in mice. The NOAEL and LOAEL selected for the cRfD are based on hepatotoxicity and nephrotoxicity observed at doses lower than the liver tumour response. Thus, the cRfD is protective of the cancer effects. The chronic reference dose or RfD (USEPA 2006) is 0.25 mg/kg/d. No appropriate endpoint attributable to a single dose (acute toxicity) was identified. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.25 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for metrafenone is 1.75 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.25 mg/kg body weight, with a NOEL of 24.9 mg/kg bw (<https://apvma.gov.au/>); an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose.

JMPR (2014) quotes an ADI of 0.3 mg/kg bw, and that an ARfD is not needed.

### Derivation of Maximum Acceptable Value

No MAV.

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# Metribuzin

CAS No. 21087-64-9. IUPAC name: 4-amino-6-tert-butyl-4,5-dihydro-3-methylthio-1,2,4-triazin-5-one, or: 4-amino-6-tert-butyl-3-methylthio-1,2,4-triazin-5(4H)-one. The CAS name is 4-amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one.

### Maximum Acceptable Value (Provisional)

Based on health considerations, the concentration of metribuzin in drinking-water should not exceed 0.07 mg/L (70 μg/L). Metribuzin is not mentioned in the WHO Guidelines.

The maximum acceptable concentration for metribuzin in Canada is 0.08 mg/L.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.07 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.001 mg/L (1 µg/L) for metribuzin in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Metribuzin is a triazine (or triazinone) herbicide used pre- and post-emergent for the control of broad-leaf weeds and grasses in agricultural crops.

Metribuzin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is available in four different formulations and is used for pre- and post-emergent weed control. Some trade names include Lexone DF, Metriphar 48SC, Python and Sencor DF. It is applied by various methods including aerial, chemigation, and ground application.

No information is available on the annual usage of specific active ingredients in New Zealand, although metribuzin is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Metribuzin is very soluble in water: 1,200 mg/L (Merck & Co 1996). Its vapour pressure at 20°C is less than 1.3 x 10-3 Pa. The log octanol-water partition coefficient of metribuzin has been reported to be 1.70; therefore, it is not likely to bioaccumulate significantly (Health Canada 1986/89).

Microbial degradation is the principal route of removal of metribuzin from the soil (Health Canada 1986). Metribuzin also adsorbs moderately to soil with high clay and/or organic matter content; adsorption decreases as soil pH increases (WSSA 1983, cited in Health Canada 1986). Its half-life in soil ranges between 2.5 and 4 months. It has a mobility (as Koc) of 60, which indicates that it is weakly adsorbed to organic soil and therefore has the potential to migrate through soil to reach groundwater.

Once in groundwater, metribuzin is expected to persist due to its stability to hydrolysis and the lack of light penetration. Conversely, residues of metribuzin are not likely to persist in clear, well-mixed, shallow surface water with good light penetration since parent metribuzin degrades rapidly by aqueous photolysis (USEPA 1998). The half-life of metribuzin in pond water is approximately seven days. If present, metribuzin would most likely be found in the water column rather than the sediment, due to its low binding affinity and high water solubility.

NPIC (1994) quotes for metribuzin a soil half-life of 40 days, water solubility of 1,220 mg/L and a sorption coefficient (soil Koc) of 60. This resulted in a pesticide movement to groundwater rating of high. Its GUS score is 3.82, indicating that it will leach to groundwater.

USGS (2006) give the following values: log Kow = 1.60; log Koc (where Koc is in mL/g) = 1.72; water solubility = 1,000 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -5.31; half-life in aerobic soil = 172 days; half-life in water = >200 days.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included metribuzin.

In the New Zealand national pesticides surveys, conducted every four years since 1990, metribuzin has been detected in groundwater twice, at concentrations of 0.00014 and 0.0012 mg/L (Close et al 2001). In the Waikato region, metribuzin has been detected in groundwater at three sites. Concentrations ranged from 0.00002–0.00028 mg/L (Hadfield and Smith 1999, p12). Metribuzin has been detected in groundwater at one location in the Edendale area at concentrations ranging between  
0.00003–0.00014 mg/L (Hughes 2000).

Metribuzin has been found ten times in groundwaters in Waikato, Canterbury and Southland, ranging from 0.00002 to 0.012 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Metribuzin occurred at 0.14 to 1.2 µg/L, ie, 0.0012 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Metribuzin occurred at 0.27 µg/L, ie, 0.00027 mg/L.

Metribuzin was found in 1 bore water during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.000088 mg/L. The bore was in the Manawatu region.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Metribuzin was found in five wells, up to 1.7 µg/L, ie, up to 0.0017 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Metribuzin was found in one sample, at 0.06 µg/L, ie, 0.00006 mg/L.

Ten water utilities in the US reported detecting metribuzin in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0024 mg/L.

Metribuzin was detected in 26 of 1,140 samples from municipal and private water supplies in Prince Edward Island (time period not reported) Nova Scotia (1986), Ontario (1979 to 1986), Manitoba (1986) and Alberta (1978 to 1986). Detection limits ranged from 0.00001 to 0.001 mg/L. The maximum concentration of metribuzin, determined in a sample from a well in Ontario, was 0.3 mg/L (Hiebsch 1988, cited in Health Canada 1986/89).

### Removal methods

Oxidation of triazines by ozone is reported to be effective (Chiron et al 2000). The water chemistry, in particular the alkalinity and pH, will affect the oxidation rate. Use of activated carbon following ozonisation should be considered to adsorb oxidation products.

Nanofiltration of water with a low natural organic matter concentration is reported to remove approximately 50 percent of atrazine and simazine (Agbekodo et al 1996). The percentage is increased to 90–100 percent when 3.6 mg/L of natural organic matter is present. Similar results may be expected for metribuzin as it is from the same chemical family and of comparable molecular size.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of metribuzin, although a guide to the efficiency of the process cannot be provided.

Treatment by coagulation and sedimentation with alum or iron salts may remove up to 50 percent of the metribuzin. Two different granular activated carbon adsorption columns were found to be effective in the removal of metribuzin from water (96 and 100 percent for an initial concentration of 140 mg/L) (Health Canada 1986/89).

### Recommended analytical techniques

#### Referee method

Liquid/liquid extraction/gas chromatography-nitrogen/phosphorus detector (EPA 507).

#### Some alternative methods

Liquid/solid extraction/gas chromatography-mass spectrometer (EPA 525.2) or liquid/solid extraction/gas chromatography-mass spectrometer (EPA 508.1).

### Health considerations

There is no information available regarding the greatest source of exposure to metribuzin for New Zealanders (ie, dermal contact, inhalation, diet: food, water), however, food is likely to be the most important route. The USEPA indicates that dietary exposure to metribuzin residues in food are not of concern. Of greater concern is the inhalation exposure risk posed to metribuzin handlers, particularly mixers/loaders/applicators and field workers.

Rats administered 1 or 200 mg/kg body weight of radioactively labelled metribuzin by stomach tube were reported to eliminate about 80 percent in the first day following administration, and 95 percent by the second day. Almost equal amounts were found in the urine and faeces (Health Canada 1986).

#### Acute poisoning

In studies using laboratory animals, metribuzin generally has been shown to be of low acute toxicity. It is slightly toxic by the oral and inhalation routes and has been placed in Toxicity Category III (the second lowest of four categories) for this effect (USEPA 1998).

The acute oral LD50 for rats is 2,200 mg/kg, mice 698–711 mg/kg, guinea pigs 250 mg/kg (RSocC 1987). These levels suggest a moderate acute oral toxicity when compared with other pesticides.

Effects of high acute exposure in metribuzin poisoned rats included narcosis (stupor) and laboured breathing. Deaths occurred within 24 hours, and survivors recovered slowly without permanent effects. In single high dose studies, metribuzin appears to depress the central nervous system. Other studies indicate that the target organs of metribuzin are the thyroid gland and the liver (EXTOXNET 1996).

#### Chronic exposure

In two-year feeding studies with rats and dogs, results showed no observable effects at doses of 5 mg/kg/day in rats and 2.5 mg/kg/day in dogs. Reduced weight gain, an increase in the number of deaths, blood chemistry changes, and liver and kidney damage were observed in a two-year study in which dogs were given 1,500 ppm or 37.5 mg/kg/day of metribuzin (EXTOXNET 1996).

Results of three developmental toxicity studies and one reproduction study suggest that although metribuzin is not considered a developmental toxicant, it is associated with developmental toxicity effects (USEPA 1998).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw from a long-term rat study. The NOEL is based on decreased absolute and relative heart weights. The ADI incorporates a safety factor of 100. The ARfD adopted in Australia is 0.25 mg/kg body weight, with a NOEL of 25 mg/kg bw based on a NOEL of 25 mg/kg bw/day from a developmental study in rats. The ARfD incorporates a safety factor of 100. In Jan 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EC (2006) adopted an ADI of 0.013 mg/kg/d and an ARfD of 0.02 mg/kg/d.

EFSA (2016) reports an acceptable daily intake (ADI) of 0.013 mg/kg body weight (bw) per day and an acute reference dose (ARfD) of 0.02 mg/kg bw.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.01 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.35 mg/L. The oral RfD had earlier been 0.025 mg/kg/d (USEPA 1995).

The International Agency for Research on Cancer (IARC) has not classified metribuzin, and as at September 2008 the USEPA has classified it in Group D: not classifiable as to human carcinogenicity. Metribuzin is not considered to be genotoxic, based on in vitro and in vivo short-term studies.

USEPA (2015) found that for the androgen pathway, metribuzin was negative in the in vitro estrogen receptor (ER) binding and ER transactivation assay, and was equivocal in the aromatase assay. It was positive in the steroidogenesis assay. In the in vivo Tier 1 assays, metribuzin showed no evidence for potential estrogen-related effects in the uterotrophic and female pubertal assays. For the androgen pathway, metribuzin was negative in the in vitro Tier 1 AR binding assay and the steroidogenesis assay. There was convincing evidence of potential interaction with the thyroid pathway.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for metribuzin in drinking-water, as follows:

2 mg/kg body weight per day x 70 kg x 0.1 = 0.07 mg/L

2 L x 100

where:

* no observable adverse effect level = 2 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for metribuzin is 0.2 mg/L.

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# Metsulfuron

CAS No. 79510-48-8. The IUPAC name for metsulfuron is 2-(4-methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl)benzoic acid. The CAS name is 2-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]benzoic acid.

When this substance is used as an ester or a salt, its identity should be stated, for example, [metsulfuron-methyl](http://www.alanwood.net/pesticides/derivatives/metsulfuron-methyl.html): CAS No. 74223-64-6. Also listed as CAS No. 5585-64-8. Also written as [metsulfuron methyl](http://www.alanwood.net/pesticides/derivatives/metsulfuron-methyl.html).

Trade names include Escort, Meturon, Mustang, Meteor 600, Eradicate 600, Matrix.

### Maximum Acceptable Value

Metsulfuron-methyl is not mentioned in the WHO Guidelines and does not have a MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2016) include a guideline value of 0.04 mg/L for metsulfuron-methyl; excursions above this level would need to occur over a significant period to be a health concern, because the health-based guideline is based on long-term effects.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for metsulfuron-methyl in water (set by an approval under Part 5 of the HSNO Act) of 8.4 ng/L (0.0084 µg/L).

### Sources to water

Sulfonylurea herbicides have been registered for use in New Zealand since 1986. Metsulfuron-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Four herbicides (metsulfuron methyl, haloxyfop methyl, imazapyr isopropylamine and triclopyr triethylamine (TEA)) have been approved by the New Zealand Environmental Protection Agency (EPA) for restricted use over water, by authorised agencies, under a set of conditions (EPA 2014). Metsulfuron methyl provides control of alligator weed, yellow flag and arrowhead. It is rapidly taken up by plant roots and foliage, is translocated throughout the plant, but is not persistent (Auckland City 2013).

Metsulfuron acts systemically (ie, will spread through entire plant to roots) on ferns, conifers and most broadleafs except Solanum spp. Generally not effective on grasses or other monocots, however high rates will kill almost anything. Preferred for hard-to-kill shrubs, trees. Very useful for vines. Recommended for stem/stump treatment, blackberry and gorse.

Metsulfuron-methyl is a degradation product of iodosulfuron-methyl-sodium (qv).

### Forms and fate in the environment

The breakdown of metsulfuron-methyl in soils is largely dependant on soil temperature, moisture content, and pH. The chemical will degrade faster under acidic conditions, and in soils with higher moisture content and higher temperature. Metsulfuron-methyl has a higher mobility potential in alkaline soils than in acidic soils, as it is more soluble under alkaline conditions. Metsulfuron methyl is not expected to volatilise from dry soil surfaces based on its vapour pressure. Metsulfuron-methyl is stable to photolysis, but will break down in ultraviolet light. Half-life estimates for metsulfuron-methyl in soil are wide ranging from 14–180 days, with an overall average of reported values of 30 days, ie, it has medium persistent. Major metabolites are sulfonamide and saccharin (EC 2000).

Solubility in water at 25°C and pH 7.0 is about 2,800 mg/L; at pH 5 the solubility is about 550 mg/L, and 21.3 percent at pH 9. If released into water, metsulfuron methyl is expected to have little to no adsorption to suspended solids and sediment based on its range of Koc values. Metsulfuron-methyl is stable to breakdown by water (hydrolysis) at neutral and alkaline pHs. It has an estimated three-week half-life in water at acidic pH. The degradation/dissipation of metsulfuron-methyl was investigated in four water/sediment systems (pH 7.6–8.26). Metsulfuron-methyl degraded in the whole systems with half-lifes between 50.2 and 579 days. Metabolites triazine amine (IN‑A4098), metsulfuron (IN-F5438) and bis-O-demethylmetsulfuron-methyl (IN-JX909) exceeded 10 percent AR in the water phase. No major metabolites were found in the sediment.

NPIC (1994) quotes for metsulfuron-methyl a soil half-life of 30 days, water solubility of 9,500 mg/L and a sorption coefficient (soil Koc) of 35. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

Has occasionally been reported in Australian drinking waters, but unlikely to be found at levels that may cause health concerns (NHMRC, NRMMC 2011).

### Removal methods

The high solubility suggests that treatment processes that remove particulate matter should be fairly ineffective at reducing the concentration of metsulfuron-methyl in water. Activated carbon treatment may be more effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

Appropriate HPLC-MS/MS method with a LOQ of 0.01 μg/L exists for monitoring metsulfuron-methyl in surface water and drinking water (EFSA 2015).

### Health considerations

JMPR (2001) states that metsulfuron methyl has not been evaluated by the FAO/WHO JMPR and WHO/PCS.

Metsulfuron-methyl is almost completely absorbed after oral administration, it is widely distributed, poorly metabolised and rapidly excreted mainly via urine; no potential for accumulation was observed.

Metsulfuron-methyl has very low toxicity in mammals and aquatic organisms. A two-year chronic toxicity feeding study in rats resulted in a No Observable Effects Level (NOAEL) of 25.0 mg/kg/day, based on decreased body weights seen at 250 mg/kg/day which was the highest dose tested; an uncertainty factor of 100 was applied. Based on this, the USEPA reference dose or cRfD (also the cPAD) is 0.25 mg/kg/day based on a NOAEL of 25 mg/kg/d and UF = 100. The RfD is the amount of daily pesticide exposure judged to pose no appreciable risk over a 70-year lifetime. An endpoint attributable to a single dose was not identified, therefore quantitation of acute dietary risk or aRfD is not appropriate (USEPA 2002).

JMPR (2001) quotes the EU review of metsulfuron methyl which established the following toxicological reference dose: ADI 0–0.22 mg/kg bw/day. The compound was not teratogenic and was considered by the EU review not to be genotoxic, although one test result was questioned.

The Acceptable Daily Intake (ADI) adopted in Australia for metsulfuron-methyl is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw from a long-term (two-year) dietary rat study. The NOEL is based on decreased bodyweight gain. The ADI incorporates a safety factor of 100.

EC (2000) adopted an ADI of 0.22 mg/kg/d for metsulfuron-methyl; an ARfD was considered unnecessary.

The ADI of metsulfuron-methyl is 0.22 mg/kg bw per day, based on the NOAEL of 22.4 mg/kg bw per day for reduced body weight gain from the two-year toxicity study in rats and applying the standard uncertainty factor (UF) of 100. The acute reference dose (ARfD) is 0.25 mg/kg bw based on the maternal NOAEL of 25 mg/kg bw per day for reduced body weight gain in the first days of dosing from the rabbit developmental toxicity study, 100 UF applied (EFSA 2015).

There is no evidence that metsulfuron-methyl causes birth defects, reproductive problems, nerve damage, or cancer. As at September 2008, the USEPA has classified metsulfuron-methyl as Class E: “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

No MAV.

The USEPA has not established a maximum contaminant level (MCL) for residues of metsulfuron methyl in drinking water. No health advisory levels for metsulfuron methyl in drinking water have been established. Taking into account the present uses and uses proposed, the USEPA concludes with reasonable certainty that residues of metsulfuron methyl in drinking water (when considered along with other sources of chronic exposure for which EPA has reliable data) would not result in an unacceptable estimate of acute aggregate human health risk at this time.

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# Milbemectin

CAS No. 51596-10-2 (milbemycin A3) plus 51596-11-3 (milbemycin A4). The commercial product is a 30:70 mixture (approx.).

The IUPAC name for milbemectin is extended von Baeyer nomenclature: mixture of 70 percent (10E,14E,16E)-(1R,4S,5′S,6R,6′R,8R,13R,20R,21R,24S)-6′-ethyl-21,24-dihydroxy-5′,11,13,22-tetramethyl-(3,7,19-trioxatetracyclo[15.6.1.14,8.020,24]pentacosa-10,14,16,22-tetraene)-6-spiro-2′-(tetrahydropyran)-2-one and 30 percent (10E,14E,16E)-(1R,4S,5′S,6R,6′R,8R,13R,20R,21R,24S)-21,24-dihydroxy-5′,6′,11,13,22-pentamethyl-(3,7,19-trioxatetracyclo[15.6.1.14,8.020,24]pentacosa-10,14,16,22-tetraene)-6-spiro-2′-(tetrahydropyran)-2-one or bridged fused ring systems nomenclature: mixture of 70 percent (2aE,4E,8E)-(5′S,6R,6′R,11R,13R,15S,17aR,20R,20aR,20bS)-6′-ethyl-3′,4′,5′,6,6′,7,10,11,14,15,17a,20,20a,20b-tetradecahydro-20,20b-dihydroxy-5′,6,8,19-tetramethylspiro[11,15-methano-2H,13H,17H-furo[4,3,2-pq][2,6]benzodioxacyclooctadecin-13,2′-[2H]pyran]-17-one and 30 percent (2aE,4E,8E)-(5′S,6R,6′R,11R,13R,15S,17aR,20R,20aR,20bS)-3′,4′,5′,6,6′,7,10,11,14,15,17a,20,20a,20b-tetradecahydro-20,20b-dihydroxy-5′,6,6′,8,19-pentamethylspiro[11,15-methano-2H,13H,17H-furo[4,3,2-pq][2,6]benzodioxacyclooctadecin-13,2′-[2H]pyran]-17-one.

The CAS name is (6R,25R)-5-O-demethyl-28-deoxy-6,28-epoxy-25-ethylmilbemycin B mixture with (6R,25R)-5-O-demethyl-28-deoxy-6,28-epoxy-25-methylmilbemycin B.

### Maximum Acceptable Value

Milbemectin does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Milbemectin is a mixture of milbemycin A3 (about 30 percent) and milbemycin A4 (about 70 percent), and is used as an acaricide, nematicide and insecticide on a range of fruit and vegetables by acting on the targets’ nervous system.

Milbemectin (and milbemycin oxime) appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Milbemycins are products of [fermentation](http://en.wikipedia.org/wiki/Fermentation_(biochemistry)) by [Streptomyces](http://en.wikipedia.org/wiki/Streptomyces) species. Milbemectin and milbemycin oxime are produced by Streptomyces hygroscopicus aureolacrimosus.

### Forms and fate in the environment

Soil dissipation studies imply a half-life of one to two weeks. Dissipation from water was dominated by adsorption to sediment. EFSA (2012) state that milbemectin is persistent in soil and that DT90 values exceed the trigger value of 100 days.

Water solubility is about 2.7 mg/L (milbemycin A3) and 4.6 mg/L (milbemycin A4) (EC 2005); Mitsui quotes 7.23 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed. See EFSA (2012).

### Health considerations

The lowest relevant short-term oral NOAEL / NOEL is 3 mg/kg/d based on 90-day and 12‑month dog studies. The lowest relevant long-term oral NOAEL / NOEL is 0.7 mg/kg/d based on a two-year rat study.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.007 mg/kg body weight, with a NOEL of 0.7 mg/kg bw (based on a two-year rat study), and the ARfD is 0.06 mg/kg bw. Note that their (mis)spelling in the ADI List is mibemectin. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EC (2005) quotes an ADI of 0.03 mg/kg bw, and an ARfD also of 0.03 mg/kg/d. These values were reaffirmed by EFSA (2012); both toxicological reference values were established for milbemycin A4 and milbemycin A3.

Carcinogenicity studies suggest increased incidence of neoplastic changes in the uterus of rats (EC 2005).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Mirex

CAS No. 2385-85-5. IUPAC name for mirex is dodecachloropentacyclo[5.3.0.02,6.03,9.04,8]decane, or perchloropentacyclo[5.3.0.02,6.03,9.04,8]decane. The CAS name is 1,1a,2,2,3,3a,4,5,5,5a,5b,6-dodecachlorooctahydro-1,3,4-metheno-1H-cyclobuta[cd]pentalene. Mirex has also been called perchloropentacyclodecane. Has also been called hexachlorocyclopentadiene dimer and perchloropentacyclodecane.

### Maximum Acceptable Value

WHO (2004) states that because mirex is unlikely to be found in drinking-water, the establishment of a guideline value is not deemed necessary. WHO (2011) states that mirex is unlikely to occur in drinking-water.

### Sources to water

Mirex is a fully chlorinated organic compound, based on two linked five member carbon rings. Mirex was used as a stomach insecticide to control [fire ants](http://en.wikipedia.org/wiki/Fire_ants), leaf cutters and mealy bug, and as a [flame retardant](http://en.wikipedia.org/wiki/Flame_retardant) in [plastic](http://en.wikipedia.org/wiki/Plastic), [rubber](http://en.wikipedia.org/wiki/Rubber), paint, paper and electronics. About 75 percent of the mirex produced was used as a fire retardant additive, while 25 percent was used as a pesticide.

Mirex does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The [Stockholm Convention](http://en.wikipedia.org/wiki/Stockholm_Convention) banned production and use of several [persistent organic pollutant](http://en.wikipedia.org/wiki/Persistent_organic_pollutant) and mirex was one of the dirty dozen, naming the worst offenders. It is not registered for use in New Zealand, as at 2008. Mirex and chlordecone (a structurally similar product) have not been manufactured or used in the United States since 1978. The technical grade was about 95 percent mirex, plus about 2.5 percent chlordecane, which was also manufactured as an insecticide (but no longer).

### Forms and fate in the environment

Mirex is one of the most stable of the organochlorine insecticides, the half-life can be >12 years. Mirex is very resistant to microbiological degradation and is only slowly dechlorinated to a monohydro derivative by anaerobic microbial action.

Although general environmental levels are low, it is widespread in the biotic and abiotic environment. Mirex is both accumulated and biomagnified. Mirex is strongly adsorbed on sediments and has a very low water solubility (<1 mg/L).

NPIC (1994) quotes for mirex a soil half-life of 3,000 days, water solubility of 0.00007 mg/L and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

Mirex adsorbs strongly to soil so is not likely to travel far through the soil and into underground water.

Two water utilities in the US reported detecting mirex in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0012 mg/L.

### Removal methods

Being strongly adsorbed to soil particles suggests that mirex will be removed by coagulation processes and many filtration techniques.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See section 6 of ATSDR (1996).

### Health considerations

The USEPA suggests that ingesting an amount of mirex equal to 200 picograms (pg) per kilogram (kg) of body weight per day is not likely to cause significant harmful health effects. Mirex is transported across [placenta](http://en.wikipedia.org/wiki/Placenta) and is excreted with milk. Mirex is foetotoxic and produces teratogenic effects. Photomirex and kepone are major degradation products.

The oral RfD for mirex was calculated at 0.0002 mg/kg/d (USEPA 1992).

IARC (1979) stated there is sufficient evidence that mirex is carcinogenic in mice and rats. In the absence of adequate data in humans, it is reasonable, for practical purposes, to regard mirex as if it presented a carcinogenic risk to humans. In 1987 IARC placed mirex in Group 2B – a probable human carcinogen.

Mirex is classified by the USEPA as probably causing cancer in humans, although it is not on their 2008 list. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Mirex is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of 0.0008 mg/kg/day for chronic-duration oral exposure (>364 days) to mirex.

### Derivation of Maximum Acceptable Value

No MAV.

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# Molinate

CAS No. 2212-67-1. The IUPAC name for molinate is S-ethylazepane-1-carbothiate, or S-ethyl perhydroazepine-1-carbothioate, or S-ethyl perhydroazepine-1-thiocarboxylate. The CAS name is S-ethyl hexahydro-1H-azepine-1-carbothioate.

### Maximum Acceptable Value

Based on health considerations, the concentration of molinate in drinking-water should not exceed 0.007 mg/L (7 g/L).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.004 mg/L; excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

The USEPA concluded on 22 September 2009 that molinate is known or anticipated to occur in PWSs and may require regulation. Therefore they added molinate to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

### Sources to water

Molinate, a thiocarbamate, may enter source waters as a result of its use as a post-emergence herbicide to control germinating broadleaved and grassy weeds in rice. It has been detected in irrigation drains after application to rice fields in NSW at levels up to 0.7 mg/L.

Molinate has never been registered for use in New Zealand.

### Forms and fate in the environment

The available data suggest that groundwater pollution by molinate is restricted to some rice-growing regions.

Volatilisation is the main route of loss of molinate from soil and rice fields. Photochemical degradation occurs to a lesser extent. Molinate has a low persistence in soil and water with half-lifes ranging from 5 to 30 days. EFSA (2013) states that data from soil dissipation studies evaluated during the peer-review show that molinate DT90field soil post-flood varies between 90 and 115 days. The main soil metabolite is molinate sulfoxide (EC 2003).

The water solubility of molinate is about 1,000 mg/L and the sorption coefficient is 190 mL/g.

### Typical concentrations in drinking-water

Molinate has never been used in New Zealand.

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of molinate (limit of detection = 0.0001 mg/L) (ESR 2001).

In 1987–88, water from 1288 drinking-water wells in the Lombardy region of Italy was analysed for molinate; it was detected in 27 wells at levels above 0.001 mg/L and in 220 wells at levels between 0.0001 and 0.001 mg/L. In the Piedmont region, molinate was detected in 25 wells used as a source of drinking-water; in five of them, levels were above 0.001 mg/L.

One water utility reported detecting molinate (ordram) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.001 mg/L.

NPIC (1994) quotes for molinate a soil half-life of 21 days, water solubility of 970 mg/L and a sorption coefficient (soil Koc) of 190. This resulted in a pesticide movement to groundwater rating of moderate.

USGS (2006) give the following values: log Kow = 3.21; log Koc (where Koc is in mL/g) = 1.92; water solubility = 970 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -0.839; half-life in aerobic soil = 21 days; half-life in water = >200 days.

### Removal methods

WHO (2011/2017) states that a concentration as low as 0.001 mg/L should be achievable using GAC. NHMRC, NRMMC (2011) states that ozonation, granular activated carbon, preoxidation by chlorine and preoxidation by chlorine combined with activated carbon adsorption removes 100 percent of molinate during drinking water treatment.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector (EPA 507).

#### Some alternative methods

No alternative methods have been recommended for molinate because no methods meet the required criteria. See WHO (2003) for further information.

### Health considerations

Molinate is not absorbed percutaneously. In rats, it is metabolised primarily to the sulfoxide, then to mercapturic acid.

The oral RfD for molinate was calculated at 0.002 mg/kg/d (USEPA 1991).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw from a three-generation rat reproduction study. The NOEL is based on reduced litter numbers, litter size and pup survival at the next highest dose of 0.63 mg/kg bw/day. The ADI incorporates a safety factor of 100.

EC (2003) report kidney tumours (benign and malignant) in the rat. EC (2003) adopted an ADI of 0.008 mg/kg/d, and an ARfD of 0.1 mg/kg/d. Reaffirmed by EFSA (2013).

Molinate has not shown evidence of mutagenic activity in a range of bacterial assays.

Based on the limited data available, molinate does not seem to be carcinogenic to animals. Evidence suggests that impairment of the reproductive performance of the male rat is the most sensitive indicator of molinate exposure. However, a review of epidemiological data based on the examination of workers involved in molinate production does not indicate an effect on human fertility.

As at May 2002 the USEPA has classified molinate in Group C: a possible human carcinogen. However, as at September 2008 the USEPA considered there was suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.

### Derivation of Maximum Acceptable Value

A tolerable daily approach has been used for the derivation of the MAV for molinate in drinking-water. The no-observable-adverse-effect level used in the derivation is for reproductive toxicity in the rat.

The MAV for molinate in drinking-water was derived as follows:

0.2 mg/kg body weight/day x 70 kg x 0.1 = 0.007 mg/L (7 g/L)

2 L/day x 100

where:

* no observable adverse effect level = 0.2 mg/kg body weight per day for reproductive toxicity in the rat
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter and intra-species variation).

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# Monocrotophos

CAS No. 6923-22-4. The IUPAC name for monocrotophos is dimethyl (E)-1-methyl-2-(methylcarbamoyl)vinyl phosphate, or 3-dimethoxyphosphinoyloxy-N-methylisocrotonamide. The CAS name is dimethyl (1E)-1-methyl-3-(methylamino)-3-oxo-1-propenyl phosphate.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because monocrotophos has been withdrawn from use in many countries, it is unlikely to be found in drinking-water, the establishment of a guideline value is not deemed necessary.

### Sources to water

Monocrotophos (a mixture of isomers) is a broad spectrum, non-specific, systemic, fast-acting organophosphate insecticide and acaricide, used to control common mites, ticks and spiders. It is acutely [toxic](http://en.wikipedia.org/wiki/Toxic) to [birds](http://en.wikipedia.org/wiki/Birds) and bees and for that reason has been banned in the US and many other countries. While mainly applied against cotton pests, it was used on citrus, olives, rice, maize, sorghum, sugar cane, sugar beet, peanuts, potatoes, soya beans, vegetables, ornamentals and tobacco.

Monocrotophos does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. Monocrotophos appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

### Forms and fate in the environment

In the environment, monocrotophos is degraded mainly via hydrolysis and oxidation. The products of these degradation pathways are non-cholinesterase inhibiting and of low toxicity. Volatilisation appears to be the major factor in the rapid loss of residues following application.

Monocrotophos has a half-life of 14–21 days at pH 9 and 25°C, with the rate decreasing at lower pHs and increasing at higher temperatures. Degradation on soil exposed to natural sunlight is rapid (half-life less than seven days) and on dark control samples is slower (half-life approximately 30 days). Monocrotophos is mobile in soil, and although it degrades rapidly it may possess potential for groundwater contamination. It is extremely soluble in water, about 100 percent.

NPIC (1994) quotes for monocrotophos a soil half-life of 30 days, water solubility of 100 percent and a sorption coefficient (soil Koc) of 1. This resulted in a pesticide movement to groundwater rating of very high.

### Removal methods

Oxidative processes are the most likely to succeed; aeration may enhance the process.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See section 6 of ATSDR (1996).

### Health considerations

The most likely route of exposure to monocrotophos for the public is via residues in food. From the 1994 Australian Market Basket Survey, the estimated intake in the group with the highest consumption of monocrotophos residues (toddlers aged two), based on average energy intake, was 0.0000072 mg/kg bw/day. This makes up less than 3 percent of the ADI.

JMPR (1993) stated that in 1991 the ADI was changed to 0–0.00005 mg/kg bw, based on an NOAEL of 0.005 mg/kg bw/day in a two-year study in rats. In a new teratogenicity study in rats, no evidence of teratogenicity or embryo/fetotoxicity was observed at any doses tested (up to 2 mg/kg bw/day by gavage). Malformations of the brain were not observed. The NOAEL for maternal toxicity was 0.3 mg/kg bw/day. The 1993 Meeting allocated an ADI of 0–0.0006 mg/kg bw on the basis of the 30-day human volunteer study with an NOAEL of 0.006 mg/kg bw/day based on the absence of erythrocyte cholinesterase inhibition, using a 10-fold safety factor. JMPR (1994) confirms the ADI of 0.0006 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.0003 mg/kg body weight, with a NOEL of 0.0036 mg/kg bw, and the ARfD is 0.0006 mg/kg bw.

EXTOXNET (1996) quotes an ADI of 0.0006 mg/kg/d.

Carcinogenicity studies in mice and rats evaluated by the 1991 Joint Meeting were negative (JMPR 1993).

### Derivation of Maximum Acceptable Value

No MAV.

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# Myclobutanil

CAS No. 88671-89-0. The IUPAC name for myclobutanil is (RS)-2-(4-chlorophenyl)-2-(1H-1,2,4-triazol-1-ylmethyl)hexanenitrile. The CAS name is α-butyl-α-(4-chlorophenyl)-1H-1,2,4-triazole-1-propanenitrile. Sometimes called systhane in the US.

### Maximum Acceptable Value

Myclobutanil does not have a MAV in the DWSNZ; myclobutanil is not mentioned in the WHO Guidelines.

### Sources to water

Myclobutanil is a systemic conazole or triazole fungicide, often used on grapes, hops, strawberries, apples and pears. It is a steroid demethylation inhibitor, specifically inhibiting [ergosterol](http://en.wikipedia.org/wiki/Ergosterol) biosynthesis. Ergosterol is a critical component of fungal cell membranes.

Myclobutanil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life in soil, depending on soil-type and conditions, may be about two months; some sources quote >>1 year. Myclobutanil shares common metabolites with other triazole-derivative chemicals, including free triazole (1,2,4-triazole) and triazole-conjugated plant metabolites (such as triazole alanine and triazole acetic acid). These common metabolites have been the subject of separate risk assessments (USEPA 2006).

Because it is persistent and somewhat mobile, myclobutanil may be a potential threat to groundwater in vulnerable soils. Water solubility is about 140 mg/L.

NPIC (1994) quotes for myclobutanil a soil half-life of 66 days, water solubility of 142 mg/L and a sorption coefficient (soil Koc) of 500. This resulted in a pesticide movement to groundwater rating of moderate.

JMPR (2014) reports: Henry’s Law constant = 4.33 x 10–4 kPa m3/mol. The octanol-water partition coefficient at 22°C = log POW = 2.556. Water solubility is 11 to 13 percent from pH 4 to 9. At 25°C myclobutanil is hydrolytically stable more than one year at pH 4, 7 and 9. Aerobic soil degradation studies showed half-lifes to be from 61 to 71 days for degradation of parent compound, with some results exceeding 500 days. Myclobutanil did not photodegrade to any appreciable extent, even under the greater intensities of the shorter wavelengths.

### Typical concentrations in drinking-water

Available information indicates that there will be little, if any exposure to myclobutanil in drinking-water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Myclobutanil was only slightly toxic upon acute oral administration to rats and mice. WHO has classified myclobutanil as slightly hazardous (Class III).

The primary target organ upon repeated dietary exposure to myclobutanil was the liver. IPCS summarised various studies on mice, rats and dogs that found NOAELs in the range of 2.5 to 3.6 mg/kg/day, and derived an acceptable daily intake (ADI) of 0.03 mg/kg body weight. NZFS (2008) adopted the same value.

JMPR (1998) quotes an ADI of 0.03 mg/kg/d, confirmed in JMPR (2014). The 2014 Meeting established an ARfD of 0.3 mg/kg bw for women of childbearing age only; an ARfD was unnecessary for the general population.

USEPA (1995/1998) established a chronic RfD of 0.025 mg/kg/d, they did not recommend an acute dietary endpoint. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.60 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for myclobutanil is 19.8 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 2.6 mg/kg bw. EC (2010) adopted an ADI of 0.025 mg/kg/d, and an ARfD of 0.03 mg/kg/d. See datasheet for triazole metabolites for latest ADI and ARfD.

As at September 2008 the USEPA has classified myclobutanil in Group E: evidence of non-carcinogenicity for humans. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. After reviewing the available genotoxicity data, IPCS concluded that myclobutanil was not genotoxic. The other conazoles, triademefon and propiconazole, have been reported to cause liver tumours in mice.

USEPA (2015) found that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for myclobutanil since additional testing related to the estrogen, androgen or thyroid pathways is unlikely to impact the current EPA established regulatory endpoints for human risk assessments.

### Derivation of Maximum Acceptable Value

No MAV.

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# Naphthenates

Copper naphthenate CAS No. 1338-02-9. A New Zealand trade name is metalex. Tributyltin naphthenate (or TBTN) CAS No. 85409-17-2.

Some organotin compounds are also discussed in the Organic Chemicals section, and copper compounds in the Inorganic Chemicals section.

### Maximum Acceptable Value

Naphthenates are not mentioned in the WHO Guidelines and do not have a MAV in the DWSNZ.

### Sources to water

Naphthenates are the [salts](http://en.wikipedia.org/wiki/Salt_(chemistry)) of [naphthenic acids](http://en.wikipedia.org/wiki/Naphthenic_acid), which are an acidic fraction from [petroleum](http://en.wikipedia.org/wiki/Petroleum) processing, comprising a mixture of organic acids, especially cycloalkyl [based](http://en.wikipedia.org/wiki/Carboxylic_acid). The naphthenate portion is poorly characterised; its composition depends on the petroleum source. Typical crude petroleum contains 0.5 to 2 percent naphthenic acids by weight. Naphthenic acid may contain such constituents as cyclopentylacetic acid, alkyl-substituted cyclopentylacetic acids, fused chains of cyclopentylacetic acids, cyclohexylacetic acids, cyclopentanoic acids, and various low-molecular-weight fatty acids. It may also be contaminated up to 25 percent with hydrocarbons such as benzene from the petroleum source.

Naphthenic acids and their salts have industrial applications including synthetic [detergents](http://en.wikipedia.org/wiki/Detergent), [lubricants](http://en.wikipedia.org/wiki/Lubricant), corrosion inhibitors, fuel and lubricating oil additives, wood (above and below ground) preservations, [insecticides](http://en.wikipedia.org/wiki/Insecticide), [fungicides](http://en.wikipedia.org/wiki/Fungicide), [acaricides](http://en.wikipedia.org/wiki/Acaricide), [wetting agents](http://en.wikipedia.org/wiki/Wetting_agent), and [oil drying agents](http://en.wikipedia.org/wiki/Oil_drying_agent) used in painting and wood surface treatment.

Copper naphthenate has been used for >100 years overseas. Copper naphthenate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). The copper component is usually about 20 percent, although domestic products may be <5 percent.

Tributyltin naphthenate appears on ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Chemicals) Transfer Notice 2004 (As Amended), as at 22 May 2008. (See <http://www.archive.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It also appears in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …).

### Forms and fate in the environment

Treated wood leaches copper, tributyltin and naphthenates very slowly. Naphthenates have a very low water solubility. Naphthenate salts are likely to evaporate from water surfaces to a high degree and likely to contaminate surface water by way of soil run-off. Copper and zinc naphthenate are likely to persist in water and soils around the treated wood (USEPA 2007).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Because petroleum contains many acutely toxic, chronically toxic, and carcinogenic compounds such as benzene, it must be assumed that some of them are present in naphthenates. Despite that, little toxicological information exists. Some data is summarised in CEPA (2000). Some literature suggests that the copper or tributyltin component may be more toxic than the naphthenate fraction.

Rats fed a diet of 0.5 percent zinc naphthenate experienced a significant weight loss but no effect on mating or offspring viability over two generations (US Army 1988).

Copper naphthenate wood preservatives are not the subject of a USEPA special review under 40 CFR section 154.7, nor will they be in the future, because:

1. they do not pose a risk of serious acute injury to humans or domestic animals; and

2. they do not pose a significant risk of inducing oncogenic, heritable genetic, teratogenic, fetotoxic or reproductive effects in humans.

The NOAEL for the short- and intermediate-term (1–30 days) incidental oral endpoint is 30 mg/kg/day, based on a developmental toxicity study in the rat (copper naphthenate). The NOAEL is based on decreased body weight and food consumption (USEPA 2007).

Broadly similar toxicological effects were obtained for tributyltin naphthenate and tributyltin oxide (qv) following oral or intravenous administration in the rat (DEFRA 1994).

### Derivation of Maximum Acceptable Value

No MAV.

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# 1-Naphthylacetic acid

CAS No. 86-87-3. The IUPAC name is 1-naphthylacetic acid or naphthalen-1-yl acetic acid. The CAS name is 1-naphthaleneacetic acid. It has also been called α‑naphthaleneacetic acid, [2-naphthalen-1-ylacetic acid](http://www.chemindustry.com/chemicals/0208166.html), 2-(alpha-naphthyl) ethanoic acid, naphthylacetic acid, 2-(1-naphthyl)acetic acid and NAA. It can also be sold as salts and esters, eg, 2-(1-naphthyl) acetamide and naphthylacetic acid hydrazide. Sometimes collectively called naphthalene acetates.

Some information on 2-naphthyloxyacetic acid (2-NOA) has been included in this datasheet. CAS No. 120-23-0. Also called (2-naphthyloxy)acetic acid, 2-naphthoxyacetic acid or β-naphthyloxyacetic acid (BNOA).

Some information on 1-naphthylacetamide has been included in this datasheet. CAS No. 86-86-2. Also called 2-naphthalen-1-ylacetamide.

The USEPA collectively refers to ‘naphthalene acetates’. This includes 1-naphthylacetic acid and 1-naphthylacetamide (as above), plus sodium 1-naphthaleneacetate (CAS No. 61-31-4); ethyl 1-naphthaleneacetate (2122-70-5); potassium 1-naphthaleneacetate (15165-79-4); ammonium 1-naphthaleneacetate (25545-89-5).

### Maximum Acceptable Value

1-Naphthylacetic acid and 2-naphthyloxyacetic acid are not mentioned in the WHO Guidelines and do not have a MAV in the DWSNZ.

### Sources to water

1-Naphthylacetic acid is used as a plant growth regulator (a synthetic hormone in the auxin family), and is an ingredient in many commercial [plant rooting](http://en.wikipedia.org/wiki/Rooting) [horticultural](http://en.wikipedia.org/wiki/Horticultural) products. It is a rooting agent and used for the [vegetative propagation](http://en.wikipedia.org/wiki/Vegetative_propagation) of plants from stem and leaf cutting. It is also used to improve setting in fruit and to prevent pre-harvest drop. It may also used for [plant tissue culture](http://en.wikipedia.org/wiki/Plant_tissue_culture).

1-Naphthylacetic acid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). [But 1-naphthylacetamide is not.]

The related substances 2-naphthoxyacetic acid and 2-(1-naphthyl)acetamide appear on ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008. (See <http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides). The use of 2-NOA is no longer authorised within the EU.

1-Naphthylacetic acid is also classified as a polyaromatic hydrocarbon (PAH).

EFSA (2015) reports that 1-naphthylacetamide is applied as an outdoor foliar treatment on apple, pear and cherries and 1-naphthylacetic acid is applied as an indoor and outdoor foliar treatment to a variety of crops in northern and southern Europe as well as a seed treatment on potatoes in southern Europe. 1-Naphthylacetamide and 1‑napthylacetic acid are co-applied as an indoor and outdoor foliar treatment to a variety of crops and as a root treatment in grapes and artichoke prior to planting.

### Forms and fate in the environment

ERMA (accessed 2009) stated data regarding the biodegradation of 1‑naphthaleneacetic acid in soil were not available. 1-Naphthaleneacetic acid is not expected to undergo hydrolysis in soils, yet may undergo direct photolysis in sunlit surface soils. 1-Naphthoic and phthalic acids were identified as the photolysis products of 1-naphthaleneacetic acid in sunlight exposed aqueous solution. An estimated Koc range of 160 to 610 suggests that 1-naphthaleneacetic acid will have a medium to low mobility class in soil. An estimated Henrys Law constant of 1.17 x 10-9 atm-cu m/mole at 25°C, suggests the volatilisation of 1-naphthaleneacetic from moist soils will not be important.

EFSA (2011) stated that 1-naphthylacetic acid exhibited high to very high mobility in soil, and that volatilisation from plant surfaces and soil may be expected. The soil DT90 value of 1-naphthylacetic acid is about 15 days. 1-Naphthylacetic acid is the major metabolite of 1-naphthylacetamide in soil.

Water solubility of 1-naphthylacetic acid is about 400 mg/L. Water solubility of 2‑naphthyloxyacetic acid is about 200 mg/L, and 170 mg/L for 1-naphthylacetamide.

NPIC (1994) quotes for NAA ethyl ester a soil half-life of 10 days, water solubility of 105 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of low. NAA sodium salt has a soil half-life of 10 days, water solubility of 42 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

1-Naphthylacetic acid has been detected in groundwater contaminated with coal gas plant wastes (Ohlenbusch et al 2002).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

USEPA. 2007. stated that for the purpose of the human health risk assessment, all forms of the naphthalene acetates were combined (1-naphthaleneacetic acid (NAA), its salts, ester, and acetamide) because they are structurally related and are metabolised to the acid form and eliminated from the body as glycine and glucuronic acid conjugates within 48 hours after exposure. The naphthalene acetates show low acute toxicity, are not mutagenic, and are not expected to be carcinogenic. The USEPA has not identified any metabolites of toxicological concern. The chronic dietary assessment derived a PAD (population adjusted dose) of 0.15 mg/kg/d based on a NOAEL of 50 mg/kg/d from rat studies.

NZFSA (2008) established a maximum residue limit for 1-naphthylacetic acid of 0.01 mg/kg in mandarins, and quotes an acceptable daily intake (dietary ADI) of 0.15 mg/kg bw.

The Acceptable Daily Intake (ADI) for 1-naphthylacetic acid is 0.1 mg/kg bw/day (a Safety Factor (SF) of 150 was applied). The Acute Reference Dose (ARfD) is 0.1 mg/kg bw (SF of 150) (EFSA 2011 and 2015).

EFSA (2015) established the same toxicological reference values for 1‑naphthylacetamide.

1-Naphthylacetic acid does not appear in any of the common lists of carcinogenic substances.

The toxicological profile of 2-naphthyloxyacetic acid (2-NOA) was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.01 mg/kg bw per day and 0.6 mg/kg bw, respectively (EFSA 2013).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.15 mg/kg/d, and an ARfD of 0.50 mg/kg/d for naphthalene acetates. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for naphthalene acetates is 5.0 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

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# Neem oil

The CAS No. for neem oil is 8002-65-1. Neem extracts contain azadirachtin, a convenient collective term for the active ingredient that consists of a complex group of insecticidally active tetraterpene limonoid compounds; the CAS No. for azadirachtin A is 11141-17-6. Besides azadirachtin A, azadirachtin contains other compounds that also have biological activity.

22,23-Dihydroazadirachtin and its related metabolites are extracts of the seed kernels of the neem tree, Azadirachtin indica, are chemically similar to azadirachtin, the naturally-occurring neem plant extract, but differ by a single double bond, and are biologically equivalent to azadirachtin in its functionality when tested as a growth regulator against the Mexican bean beetle, Epilachna varivestis (USEPA 1996).

Besides azadirachtin A, azadirachtin contains other compounds that also have biological activity. It is concluded by EFSA (2011) that azadirachtin A is not a sufficient marker to identify the different materials. It should be emphasised that the manufacturing process has a strong influence on the composition of the technical concentrate and it is necessary to link the specification of the technical concentrates to their respective manufacturing processes.

### Maximum Acceptable Value

Neem oil products are not mentioned in the WHO Guidelines and do not have a MAV in the DWSNZ.

### Sources to water

Neem oil repels a wide variety of pests and is often used in organic farming. Azadirachtin is broad-spectrum insect growth regulator, used on plants and against animal ectoparasites for the control of insects in many orders.

Neem oil comprises mainly [triglycerides](http://en.wikipedia.org/wiki/Triglyceride) and large amounts of [triterpenoid](http://en.wikipedia.org/wiki/Triterpenoid) compounds. Neem oil also contains [steroids](http://en.wikipedia.org/wiki/Steroids) ([campesterol](http://en.wikipedia.org/wiki/Campesterol), [beta-sitosterol](http://en.wikipedia.org/wiki/Beta-sitosterol), [stigmasterol](http://en.wikipedia.org/wiki/Stigmasterol)) and many [triterpenoids](http://en.wikipedia.org/wiki/Triterpenoid) of which [azadirachtin](http://en.wikipedia.org/wiki/Azadirachtin) (the primary active pesticidal ingredient in neem oil) is the most well known and studied. The azadirachtin content of neem oil varies from 300 ppm to over 2,500 ppm depending on the extraction technology and quality of the neem seeds crushed.

USEPA (1995) states that the clarified hydrophobic extract is prepared from the crude botanical extract of the seed kernels of the neem tree, Azadiracta indica. The constituents of clarified hydrophobic extract of neem oil are long-chain fatty acids and glycerides. Long-chain fatty acids and glycerides are “generally recognised as safe” (GRAS) for use in foods by the US Food and Drug Administration (FDA). Under title 21 of the Code of Federal Regulations (CFR) (21 CFR 172.860), oleic acid derived from tall oil fatty acids (21 CFR 172.862), and linoleic acid (21 CFR 184.1065), glyceryl monooleate (21 CFR 184.1323), glyceryl monostearate (21 CFR 184.1324), and mono- and diglycerides (21 CFR 184.1505) are considered as GRAS.

Neem oil products, and azadirachtin, appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Neem products also appear in some soaps and body lotions.

In commercial azadirachtin the FAO limits the concentration of aflatoxins (sum of aflatoxins B1, B2, G1 and G2) to a maximum of 0.00003 percent (300 μg/kg) of the azadirachtin A.

### Forms and fate in the environment

Residual insecticidal activity of azadirachtin is evident for 7 to 10 days or longer, depending on insect and application rate. In most soil and aquatic environments, these constituents of clarified hydrophobic extract of neem oil would be readily metabolised by endemic microbial populations and should not accumulate. Azadirachtin breaks down rapidly (in 100 hours) in water or light, and will not cause long-term effects (EXTOXNET 1995).

The half-life of azadirachtin in soil ranges from 3–44 days. In water, the half-life ranges from 48 minutes to four days. The remaining components of neem oil are broken down by microbes in most soil and water environments (NPIC).

None of the degradation products identified show any major transformation on the polycyclic structure of azadirachtin and therefore all known degradation products may be presumed to retain, at least in part, the biological properties attributed to this family of compounds. Sufficient information is available on the rate of degradation of azadirachtin A in soil under aerobic conditions (six soils). Under these conditions azadirachtin A exhibits low to moderate persistence. Both azadirachtin A and B hydrolyse in water (likely to form the C3 hydroxyl derivative, azadirachtin H\*) at environmental pHs (pH 4–8). Hydrolysis is faster at more alkaline pHs (EFSA (2011/2018).

Water solubility of azadirachtin A is about 3,000 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Long-chain fatty acids and glycerides are readily synthesised by most forms of life and are common constituents of human, avian, and other mammalian diets. The USEPA knows of no reported cases of adverse effects from exposure to low amounts of fatty acids. The USEPA concluded that establishment of a tolerance for clarified hydrophobic extract of neem oil is not necessary to protect the public health.

The toxicology data provided are sufficient to demonstrate that there are no foreseeable human health hazards likely to arise from the use of dihydroazadirachtin (USEPA 1996).

Neem oil and other neem products such as neem leaves and neem tea should not be consumed by pregnant women, women trying to conceive, or children.

The following reference values for the azadirachtin extracts have been finalised as part of the EU re-evaluation:

ADI 0.1 mg/kg bw/day; ARfD 0.75 mg/kg bw.

EFSA (2011) states that the acceptable daily intake (ADI) of azadirachtin extracts is 0.1 mg/kg bw/day, based on the 90-day study in rat, applying a safety factor of 300 and an additional safety factor of 3 due to the missing toxicological information on long-term, carcinogenicity and rabbit developmental study. The acute reference dose (ARfD) is 0.75 mg/kg bw based on the developmental study in rat with a maternal NOAEL of 225 mg/kg bw/day, and applying a safety factor of 300 due to the missing rabbit developmental study. The reference values are expressed in terms of whole extract and not in terms of the azadirachtin A compound. These values were reaffirmed by EFSA (2018).

### Derivation of Maximum Acceptable Value

No MAV.

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# Nicarbazin

Nicarbazin is an equimolar complex of two compounds, 4,4’-dinitrocarbanilide or 1,3‑N,N’-bis(4-nitrophenyl)urea (DNC), plus 4,6-dimethyl-2-pyrimidinol or 4,6‑dimethyl-2(1 H)-pyrimidone (HDP). DNC is considered to be the active component, while HDP aids in absorption.

Nicarbazin: CAS No. 330-95-0, made up of 1,3-bis(4-nitrophenyl)urea: CAS No. 587‑90‑6 and 4,6-dimethyl-2-pyrimidinol: CAS No. 108-79-2.

### Maximum Acceptable Value

Nicarbazin is not mentioned in the WHO Guidelines and does not have a MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 1 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Nicarbazin interferes with the formation of the vitelline membrane, separating the egg yolk and egg white, so is used to control unwanted bird populations, for example at airports. Also, nicarbazin is a non-ionophoric parasiticide that is used as a coccidiostat feed additive for the prevention of faecal and intestinal coccidiosis in broiler chickens; it has US Food and Drug Administration (FDA) approval since 1955. When nicarbazin levels over 1 mg/kg are found in chicken liver in the UK they are followed up on-farm by the Animal Medicines Inspectorate and/or Animal Health. The Animal Medicines Inspectorate may also visit the feed mill if necessary (<http://www.thepoultrysite.com/articles/1057/reducing-nicarbazin-levels-in-british-chicken>).

Nicarbazin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Monimax® is considered a safe feed additive for turkeys for fattening at the highest use level of 50 mg monensin sodium and 50 mg nicarbazin/kg complete feed. Nicarbazin impurities p-nitroaniline and methyl(4-nitrophenyl) carbamate do not pose safety concerns when used to fattening animals. Monensin has a selective antimicrobial activity against Gram-positive bacterial species while many Enterobacteriaceae are naturally resistant. Induction of cross-resistance with clinically relevant antimicrobials or increased shedding of enteropathogenic bacteria are not reported. Nicarbazin has no antimicrobial activity (EFSA 2017).

### Forms and fate in the environment

Nicarbazin is inherently stable under extreme conditions. Half-lifes in silt loams have been reported from 85 to 301 days. DNC is reported to be virtually immobile (New York State 2007).

The use of monensin sodium from Monimax® in complete feed for turkeys and chickens for fattening does not pose a risk for the aquatic compartment and sediment, while a risk cannot be excluded for the terrestrial compartment. A final conclusion on the risk resulting from the use of nicarbazin from Monimax® cannot be made because (i) DNC refined predicted environmental concentrations (PECs) show uncertainties linked to the very high persistence of the compound (ii) DNC might accumulate in the sediment compartment and (iii) DNC can potentially bioaccumulate and may cause secondary poisoning. No concerns would arise for the HDP moiety of nicarbazin excreted from chickens fed Monimax® (EFSA 2017).

The water solubility of DNC is about 45 to 50 mg/L, and 20,000 mg/L for HDP (pH 5 to 9).

### Removal methods

Some newer advanced oxidation processes may be effective in breaking down nicarbazin.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

No suitable analytical techniques have been identified, but the use of high performance liquid chromatography–tandem mass spectrometry is expected to be suitable for residue levels of this pesticide in water. This technique has previously been used for the analysis of nicarbazin in poultry products (NHMRC, NRMMC 2011).

### Health considerations

Ingested nicarbazin rapidly splits into its two components, 2-hydroxy-4,6-dimethylpyrimidine (HDP) and 4,4’-dinitrocarbanilide (DNC), which behave independently with respect to their pharmacokinetics and metabolism. DNC from nicarbazin is considerably more available for the animal than DNC given alone or administered simultaneously with HDP in similar proportions as in nicarbazin. DNC appears as the marker residue, and liver is the target tissue. DNC residues decline rapidly from tissues following nicarbazin withdrawal. HDP-related residues are much lower than those derived from DNC. Food is expected to be the predominant route for ingestion.

p-Nitroaniline, a nicarbazin associated impurity, is a suspected carcinogen. Considering the p-nitroaniline disposition data in rats and its maximum recommended level in nicarbazin, an exposure of the consumer to p-nitroaniline resulting from the consumption of tissues from chickens for fattening fed diets supplemented with Koffogran at the maximum proposed level would be negligibly low.

WHO studies indicate that non-target mammals (including humans) would have to consume prohibitively large amounts of the product to produce any toxic effects. On a chronic basis, using the results of a two-year chronic study in rats (NOEL = 400 mg/kg bw/day, based on HDT no treatment related toxicity), the no-effect quantities of bait on a daily consumption basis are 2.4 kg and 1.6 kg for the rest of their lives. Again, the consumption of bait on a daily basis is not realistic and consumption values are not physically possible.

WHO established an ADI of 0.4 mg/kg/d based on the NOEL of 200 mg/kg/d from the rat developmental toxicity study and an uncertainty factor of 500 (quoted from New York State 2007).

The JPMR Committee established an ADI of 0–0.4 mg/kg bw on the basis of the NOEL of 200 mg/kg bw per day in the study of developmental toxicity in rats and using a safety factor of 500, chosen to account for the limitations in the database (INCHEM 1998).

The Acceptable Daily Intake (ADI) adopted in Australia for nicarbazin is 0.4 mg/kg body weight, with a NOEL of 200 mg/kg from a two-year rat dietary study. The ADI incorporated a safety factor of 100. The current acute reference dose (ARfD) is 0.4 mg/kg bw, based on a NOEL of 200 mg/kg bw/day in a rat developmental study with a safety factor of 500.

The lowest no observed effect level (NOEL) identified for monensin sodium in a developmental study in rabbits was 0.3 mg monensin sodium/kg body weight (bw) per day for maternal toxicity in rabbits. The lowest no observed adverse effect level (NOAEL) identified in a 52-week study in rat using DNC + HDP was 20 mg DNC + 8 mg HDP/kg bw per day. No significant interaction between monensin sodium and nicarbazin is expected from toxicological studies (EFSA 2017).

Based on long-term studies in rats, there is no evidence of carcinogenicity for nicarbazin. Nicarbazin was weakly positive in in vitro bacterial studies, but in vivo studies were negative. There is insufficient information to determine its genotoxic potential (NHMRC, NRMMC 2011).

### Derivation of Maximum Acceptable Value

No MAV.

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# Niclosamide

CAS No. 50-65-7. The IUPAC name for niclosamide is 2′,5-dichloro-4′-nitrosalicylanilide. The CAS name is 5-chloro-N-(2-chloro-4-nitrophenyl)-2-hydroxybenzamide. The name “clonitralid” is used for the ethanolamine salt. Niclosamide monohydrate has the CAS No. 7336-56-2.

When this substance is used as an ester or a salt, its identity should be stated, for example [niclosamide-olamine](http://www.alanwood.net/pesticides/derivatives/niclosamide-olamine.html) or [niclosamide-ethanolamine](http://www.alanwood.net/pesticides/derivatives/niclosamide-olamine.html) (CAS No. 1420-04-8). It may also appear as the piperazine salt (CAS No. 34892-17-6), or as niclosamide monohydrate (CAS No. 7336-56-2).

### Maximum Acceptable Value

Niclosamide is not mentioned in the WHO Guidelines and does not have a MAV in the DWSNZ.

### Sources to water

Niclosamide, a chloronitrophenol derivative, is classified as a molluscicide. It is also used as an piscicide, anthelmintic and lampricide. Niclosamide is a relatively selective, non-cumulative pesticide, principally used against aquatic snails at a dose of 0.6 to 1.0 mg/L, particularly in tropical areas for control of schistosomiasis and fascioliasis, but also as an antiparasitic and antihelminthic drug in human and veterinary medicine. It has been used overseas as a piscicide; the LC50 for many fish is well below 1 mg/L.

In the US, water cannot be abstracted for drinking purposes while it is being treated with niclosamide (USEPA 1999).

Niclosamide appears as an endoparasiticide on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Niclosamide is quickly metabolised in water and does not exhibit a long-term effect. After an application of 1.1 kg/ha to a 0.06-ha pond, niclosamide was detected in the water at a concentration of 0.2–0.4 mg/L after 1 hour, and 0.2 mg/L after 25 hours. In the pond sediment, niclosamide was transiently detected seven hours after treatment, but not 18 hours or 25 hours after treatment (ie, <0.3 mg/L) (DoC 2008).

Niclosamide did not degrade either in buffered solutions adjusted to pH 5.0, 6.9, or 8.7; or in pond water (pH 7.0–7.8) when incubated in the dark for up to 56 days (WHO 2002); it is subject to photolysis by long wavelength ultraviolet light.

In addition to dilution and dispersion, sorption to sediments and suspended particulates and possibly photodegradation (in clear shallow waters), are the major routes of dissipation of niclosamide. Neither hydrolysis nor volatilisation from soil or water surfaces should be major fate processes for this compound (USEPA 1999).

Water solubility of niclosamide and [niclosamide-olamine](http://www.alanwood.net/pesticides/derivatives/niclosamide-olamine.html) is 0.005 mg/L at pH 4, 0.2 mg/L at pH 7 and 40 mg/L at pH 9 (WHO 2002).

### Removal methods

Any niclosamide attached to sediments should be removed by treatment processes that remove particulate matter.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See WHO (2002).

### Health considerations

Clearly niclosamide has limited adverse health effects: in humans over the age of eight, two oral doses of 1 gram each, one hour apart for five successive days are usually effective against dwarf tapeworm, and 500 mg for younger children. In veterinary medicine single doses ranging from 83 to 500 mg/kg are recommended. However, niclosamide is very toxic to many aquatic species (WHO 1988).

Summary study results provided indicated no evidence for carcinogenicity, embryo toxicity or teratogenicity (WHO 2002).

APVMA adopted an ADI of 0.1 mg/kg/d for Australia (<https://apvma.gov.au/>). In September 2016 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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USEPA. 1999. *Pesticide Registration: Niclosamide*. EPA-738-F99-013 [9 pp]. <http://www.epa.gov/oppsrrd1/REDs/factsheets/2455fact.pdf>

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WHO. 2002. Niclosamide. *WHO Specifications and Evaluations for Public Health Pesticides* [24 pp]. <http://www.who.int/whopes/quality/en/Niclosamide.pdf>

# Nicosulfuron

CAS No. 111991-09-4. The IUPAC name for nicosulfuron is 2-[(4,6-dimethoxypyrimidin-2-ylcarbamoyl)sulfamoyl]-N,N-dimethylnicotinamide or 1-(4,6-dimethoxypyrimidin-2-yl)-3-(3-dimethylcarbamoyl-2-pyridylsulfonyl)urea. The CAS name is 2-[[[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]amino]sulfonyl]-N,N-dimethyl-3-pyridinecarboxamide.

### Maximum Acceptable Value

Nicosulfuron is not mentioned in the WHO Guidelines and does not have a MAV in the DWSNZ.

### Sources to water

Nicosulfuron is a member of the sulfonylurea family of herbicides, with a toxicity classification in the US of IV (relatively non-toxic). It controls weeds (commonly in maize) systemically by inhibiting the plant enzyme acetolactate synthase.

Nicosulfuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Biodegradation is an important degradation mechanism for nicosulfuron. The half-life in a silt clay soil is 26 days. However, anaerobic conditions slow down the degradation process. The half-life of nicosulfuron in silt clay soil/water is 63 days. The main degradates are pyridine sulfonamide and pyrimidine amine. Nicosulfuron is very mobile in sandy loam and silt loam soils, so is likely to be found in groundwater. The pyridine sulfonamide degradate is more mobile than the parent compound. The pyrimidine amine degradate is the least mobile.

In 1998, 210 water samples were collected during post-application run-off events at 75 surface-water and 25 groundwater sites in the US Midwest (USGS 2004) to gain an understanding of the occurrence of 16 sulfonylurea, sulfonamide, and imidazolinone herbicides, being the newer products for which data is relatively sparse. Imazethapyr was detected most frequently (69 percent of samples) followed by flumetsulam (62 percent) and nicosulfuron (51 percent).

The formulated product has a photolysis half-life at 25°C of 200–250 days at a pH of 7. It is stable to hydrolysis at pH 7 and 9, but hydrolyses with a half-life of 15 days at pH 5. Photolysis of nicosulfuron is quite slow. Water solubility is very dependent upon pH (410; 7,100; and 46,000 mg/L at 25°C at pH 5, 7 and 9 respectively). Effects of nicosulfuron on some freshwater algae were reported by Leboulanger et al (2001).

NPIC (1994) quotes for nicosulfuron a soil half-life of 21 days, water solubility of 2.2 percent and a sorption coefficient (soil Koc) of 30. This resulted in a pesticide movement to groundwater rating of high.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

JMPR (2006) states that nicosulfuron has not been evaluated by the FAO, JMPR or WHO/IPCS.

The acute oral LD50 for technical nicosulfuron was reported to be >5,000 mg/kg body weight. A 90-day subchronic toxicity study reported no effects up to 20,000 ppm for rats and dogs and 300 ppm for mice. In 28-day feeding trials to mice and rats, no adverse effects were noted up to 30 gm/kg.

The chronic aggregate exposure (food + water) for nicosulfuron dietary exposure and risk is below the USEPA’s level of concern. For the chronic dietary risk assessment, a chronic dog feeding study with a No Observable Adverse Effect Level (NOAEL) of 125 mg/kg/day and a Lowest Observed Adverse Effect Dose (LOAEL) of 500 mg/kg/day were used. All population subgroups’ Chronic Population Adjusted Dose are less than 1 percent which is below the Agency’s Level of Concern. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 1.25 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for nicosulfuron is 8.75 mg/L (no acute one-day value available.)

The EC (2008) adopted an ADI of 2 mg/kg bw/day; based on its low toxicity, an ARfD was considered unnecessary (reaffirmed by EFSA 2012). With particular regard to residues, the review established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is <1 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems.

As at September 2008 the USEPA has classified nicosulfuron in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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USEPA. 2004. *Report of the Food Quality Protection Act (FQPA) Tolerance Reassessment Progress and Risk Management Decision (TRED) for Nicosulfuron* [6 pp]. See <http://www.epa.gov/pesticides/reregistration/status.htm>

USGS. 2004. *Sulfonylurea, Sulfonamide, Imidazolinone, and Other Pesticides*. <http://co.water.usgs.gov/midconherb/html/sulfonylurea.html>

# Nitenpyram

CAS No. 150824-47-8. The IUPAC name for nitenpyram is (E)-N-(6-chloro-3-pyridylmethyl)-N-ethyl-N′-methyl-2-nitrovinylidenediamine. The CAS name is (1E)‑N‑[(6-chloro-3-pyridinyl)methyl]-N-ethyl-N′-methyl-2-nitro-1,1-ethenediamine.

### Maximum Acceptable Value

Nitenpyram is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Nitenpyram is a [nitromethylene neonicotinoid](http://www.alanwood.net/pesticides/class_insecticides.html#nitromethylene_neonicotinoid_insecticides) or [pyridylmethylamine neonicotinoid insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#pyridylmethylamine_neonicotinoid_insecticides). In veterinary medicine, it is used orally with [dogs](http://en.wikipedia.org/wiki/Dogs) and [cats](http://en.wikipedia.org/wiki/Cats) to control fleas, often under the trade name Capstar. Nitenpyram interferes with normal nerve transmission and leads to the death of the insect. Nitenpyram does not inhibit acetylcholinesterase.

Nitenpyram appears as an ectoparasiticide on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2013 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register).

### Forms and fate in the environment

Nitenpyram has been used as a replacement for endosulfan. Although it is highly toxic to bees, it has not attracted much of the negative attention of the other neonicotinoids.

Water solubility of norflurazon is very high, about 80 percent. Its aerobic soil half-life is about eight days. It is stable in water from pH 3 to 7, with a half-life of around three days at pH 9.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Nitenpyram is administered orally at a dose of about 1 mg/kg and is rapidly and to over 90 percent absorbed from the gastrointestinal tract of cats and dogs. More than 90 percent is eliminated in the urine within one day in dogs and two days in cats, mainly as the unchanged molecule.

Nitenpyram can be used during pregnancy and lactation. Studies in laboratory animals (rats and rabbits) have produced no evidence of teratogenic or feototoxic effects and the safety of the product was demonstrated in pregnant and lactating cats and dogs.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Novartis. CAPSTAR™ (nitenpyram) tablets. NADA 141–75. *Freedom of Information Summary* [30 pp]. http://www.fda.gov/downloads/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/FOIADrugSummaries/ucm117258.pdf

# Norbormide

CAS No. 991-42-4. The IUPAC name for norbormide is 5-(α-hydroxy-α-2-pyridylbenzyl)-7-(α-2-pyridylbenzylidene)-8,9,10-trinorborn-5-ene-2,3-dicarboximide, or 5-(α-hydroxy-α-2-pyridylbenzyl)-7-(α-2-pyridylbenzylidene)bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide. The CAS name is 3a,4,7,7a-tetrahydro-5-(hydroxyphenyl-2-pyridinylmethyl)-8-(phenyl-2-pyridinylmethylene)-4,7-methano-1H-isoindole-1,3(2H)-dione. Sometimes called NRB.

There are eight possible stereoisomers of norbormide. Only the endo isomers are toxic in rats and the threo isomers are 10 times as potent as the erythro isomers.

### Maximum Acceptable Value

Norbormide is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Norbormide is an unclassified rodenticide. Norbormide is a selective rat toxicant, being specifically toxic to Norway rats. Ship rats are less susceptible, and mice and all other species are resistant to this toxin. It was developed in the 1960s, but its use was discontinued in the 1970s as anticoagulant toxins became more popular. Taste aversion limited its effectiveness and field efficacy results were poor. Landcare Research New Zealand has been investigating ways of overcoming taste aversion to norbormide and the development of analogues (DoC 2009).

Norbormide does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2016 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register).

At the current rate of development it is expected new forms of norbormide could be registered and available for field use within the next five years and registration dossiers are being prepared in New Zealand. Because of the uniqueness of norbormide, based on an understanding of unique rodent specific receptors greater interest has been stimulated in genome screening for pest-specific toxin receptor targets which could result in new toxins for other species in the future (Cawthron Institute 2015).

### Forms and fate in the environment

Water solubility of norbormide is about 60 mg/L. Octanol-water partition coefficient at pH 7, 20oC = 3.2.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Moderately to highly toxic to humans; toxic to humans only in huge suicidal doses.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Cawthron Institute. 2015. *Trends in Vertebrate Pesticide Use and the Importance of a Research Pipeline for Mammalian Pest Control in New Zealand*. Prepared for Envirolink, MBIE on behalf of Northland Regional Council. Cawthron Report No. 2754 [49 pp]. <http://www.cawthron.org.nz/media_new/publications/pdf/2016_05/CawRpt_2754.pdf>

DoC. 2009. A re-evaluation of potential rodenticides for aerial control of rodents. *DoC Research & Development Series* 312. Eason CT, Ogilvie S. [34 pp]. <http://www.doc.govt.nz/documents/science-and-technical/drds312entire.pdf>

# Norflurazon

CAS No. 27314-13-2. The IUPAC name for norflurazon is 4-chloro-5-methylamino-2-(α,α,α-trifluoro-m-tolyl)pyridazin-3(2H)-one. The CAS name is 4-chloro-5-(methylamino)-2-[3-(trifluoromethyl)phenyl]-3(2H)-pyridazinone.

A similar herbicide, metflurazon, CAS No. 23576-23-0, has the IUPAC name of 4‑chloro-5-dimethylamino-2-(α,α,α-trifluoro-m-tolyl)pyridazin-3(2H)-one; and CAS 4‑chloro-5-(dimethylamino)-2-[(3-trifluoromethyl)phenyl]-3(2H)-pyridazinone.

### Maximum Acceptable Value

Norflurazon is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.05 mg/L for norflurazon; excursions above this level over a short to medium term are of concern as the health-based guideline is based on effects observed in a three-month study.

### Sources to water

Norflurazon, a fluorinated pyridazinone pre-emergence herbicide which inhibits carotenoid synthesis, has been used on a range of crops, and in non-crop areas.

Norflurazon does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). Despite that, ERMA’s Summary of Approvals of Substances transferred under the Hazardous Substances (Pesticides) Transfer Notice 2004 (As Amended), as at 22 May 2008 lists “water dispersible granule containing 400 g/kg diuron and 400 g/kg norflurazon”.

It is also listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals).

Maize has been reported (Strang and Rogers 1974) to degrade metflurazon rapidly (by demethylation) to norflurazon, but metflurazon is not on the ACVM or ERMA lists.

### Forms and fate in the environment

In general, norflurazon may be described as a persistent and mobile compound, so is likely to reach groundwater. Substantial fractions of applied norflurazon could be available for run-off for several months post-application.

Water solubility of norflurazon is about 34 mg/L. Its aerobic soil half-life is up to about 172 days, anaerobic about 348 days. Two breakdown products have been recorded: demethylnorflurazon (CAS No. 112748-69-3) and (more predominantly) desmethylnorflurazon (CAS No. 23576-24-1); these are persistent too.

NPIC (1994) quotes for norflurazon a soil half-life of 30 days, water solubility of 28 mg/L and a sorption coefficient (soil Koc) of 700. This resulted in a pesticide movement to groundwater rating of low.

USGS (2006) give the following values: log Kow = 2.45; log Koc (where Koc is in mL/g) = 2.55; water solubility = 34 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -4.46; half-life in aerobic soil = 130 days; half-life in water = >200 days.

### Typical concentrations in drinking-water

Groundwater detections of norflurazon have been reported frequently in the US, mostly less than 0.03 mg/L (the Health Advisory Limit developed by the USEPA Office of Prevention, Pesticides and Toxic Substances).

Norflurazon was found in one bore water during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.000096 mg/L. The bore was in the Wellington region.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Norflurazon was detected in one well at a concentration of 0.04 µg/L, ie, 0.00004 mg/L.

### Removal methods

The reasonably high solubility suggests that treatment processes that remove particulate matter should be ineffective at reducing the concentration of norflurazon in water. Some newer advanced oxidation processes or activated carbon may be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Food is expected to be the main route for ingestion.

The USEPA (in 1995) developed a RfD for norflurazon of 0.015 mg/kg/d, from a NOAEL of 1.5 mg/kg/d based a six-month dog feeding study. The oral RfD had earlier been 0.04 mg/kg/d (USEPA 1991). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.015 mg/kg/d, and an ARfD of 0.10 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for norflurazon is 3.30 mg/L.

The USEPA classified norflurazon as a non-quantifiable Group C – possible human carcinogen – based upon statistically significant pair-wise comparisons of the incidence of liver adenomas and combined liver adenomas/carcinomas as well as statistically positive trends for these lesions in male CD-1 mice receiving 218.8 mg/kg/day norflurazon technical in the diet for up to 104 weeks.

The Acceptable Daily Intake (ADI) adopted in Australia for norflurazon is 0.02 mg/kg body weight, with a NOEL of 1.5 mg/kg from a medium-term dietary study in dogs. The NOEL is based on increased liver weights. The ADI incorporates a safety factor of 100.

Although norflurazon is deemed to have very low acute toxicity, some products may contain nitrosamines. Norflurazon is not considered to be mutagenic. Norflurazon is not considered to be genotoxic, based on in vitro and in vivo short-term studies.

USEPA (2015) found that based on weight of evidence considerations, there was no convincing evidence of potential interaction with norflurazon and the estrogen or androgen pathways. While thyroid related effects were observed in mammals, the effects are likely due to perturbation of liver function. The developmental effects observed in the AMA do not appear to be thyroid-related.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Close ME, Skinner A. 2012. Sixth national survey of pesticides in groundwater in New Zealand. *New Zealand Journal of Marine and Freshwater Research*. iFirst: 1–15.

Gaw S, Close ME, Flintoff MJ. 2008. Fifth national survey of pesticides in groundwater in New Zealand. *New Zealand Journal of Marine and Freshwater Research* 42: 397–407.

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USEPA. 2015. *Endocrine Disruptor Screening Program Tier 1 Assessments*. <http://www.epa.gov/ingredients-used-pesticide-products/endocrine-disruptor-screening-program-tier-1-assessments>

USGS. 2006 (revised February 2007). Pesticides in the nation’s streams and ground water, 1992–2001. *USGS Circular* 1291. <http://pubs.usgs.gov/circ/2005/1291/>

# Novaluron

CAS No. 116714-46-6. The IUPAC name for novaluron is (RS)-1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]-3-(2,6-difluorobenzoyl)urea. The CAS name is N-[[[3-chloro-4-[1,1,2-trifluoro-2-(trifluoromethoxy)ethoxy]phenyl]amino]carbonyl]-2,6-difluorobenzamide. It is a racemate of two enantiomers.

### Maximum Acceptable Value

The WHO Guidelines 3rd addendum (2008) and the 2017 edition state that a guideline value is not considered appropriate for pesticides used for vector control in drinking-water.

WHO has assessed novaluron for use as a mosquito larvicide in drinking-water in containers, particularly to control dengue fever. WHO (2011) recommends a maximum dosage for drinking-water of 0.05 mg/L.

### Sources to water

Novaluron, a benzoylphenylurea chitin synthesis inhibitor, has been registered as an insecticide for food crops and ornamentals in a number of countries. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

WHO has assessed novaluron for use as a mosquito larvicide in drinking-water in containers, particularly to control dengue fever. Formulations for use as a vector control agent in drinking-water sources are specified by WHO.

### Forms and fate in the environment

The half-life of novaluron in three kinds of soil was reported to be 5–20 days at 20°C after an application of 0.13 mg/kg. The primary degradation product was 1-[3-chloro-4-(1,1,2-trifluoro-2-trifluoromethoxyethoxy)phenyl]urea, and the half-life for this compound was 46–64 days at 20°C. Water solubility is about 0.003 to 0.05 mg/L. The octanol / water partition coefficient is log POW = 4.3 at 20–25°C, pH 7.1.

### Typical concentrations in drinking-water

There are no data on exposure to novaluron in drinking-water, but its high soil adsorption coefficient (Koc) and low solubility suggest that it will not be mobile in the environment and is unlikely to be found frequently in treated drinking-water.

However, where novaluron is used in drinking-water containers, there is a significant probability of some exposure. The high log octanol–water partition coefficient of 4.3 indicates that novaluron is likely to adsorb to the sides of containers, and so the actual concentration is likely to be less than the recommended dose for vector control.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

WHO (2008) states that novaluron can be determined by high-performance liquid chromatography with ultraviolet detector (detection limit 0.02 mg/L).

### Health considerations

Novaluron technical grade is of very low acute toxicity.

JMPR concluded that the existing database on novaluron was adequate to characterise the potential hazards to fetuses, infants and children and established an ADI of  
0–0.01 mg/kg of body weight on the basis of the NOAEL of 1.1 mg/kg of body weight per day for erythrocyte damage and secondary splenic and liver changes in a two-year dietary study in rats, and a safety factor of 100.

At the maximum recommended dosage for drinking-water of 0.05 mg/l, the intake of a 60 kg adult drinking two litres of water would represent only 17 percent of the upper limit of the ADI. Similarly, the intake for a 10 kg child drinking one litre of water would be 50 percent of the upper limit of the ADI, whereas a 5 kg bottle-fed infant drinking 0.75 litre of water would receive an intake of 75 percent of the upper limit of the ADI. The high log octanol–water partition coefficient of 4.3 indicates that novaluron is likely to adsorb to the sides of containers, and so the actual concentration is likely to be less than the recommended dose. Exposure to novaluron through food is not expected to be significant (WHO 2017).

USEPA (2001) derived a NOAEL of 8.3 mg/kg/d based on a subchronic rat oral study which noted histopathological parameters in the spleen. USEPA (2004) quotes a chronic RfD of 0.011 mg/kg/d based on a NOAEL of 1.1 mg/kg/d and an uncertainty factor of 100 following a combined chronic toxicity/carcinogenicity feeding in rat. An acute RfD was not necessary. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.011 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for novaluron is 0.077 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1.1 mg/kg bw. An ARfD was considered unnecessary.

JMPR also concluded (in 2005) that it was not necessary to establish an acute RfD for novaluron in view of its low acute toxicity, the absence of relevant developmental toxicity in rats and rabbits that could have occurred as a consequence of acute exposure and the absence of any other toxicological effect that would be elicited by a single dose. In view of the absence of a carcinogenic potential in rodents and the lack of genotoxic potential in vitro and in vivo, JMPR concluded that novaluron is unlikely to pose a carcinogenic risk to humans. JMPR also concluded that novaluron is not a developmental toxicant.

Novaluron gave negative results in an adequate battery of studies of genotoxicity in vitro and in vivo. In view of the absence of a carcinogenic potential in rodents and the lack of genotoxic potential in vitro and in vivo, it is concluded that novaluron is unlikely to pose a carcinogenic risk to humans. As at September 2008, the USEPA has classified novaluron as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

Novaluron is used as a larvicide for control of disease-carrying mosquitoes that breed in drinking-water containers at a dosage not exceeding 0.05 mg/L.

It is not appropriate to set a formal guideline value for novaluron as a vector control agent in drinking-water. JMPR established an ADI of 0–0.01 mg/kg of body weight for novaluron in 2005. At the recommended dose for drinking-water of 0.05 mg/L, the intake of a 60-kg adult drinking two litres of water would represent an intake of only 17 percent of the ADI. Similarly, the intake for a 10-kg child drinking 1 litre of water would be 50 percent of the ADI, whereas a 5-kg bottle-fed infant drinking 0.75 litre of water would receive an intake of 75 percent of the ADI.

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# Octhilinone

CAS No. 26530-20-1. The IUPAC name for octhilinone is 2-octyl-1,2-thiazol-3(2H)-one or 2-octylisothiazol-3(2H)-one. The CAS name is 2-octyl-3(2H)-isothiazolone. Octhilinone has trade names of Tanalith Antimould and Hiyield Plus. Sometimes referred to as OIT. See also the datasheet for 4,5-dichloro-2-octyl-3(2H)-isothiazolone.

### Maximum Acceptable Value

Octhilinone is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for octhilinone in water (set by an approval under Part 5 of the HSNO Act) of 0.00009 mg/L (0.09 µg/L).

### Sources to water

Octhilinone is a thiazole fungicide and bactericide, possibly acting as a DNA/RNA synthesis inhibitor. Tebuconazole (qv) and octhilinone are formulated in New Zealand as a fungicide paint for the treatment of European canker on pipfruit (apples and pears), silverleaf in pipfruit and summerfruit, Eutypa dieback in grapes and as a wound protectant in pipfruit, summerfruit, grapes, kiwifruit and ornamentals.

The primary use sites (in the US) for octhilinone are as a materials preservative, as an industrial mildewcide for cooling tower and air washer water systems, and as a wood preservative. Some examples of materials that can contain octhilinone include fabrics and textiles (eg, furniture, auto-upholstery, footwear, carpet, carpet-backing, tents, awnings, canvas, linens, wall and window coverings, dust towels, bedding, mattresses, pet bedding, poll liners, automotive trim, roof liners, marine upholstery, pond liners, synthetic brooms, mops, air filter media); coatings (eg, walls, paints, plasters, stuccos); sealants (eg, grouts, caulks, joint cements); adhesives (eg, wallpaper pastes, gelatin and starch based); rubber and plastics (eg, latex, acrylic, styrene, butadiene, polyvinylchloride, polymethane, vinyl, foams); leather preservation (eg, wet processes). Octhilinone is also used for metalworking fluid preservation, hydraulic fluid preservation, and industrial process and water systems including air washer water and flow-thru cooling towers. As a wood preservative, octhilinone is used as an antisapstain drench to debarked logs (USEPA 2007).

Octhilinone does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm). However, it is listed in Table 3 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides).

After 1 July 2017 antifouling paints containing octhilinone will no longer able to be manufactured in or imported into New Zealand. See EPA (2013).

### Forms and fate in the environment

OIT is stable and persistent in water under abiotic conditions with a half-life of greater than 30 days. OIT does not migrate much and the chemical binds strongly with soil. Therefore, OIT is expected to remain on surface soils, which may result in contamination of surface water via erosion. OIT’s degradation pathway appears to be through microbial biodegradation in surface soils under aerobic and anaerobic conditions within 120 days (USEPA 2007).

Water solubility is about 500 mg/L. This solubility means there is a high potential for leaching to groundwater. The Octanol/water partition coefficient: Log Kow = 3.42.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of octhilinone.

### Health considerations

The Acceptable Daily Intake (ADI) adopted in Australia for octhilinone is 0.03 mg/kg body weight, with a NOEL of 60 mg/kg bw.

The USEPA (2007) considers OIT is not mutagenic or genotoxic. The incidental oral, short-term; intermediate-term (1–30 days; 30 days–6 months) NOAEL was estimated to be 5 mg/kg/d, from a developmental toxicity study.

### Derivation of Maximum Acceptable Value

No MAV.

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# N-octyl bicycloheptene dicarboximide

CAS No. 113-48-4. The IUPAC name for N-octyl bicycloheptene dicarboximide is N‑(2‑ethylhexyl)-8,9,10-trinorborn-5-ene-2,3-dicarboximide or N‑(2‑ethylhexyl)bicyclo[2.2.1]hept-5-ene-2,3-dicarboximide. The CAS name is 2‑(2‑ethylhexyl)-3a,4,7,7a-tetrahydro-4,7-methano-1H-isoindole-1,3(2H)-dione. Sometimes referred to as MGK-264, Synergist 264, pyrodone (obsolete) or zengxiaoan.

### Maximum Acceptable Value

N-octyl bicycloheptene dicarboximide is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

N-octyl bicycloheptene dicarboximide is an ingredient in some common [pesticides](https://en.wikipedia.org/wiki/Pesticides) and has been in use since the 1940s. It has no intrinsic pesticidal activity itself, but, like piperonyl butoxide (qv), is a [synergist](https://en.wikipedia.org/wiki/Synergy#Toxicological_synergy) enhancing the potency of [pyrethroid](https://en.wikipedia.org/wiki/Pyrethroid) ingredients. It is used in a variety of household and veterinary products. Therefore its use is mainly associated with the use of pyrethrins and pyrethroids.

N-octyl bicycloheptene dicarboximide does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2016.

### Forms and fate in the environment

MGK 264 does not contain chromophores that absorb at wavelengths >290 nm and therefore is not expected to be susceptible to direct photolysis by sunlight. If released to soil, MGK 264 is expected to have low to slight mobility based upon Koc values of 636 and 3106. Volatilisation from moist soil surfaces is not expected to be an important fate process based on an estimated Henry’s Law constant of 2.8 x 10-7 atm-cu m/mole. MGK 264 has a mean aerobic half-life of 341 days, suggesting that biodegradation is not an important environmental fate process. If released to water, MGK 264 is expected to adsorb to suspended solids and sediment based upon its Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 130 suggests the potential for bioconcentration in aquatic organisms is high. MGK 264 is not expected to undergo hydrolysis in the environment as indicated by a lack of hydrolysis after 30 days at pH 5–9. The Octanol/Water Partition Coefficient is log Kow = 3.61 (cis-isomer); 3.80 (trans-isomer): 3.70 average (TOXNET 2012 revision).

Water solubility is about 13.7 mg/L.

### Typical concentrations in drinking-water

In a USEPA survey in which 783 rural domestic wells and 566 community wells were tested, MGK 264 was not detected above the minimum reporting limit of 1.0 µg/L.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of MGK 264 in water.

### Health considerations

The USEPA has classified MGK-264 as Group C, a possible human carcinogen (NPIC 2016).

### Derivation of Maximum Acceptable Value

No MAV.

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NPIC. 2016. *MGK-264 Factsheet*. National Pesticide Information Centre [4 pp]. <http://npic.orst.edu/factsheets/mgk264gen.pdf>

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# Oryzalin

CAS No. 19044-88-3. IUPAC name 3,5-dinitro-N4,N4-dipropylsulfanilamide. The CAS name is 4-(dipropylamino)-3,5-dinitrobenzenesulfonamide.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of oryzalin in drinking-water should not exceed 0.4 mg/L (400 μg/L). Oryzalin is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L

Oryzalin should not contain more than 0.5 mg/kg of N-nitroso-di-n-propylamine. The maximum level for toluene (4 g/kg) was also considered toxicologically relevant but not of concern at the proposed level (EFSA 2013).

### Sources to water

Oryzalin is a selective pre-emergence dinitroaniline (or sulphonamide) contact herbicide often used to control annual grasses and broadleaf weeds. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is available in two different formulations: granules and suspension concentrate. The granule formulation (trade name Rout Ornamental Herbicide) also contains the active ingredient oxyfluorfen. The suspension formulation has a trade name of Surflan Flo.

No information is available on the annual usage of specific active ingredients in New Zealand, although oryzalin is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Oryzalin is bound to a greater extent with increasing soil organic matter and clay content. In soils with low proportions of these, high water tables and increased rainfall, oryzalin may be mobile, and thus present a risk of contamination to groundwater.

Oryzalin has low solubility in water: 2.5 mg/L (Merck & Co 1996).

Oryzalin biodegrades slowly with a half-life of approximately two months. It is not mobile under field conditions and is not volatile.

NPIC (1994) quotes for oryzalin a soil half-life of 20 days, water solubility of 2.5 mg/L and a sorption coefficient (soil Koc) of 600. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included oryzalin, so typical concentrations in New Zealand drinking-waters are unknown.

Oryzalin has been detected once during sampling of groundwaters in the Waikato region by Environment Waikato. The concentration was 0.00019 mg/L (Hadfield and Smith 1999, p12).

### Removal methods

No information is available on the removal of oryzalin from water.

The observed adsorption to some soil types suggests that treatment processes that remove particulate matter may be effective at reducing the concentration of oryzalin in water. Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of oryzalin, although a guide to the efficiency of the process cannot be provided.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Recommended analytical techniques

#### Referee method

None listed for oryzalin in APHA 1998/2005.

### Health considerations

There is no information available regarding the greatest source of exposure to oryzalin for New Zealanders (ie, dermal contact, inhalation, diet: food, water). However, food is expected to be the main route of ingestion. Oryzalin is moderately well-absorbed from the gastrointestinal tract, metabolised and eliminated following absorption. When oryzalin was administered to male rats, 40 percent of the dose was excreted in the urine and 40 percent in the faeces within three days. Similar results were obtained in tests with rabbits, a steer, and with Rhesus monkeys (EXTOXNET 1996).

#### Acute exposure

In acute toxicity studies using laboratory animals, oryzalin is practically non-toxic by the oral route and the USEPA has placed it in Toxicity Category IV (the lowest of four categories) for this effect. Oryzalin generally is of modest acute toxicity.

The acute oral LD50 for rats and mice is greater than 10,000 mg/kg, for cats and dogs it is greater than 1,000 mg/kg (RSocC 1987). These levels suggest a low acute oral toxicity when compared with other pesticides.

USEPA. 2007. quotes an acute Reference Dose (RfD) of 0.25 mg/kg/day, for females 13–49 years old, which was calculated by dividing the NOAEL (25 mg/kg/d) by the UF (100). No appropriate endpoint for the general population was identified. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes an ARfD of 0.25 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for oryzalin is 8.25 mg/L.

#### Chronic exposure

In subchronic toxicity studies, oryzalin caused the accumulation of an iron-containing pigment in the kidneys of rats, an increase in the weights of several organs in mice, and blood, bone marrow and liver effects in beagle dogs.

Another chronic toxicity study using beagle dogs showed effects to the blood, liver, kidneys and thyroid gland. In developmental toxicity studies using rats, oryzalin caused reduced maternal body weight gain as well as decreased foetal body weights, an increase in runts and bone development effects. In rabbits, it caused reduced maternal food consumption and weight gain, foetal effects and reduced litter size. Reproduction studies using rats showed increased liver and kidney weights, and decreased food consumption and body weight gain (USEPA 1994).

A NOAEL of 14 mg/kg/d was selected (USEPA 2007) for all populations for chronic dietary exposure based on decreased body weight gain and hematology parameters, and increased microscopic findings in the thyroid at the LOAEL of 43 mg/kg/day from a two-year rat feeding study. The chronic RfD is calculated to be 0.14 mg/kg/day by dividing the NOAEL by the UF (100). The oral RfD had earlier been 0.05 mg/kg/d (USEPA 1991). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.14 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 12 mg/kg bw established in 1982. It is assumed this incorporates a safety factor of 100. The basis of this ADI cannot be traced with current records, although, according to available United States reports, it is probably based on a NOEL of 12 mg/kg bw/day from a long-term rat study.

The EU (2011) established an ADI of 0.05 mg/kg/d. An ARfD was considered not necessary. These values were reaffirmed by EFSA (2014).

The International Agency for Research on Cancer (IARC) has not classified oryzalin, but USEPA has classified it as a Group C carcinogen, that is, a possible human carcinogen for which there is limited animal evidence (USEPA 1994), and in 2008 they considered it was “likely to be carcinogenic to humans”. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for oryzalin in drinking-water, as follows:

12 mg/kg body weight per day x 70 kg x 0.1 = 0.4 mg/L

2 L x 100

where:

* no observable adverse effect level = 12 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Oxadiazon

CAS No. 19666-30-9. IUPAC name 5-tert-butyl-3-(2,4-dichloro-5-isopropoxyphenyl)-1,3,4-oxadiazol-2(3H)-one. The CAS name is 3-[2,4-dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3H)-one.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of oxadiazon in drinking-water should not exceed 0.2 mg/L (200 μg/L).

Oxadiazon is not mentioned in the WHO Guidelines.

### Sources to water

Oxadiazon is a selective pre-emergence or early post-emergent oxadiazole herbicide. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is available as an emulsifiable concentrate (trade name: Foresite 380) and as granules (trade name: Ronstar SG). The granules formulation also contains simazine as an active ingredient. In the US, 77 percent of its use is on golf courses.

No information is available on the annual usage of specific active ingredients in New Zealand, although oxadiazon is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Oxadiazon has low solubility in water: 0.7 mg/L (Merck & Co 1996). Its mobility (as Koc) is 3,200, which indicates that it is strongly adsorbed to organic soil, and therefore unlikely to be highly mobile in organic soils. Leaching from surficial soils to groundwater is expected to be low or negligible, unless the soil is very porous or has some cracks that favour preferential flow.

Based on the fate studies reviewed, oxadiazon would be stable and persistent under typical terrestrial environment conditions. Soil photolysis and hydrolysis under acidic and basic conditions do not appear to be an important dissipation mechanism. However, direct aqueous photolysis half-life of about three days (summer sunlight conditions in Florida) suggests that in clear and shallow surface water bodies where sunlight penetration can be significant, photolytic degradation of oxadiazon is possible. The photolytic effect may substantially diminish in turbid and deeper water bodies (USEPA 2003).

NPIC (1994) quotes for oxadiazon a soil half-life of 60 days, water solubility of 0.7 mg/L and a sorption coefficient (soil Koc) of 3,200. This resulted in a pesticide movement to groundwater rating of very low.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included oxadiazon, so typical concentrations in New Zealand drinking-waters are unknown.

Monitoring for pesticides in groundwater in the Waikato region has detected oxadiazon at one location, at a concentration of 0.00021 mg/L (Hadfield and Smith 1999, p12). Oxadiazon has been found twice, in groundwaters in Waikato and Otago, ranging from 0.00002 to 0.00021 mg/L (MAF 2006).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Oxadiazon occurred at 0.021 µg/L, ie, 0.000021 mg/L.

Oxadiazon was found in one bore water during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.000018 mg/L. The bore was in the Otago region.

### Removal methods

No information is available on the removal of oxadiazon from water.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of oxadiazon, although a guide to the efficiency of the process cannot be provided.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Health considerations

There is no information available regarding the greatest source of exposure to oxadiazon for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

In both subchronic and chronic studies, the major target organ of oxadiazon toxicity was the liver. Effects were consistent among the species tested (rat, dog, mouse) and typically included enlarged livers along with increases in serum clinical chemistry parameters associated with hepatotoxicity such as alkaline phosphatase and serum aspartate or alanine aminotransferase (USEPA 2003).

#### Acute exposure

The acute oral LD50 for rats and mice is greater than 8,000 mg/kg (RSocC 1987), which suggests a low acute oral toxicity when compared with other pesticides. Oxadiazon may irritate slightly the mucous membranes of the mouth if swallowed.

A short-term oral endpoint was selected for incidental oral exposure in children, using a No Observed Adverse Effect Level (NOAEL) of 12 mg/kg/day based on a statistically significant decrease in maternal body weight gains at 40 mg/kg/day (LOAEL) in a developmental study in rats (USEPA 2003).

#### Chronic exposure

The critical effect of chronic exposure is increased levels of serum proteins and increased liver weights, based on a two-year rat feeding study (USEPA 1987).

USEPA (2003)states for the purpose of assessing potential risks from drinking water, the USEPA used the chronic/oncogenicity feeding study. For the chronic drinking water assessment, an uncertainty factor of 100 was applied based on a 10x factor for intraspecies variation and a 10x factor for interspecies extrapolation. This chronic oral endpoint was based on increased incidence of swollen cells in the central lobe of the livers of male rats observed at the LOAEL of 3.5 mg/kg/day. The NOAEL in this study was 0.36 mg/kg/day. Therefore, the “theoretical chronic RfD” would be 0.0036 mg/kg/day. The oral RfD had earlier been 0.005 mg/kg/d (USEPA 1991).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw.

EC (2010) established an ADI of 0.0036 mg/kg/d, and an ARfD of 0.12 mg/kg/d.

The International Agency for Research on Cancer has not classified oxadiazon for its ability to cause cancer. As at May 2002 the USEPA had classified oxadiazon as likely to be carcinogenic to humans. Then in September 2008 the USEPA reclassified oxadiazon in Group C: a possible human carcinogen. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the PMAV for oxadiazon in drinking-water, as follows:

5 mg/kg body weight per day x 70 kg x 0.1 = 0.175 mg/L (rounded to 0.2 mg/L)

2 L x 100

where:

* no observable adverse effect level = 5 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 100.

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# Oxamyl

CAS No. 23135-22-0. The IUPAC name for oxamyl is (EZ)-N,N-dimethyl-2-methylcarbamoyloxyimino-2-(methylthio)acetamide. The CAS name is methyl 2‑(dimethylamino)-N-[[(methylamino)carbonyl]oxy]-2-oxoethanimidothioate. Has also been called N,N-dimethyl-2-methylcarbamoyloxyimino-2-(methylthio)-acetamide.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because oxamyl is unlikely to be found in drinking-water, the establishment of a guideline value is not deemed necessary.

The USEPA (2006/2009/2011) has set a maximum contaminant level (MCL) at 0.2 mg/L because USEPA believes, given present technology and resources, this is the lowest level to which water systems can reasonably be required to remove this contaminant should it occur in drinking-water.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; excursions above this level even for a short period are of concern, as the health-based guideline is based on effects on foetal bodyweight following short-term exposure.

Care during the manufacturing process limits the possibility of forming non-polar N‑nitrosamines.

### Sources to water

Oxamyl is a fast acting carbamate insecticide/acaricide/nematicide that controls a broad spectrum of insects, mites, ticks, and roundworms. It may work both through systemic distribution in the target pest and on contact. Oxamyl is used on field crops, vegetables, fruits, and ornamental plants and may be applied directly on to plants or the soil surface. It is available in both liquid and granular form, but the granular form is banned in the US.

Oxamyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Oxamyl is of low persistence in soil with reported field half-lifes of 4 to 20 days. Loss is due to decomposition by aerobic and anaerobic bacteria. Oxamyl is hydrolysed rapidly in neutral and alkaline soils and more slowly in acid soils. Photolysis is slow; sunlight hastens the degradation process. It does not readily adsorb to soil or sediments and it has been shown to leach in soil. Its adsorption is strongest in soils of high organic matter, but on sandy loam is fairly weak. In a river water study, oxamyl had a half-life of one to two days, although longer in acidic water. Since oxamyl degrades relatively quickly in the presence of bacteria, it is more likely to be found in groundwater than in surface water.

The log Octanol/Water Partition Coefficient (log Kow) is -0.47.

Oxamyl is very soluble in water: 280 g/L at 25°C (28 percent).

NPIC (1994) quotes for oxamyl a soil half-life of four days, water solubility of 28 percent and a sorption coefficient (soil Koc) of 25. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

Oxamyl was not detected in 1,370 wells sampled in 34 counties in California. Sampling occurred between 1 July 1995 and 30 June 1996. Oxamyl has been detected in groundwater in Massachusetts, New York, New Jersey, and Rhode Island (California EPA 1997).

The USEPA (2004) estimates that concentrations of oxamyl residues in surface water and groundwater are 1 and 4 µg/L, respectively.

Forty water utilities in the US reported detecting oxamyl (vydate) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.012 mg/L.

### Removal methods

The weak soil adsorption and very high water solubility suggest that treatment processes that remove particulate matter should be ineffective at reducing the concentration of oxamyl in water. Some newer advanced oxidation or activated carbon processes may be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Oxamyl is very toxic to birds. In a two-year mouse feeding study, no effects were observed at a dose of 1.25 mg/kg/day, although at the very high doses of 2.5 and 3.75 mg/kg/day there was decreased body weight and changed nutritional performance. Liver impairment was suggested by a slight biochemical change seen in dogs that were fed 3.75 mg/kg/day as a part of a two-year feeding study. Male rats fed the very high dose of 7.5 mg/kg/day oxamyl for two years had decreased organ weight of the heart, testes, and adrenals. In females, there was an increase in the relative weights of the brain, heart, lungs, and adrenals at these doses.

Being a carbamate, oxamyl can cause cholinesterase inhibition in humans; that is, it can overstimulate the nervous system causing nausea, dizziness, and confusion. The oxamyl risk assessments are based on oxamyl’s ability to cause cholinesterase inhibition as measured in plasma, red blood cells, and brain. Neither of the degradates, oxime or dimethyloxamic acid (DMOA), is expected to inhibit cholinesterase and neither is of toxicological concern. Because the current analytical method does not differentiate between the parent and the degradate (oxime), the tolerance expression for oxamyl includes both (USEPA 2007).

USEPA (2004) reports a one-day Health Advisory (HA) for a 10 kg child of 0.01 mg/L. This one-day HA for a 10 kg child also is used as a conservative estimate for the lifetime HA to be protective of public health including chronic exposure effects, maternal, and developmental effects.

EC (2006) established an ADI and ARfD of 0.001 mg/kg/d.

The USEPA (2007) did not conduct a chronic dietary risk assessment for oxamyl because it is typical of most cholinesterase-inhibiting carbamates in that cholinesterase inhibition is fully reversible around the LOAEL, where cholinesterase inhibition lasts for two to three hours (as determined in a cholinesterase reversibility study).

JMPR (2008, reaffirmed in 2017) quotes an ADI of 0.009 mg/kg bw/day and an ARfD of 0.009 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw from a developmental study in rats. The NOEL is based on reduced foetal weights. The ADI incorporates a safety factor of 100.

The oral reference dose or RfD (USEPA 2006/2009/2011) is 0.001 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.035 mg/L. The oral RfD had earlier been 0.025 mg/kg/d (USEPA 1991).

Oxamyl was negative in various genotoxicity and mutagenicity tests and in long-term carcinogenicity studies in rats and mice. There is no scientific evidence that oxamyl is a teratogen. As at September 2008 the USEPA has classified oxamyl in Group E: evidence of non-carcinogenicity for humans.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for oxamyl since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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WHO. 2011. *Guidelines for Drinking-water Quality 2011* (4th edition). Geneva: World Health Organization. Available at: [http://www.who.int/water\_sanitation\_health/publications/drinking-water-quality-guidelines-4-including-1st-addendum/en/index.html](http://www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/index.html)

# Oxathiapiprolin

CAS No. 1003318-67-9. The IUPAC name for oxathiapiprolin is 1-(4-{4-[(5RS)-5-(2,6-difluorophenyl)-4,5-dihydro-1,2-oxazol-3-yl]-1,3-thiazol-2-yl}-1-piperidyl)-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone. The CAS name is 1-[4-[4-[5-(2,6-difluorophenyl)-4,5-dihydro-3-isoxazolyl]-2-thiazolyl]-1-piperidinyl]-2-[5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl]ethanone.

The technical material is a racemic mixture.

### Maximum Acceptable Value

Oxathiapiprolin is not mentioned in the DWSNZ or in the WHO Guidelines.

### Sources to water

Oxathiapiprolin is a systemic oxazole or pyrazole or thiazole fungicide, also described as a piperidinyl-thiazole-isoxazoline fungicide.

### Forms and fate in the environment

The hydrolysis of oxathiapiprolin in sterile buffer solutions was slow. In pH 4, 7 and 9 buffer solutions, <10 percent degradation occurred at 50ºC, indicating that oxathiapiprolin is stable to hydrolysis. In sterile natural water, the photolytic half-life of oxathiapiprolin was 20.2 days under continuous irradiation.

Oxathiapiprolin data showed DT50 values of 28.2 days and 36.3 days in irradiated moist soils and in irradiated dry soils, respectively. The rate of aerobic degradation of oxathiapiprolin in the laboratory was measured in five different soils. Under laboratory conditions, the DT50 values ranged from 16 to 162 days at 20ºC. No correlation was observed between the rate of degradation of oxathiapiprolin and soil pH. Oxathiapiprolin degrades slowly under anaerobic conditions in the sandy loam soil tested with DT50 and DT90 values of 1,505 and 4,998 days, respectively.

Oxathiapiprolin and its metabolites were found generally confined to the upper soil segment (0 to 15 cm) with the highest concentration found in the 0 to 5 cm segment. The metabolites of oxathiapiprolin were slightly more mobile through the soil depths however none of these generally moved below the 15 cm depth in any significant amounts. Contamination of groundwater is unlikely (APVMA 2015). EFSA (2016) found some metabolites were present at levels that trigger a groundwater exposure assessment.

The DT50 values for oxathiapiprolin in the water phase of the aerobic sediment systems ranged from 5.5 to 13.6 days in the two water/sediment systems. The DT50 value for oxathiapiprolin in the sediment extracts ranged from 112.7 to 249.2 days in the two water/sediment systems. For the total system, the DT50 values for oxathiapiprolin ranged from 24.4 to 44.7 days in the two water/sediment systems.

During transformation in the environmental matrices soil, water and sediment, the isomer ratio of oxathiapiprolin did not change (ie, it remained a racemic mixture) (EFSA 2016).

Water solubility is about 0.2 mg/L at 20°C. The octanol-water partition coefficient at pH 7, 20°C = 4.57 x 103 or LogP = 3.66. Henry’s Law constant at 25oC (Pa m3 mol-1) = 3.521 x 10-03.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2016).

### Health considerations

The ADI is established at 4.1 mg/kg bw/d based on a NOAEL of 411 mg/kg bw/d in a two-generation reproduction rat study and applying a 100 fold safety factor (consisting of a 10–fold safety factor for both intra- and inter-species variation). An ARfD was not established since oxathiapiprolin was considered unlikely to present an acute hazard to humans, noting that no toxicologically significant acute findings were seen in any animal studies.

Oxathiapiprolin did not show carcinogenic potential in mice or rats. Oxathiapiprolin did not induce chromosomal aberrations with and without metabolic activation. The available data suggests that oxathiapiprolin should not being considered a hazard for reproductive or developmental toxicity (APVMA 2015). APVMA adopted an ADI of 4 mg/kg/d for Australia (<https://apvma.gov.au/>). An ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose.

For oxathiapiprolin, the ADI is 0.14 mg/kg bw per day based on the one-year dog study and applying an uncertainty factor of 100; whereas the ARfD is not considered necessary (EFSA 2016).

JMPR (2016) established an ADI of 0–4 mg/kg bw on the basis of the NOAEL of 430 mg/kg bw per day in a two-generation study in rats for delayed balanopreputial separation in offspring at 1,210 mg/kg bw per day. A safety factor of 100 was applied. The meeting concluded that it was not necessary to establish an ARfD for oxathiapiprolin in view of its low acute oral toxicity and the absence of any other toxicological effects, including developmental toxicity, that would likely be elicited by a single dose.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Oxine-Copper

CAS No. 10380-28-6. The IUPAC name for oxine-copper is bis(quinolin-8-olato-O,N)copper(II) or cupric 8-quinolinoxide. The CAS name is bis(8-quinolinolato-κN1,κO8)copper. It can also be called copper 8-quinolinolate, copper quinolate or copper-oxinate. Oxine-copper is the accepted name for a complex of copper and 8‑hydroxyquinoline (qv).

### Maximum Acceptable Value

Oxine-copper is not mentioned in the DWSNZ or in the WHO Guidelines.

EPA established an environmental exposure limit of 0.011 µg/L for oxine copper in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Oxine-copper is a copper fungicide. It is also used is used in formulating antiseptics, deodorants and antiperspirants. Common usages include a fungicide for preservation of above-ground timber, and as a pruning paint. In New Zealand it has been used for sapstain control in water-based solutions. Sometimes it is used in conjunction with carbendazim and permethrin. Some products include nickel 2-ethylhexanoate.

Oxine-copper does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). However, oxine-copper is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …).

Because of its low toxicity to humans and animals, oxine copper is the only USEPA registered preservative permitted by the US Food and Drug Administration for treatment of wood used in direct contact with food. Some examples of its uses in wood are commercial refrigeration units, fruit and vegetable baskets and boxes, and water tanks. Oxine copper (copper-8-quinolinolate) is an organometalic compound, and the formulation consists of at least 10 percent copper-8-quinolinolate, 10 percent nickel-2-ethylhexanoate, and 80 percent inert ingredients. It is accepted as a stand-alone preservative for above ground use for sapstain and mould control and is also used for pressure treating. A water-soluble form can be made with dodecylbenzene sulfonic acid, but the solution is corrosive to metals. Oxine copper solutions are greenish brown, odourless, toxic to both wood decay fungi and insects, and have a low toxicity to humans and animals. Oxine copper solutions have also been used on non-wood materials, such as webbing, cordage, cloth, leather, and plastics.

### Forms and fate in the environment

Copper 8-quinolinolate is hydrolytically stable at pH 5, 7 and 9 but photolytically it is not stable. More than 80 percent of it is stable in aerobic and anaerobic soils. In aerobic soils its half-life is about four months, but it may be over one year in anaerobic soils. It does not show any tendency to migrate from topsoil. It is therefore likely to contaminate surface water through surface water run-off. Its degradation pathway appears to be aqueous photolysis with a half-life of 60 to 96 hours. Leaching from (sapstain use) treated Douglas fir wood is 666 mg/1,000 board feet while for Hemlock it is 229 mg/1,000 board feet after eight stimulated rain cycles. The estimated log Kow for copper 8-quinolinolate is 2.5, which indicates that it is not likely to bioaccumulate in aquatic organisms like fish. It is persistent in water and soils.

Water solubility is about 0.7 mg/L at 25°C. EPA quotes 0.07 mg/L [(http://www.epa.govt.nz/search-databases/Pages/ccid-details.aspx?SubstanceID=2899](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\INetCache\Content.Word\(http:\www.epa.govt.nz\search-databases\Pages\ccid-details.aspx%3fSubstanceID=2899)).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In a 90-day oral toxicity test (MRID 42986802), copper 8-quinolinolate (>99.5 percent purity) was administered in feed via capsules to four dogs/sex/dose at concentrations of 0, 5, 50, or 250 mg/kg/day for males and females, respectively) for 13 weeks. The NOAEL was determined to be 5 mg/kg/day (males/females), based on vomiting, reduced total plasma protein and albumin, reddened mucosa and hyperemia in stomach and/or small intestine observed at the LOAEL of 50 mg/kg/day (USEPA 2007).

Copper 8-hydroxyquinoline has been tested in two strains of mice by oral and by single subcutaneous administration. Although a significantly increased incidence of reticulum-cell sarcomas was observed only in males of one strain following single subcutaneous injection, no evaluation of the carcinogenicity of this compound can be made on the basis of the available data (IARC 1999).

Copper 8-quinolinolate has a low order of acute toxicity via the oral route of exposure. Oxine copper is listed by the US Food and Drug Administration (FDA) as an indirect additive that can be used in packaging that may come in direct contact with food.

### Derivation of Maximum Acceptable Value

No MAV.

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USEPA. 2007. *Revised Risk Assessment Chapter for Copper 8-Quinolinolate (Oxine-Copper) in Support of the Re‑registration Eligibility Decision (RED) Document for the Copper Salts (RED Case 4026)* [83 pp]. See: [www.regulations.gov/search/Regs/contentStreamer?objectId=090000648063cd26&disposition=attachment&contentType=pdf](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Word\www.regulations.gov\search\Regs\contentStreamer%3fobjectId=090000648063cd26&disposition=attachment&contentType=pdf)

# Oxyfluorfen

CAS No. 42874-03-3. The IUPAC name for oxyfluorfen is 2-chloro-α,α,α-trifluoro-p-tolyl 3-ethoxy-4-nitrophenyl ether. The CAS name is 2-chloro-1-(3-ethoxy-4-nitrophenoxy)-4-(trifluoromethyl)benzene.

### Maximum Acceptable Value

Oxyfluorfen is not mentioned in the DWSNZ or the WHO Guidelines.

The USEPA concluded on 22 September 2009 that oxyfluorfen is known or anticipated to occur in PWSs and may require regulation. Therefore they added oxyfluorfen to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

Oxyfluorfen should not contain more than 2 g/kg of N-nitrosodimethylamine.

### Sources to water

Oxyfluorfen is a selective pre- and post-emergent contact nitrophenyl ether herbicide and algicide used to control certain annual broadleaf and grassy weeds in vegetables, fruit, cotton, ornamentals, and on non-crop areas. The biggest use in the US is on grapes. It is frequently used on onions in Australia, and onions, raspberries and strawberries in Canada.

Oxyfluorfen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Oxyfluorfen is quite persistent in most soil environments (half-life of about  
300–600 days) and is fairly resistant to microbial degradation or hydrolysis. Once oxyfluorfen is adsorbed to soil particles, it is not readily removed. It is practically insoluble in water (0.1 mg/L), and therefore is unlikely to be mobile, so should not be found in groundwater. Oxyfluorfen is stable in water, but is decomposed in the presence of light.

EFSA (2015) states that oxyfluorfen undergoes photolytic degradation in water to form metabolites. The soil DT50 for oxyfluorfen is about 138 days; the DT50 water/sediment system is 29.2 days.

NPIC (1994) quotes for oxyfluorfen a soil half-life of 35 days, water solubility of 0.1 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Removal methods

Treatment processes that remove particulate matter from water should remove oxyfluorfen as well.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Because oxyfluorfen is highly hydrophobic, it may have the potential to bioconcentrate in animal fatty tissues. Effects on the liver have been observed in long-term feeding studies with rats, mice, and dogs.

It does not appear likely that oxyfluorfen will cause reproductive effects in humans at likely levels of exposure. Data suggest oxyflurofen may have teratogenic effects, but only at very high doses. The oral Reference Dose (RfD) was estimated by the USEPA (1991) to be 0.003 mg/kg/d based on increased absolute liver weight and non-neoplastic lesions. The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.03 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for oxyfluorfen is 0.21 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.025 mg/kg body weight, with a NOEL of 2.5 mg/kg bw.

As at September 2008 the USEPA has classified oxyfluorfen in Group C: a possible human carcinogen, based on combined hepatocellular adenomas/carcinomas in the mouse carcinogenicity study. However, the USEPA concludes that residues of oxyfluorfen in food and drinking-water do not result in a chronic aggregate risk of concern.

### Derivation of Maximum Acceptable Value

No MAV.

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# Paclobutrazol

CAS No. 76738-62-0. The IUPAC name for paclobutrazol is (2RS,3RS)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1H-1,2,4-triazol-1-yl)pentan-3-ol. The CAS name is (αR,βR)-rel-β-[(4-chlorophenyl)methyl]-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol. Sometimes called PBZ.

### Maximum Acceptable Value

Paclobutrazol does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Paclobutrazol is a triazole plant growth regulator that slows vegetative growth by inhibiting gibberilin biosynthesis, thereby creating more compact plants. It is normally applied to the soil to be taken up by the roots and transported via the [xylem](http://en.wikipedia.org/wiki/Xylem) to the upper parts of the plant. Foliar application is mostly ineffective. Seeds can be soaked with PBZ to reduce seedling growth. It also has fungicidal properties.

Paclobutrazol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](https://eatsafe.nzfsa.govt.nz/web/public/acvm-register%20and%20select%20entire%20register)). Tebuconazole and cyproconazole have similar structures.

### Forms and fate in the environment

Paclobutrazol is relatively stable (little degradation after 30 days) in sterile aqueous solutions.

Paclobutrazol degraded with a half-life of more than one year in loam soil incubated at 20°C with 40 percent moisture holding capacity. Batch equilibrium testing indicated that paclobutrazol has the capacity to be mobile on some conditions such as sandy soils with low organic content, otherwise it has a low mobility. Paclobutrazol is unlikely to volatilise to any significant extent, and does not photodegrade after being exposed to 10 days of simulated sunlight. The only known degradate of paclobutrazol is its ketone analogue.

The DT90 for paclobutrazol obtained from laboratory studies was higher than 100 days, indicating that paclobutrazol is persistent. The main residues are the triazole derivative metabolites (TDMs): triazole alanine, triazole lactic acid and triazole acetic acid (EFSA 2017).

Water solubility is about 30 mg/L.

NPIC (1994) quotes for paclobutrazol a soil half-life of 200 days, water solubility of 25 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of high.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Paclobutrazol, administered orally to rats and dogs, was rapidly absorbed and excreted in urine and faeces. Tissue residues were found only in liver and kidney and declined rapidly after single or repeated dosing. Paclobutrazol is of slight to moderate acute toxicity to mice, rats, guinea pigs and rabbits.

IPCS (1988) quotes an estimate of acceptable daily intake (ADI) for man of 0 to 0.1 mg/kg body weight.

The USEPA (1987/1992) derived an oral reference dose (RfD) of 0.013 mg/kg/d based on elevated liver weights, serum cholesterol, hepatic aminopyrine N-demethylase activity, and alanine transaminase levels in a 90-day rat feeding study with a NOEL of 12.5 mg/kg/d.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

DEFRA (1995) proposed an ADI of 0.025 mg/kg body weight using a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for paclobutrazol is 0.01 mg/kg body weight, with a NOEL of 1.4 mg/kg.

EFSA (2017) reports an ADI of 0.022 mg/kg/d and an ARfD of 0.10 mg/kg bw. See datasheet for triazole metabolites for latest ADI and ARfD.

Paclobutrazol is not mutagenic in Ames tests or mouse lymphoma assays.

### Derivation of Maximum Acceptable Value

No MAV.

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# PAPP, para-aminopropiophenone

CAS No. 70-69-9. The IUPAC name for para-aminopropiophenone is 1‑(4‑aminophenyl)propan-1-one. Also called PAPP, 4-aminopropiophenone, and p‑aminophenyl ethyl ketone. Can be called Predastop.

### Maximum Acceptable Value

PAPP does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

PAPP is a new, more humane, vertebrate toxic agent, particularly effective against feral cats and stoats. It induces methaemoglobinaemia preventing oxygen from binding to red blood cells. It is still at the experimental/application stage, as a possible replacement for 1080. Rabbits and rodents appear to tolerate the pharmacological effect of PAPP quite well due to their relatively high NADH-dependent capacity to convert methaemoglobin to haemoglobin. Registration dossiers have been vetted by NZFSA and were submitted to ERMA in May 2009. PAPP products should be available from 2010 subject to NZFSA and ERMA approvals (ERMA approval 22 March 2011). In trials, baits were usually delivered as a 40 percent paste bolus or encapsulated pellet in a mince meatball. It was also applied with dimethylsulfoxide and condensed milk. It has been used in Australia to control the fox and wild dog population.

Since April 2011, 4-aminopropiophenone has appeared on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) under the trade name of PredaSTOP (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). 4-Aminopropiophenone is also listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals).

### Forms and fate in the environment

An evaluation of PAPP using OECD methodology has determined the compound as being hydrolytically stable from pH 4 to 9, and readily biodegradable (ERMA 2010). PAPP is reasonably mobile in sandy soils but retained in clays. It breaks down within a month.

The paste in the meat bait (as used in pest control operations) should disposed of by burying below the ground level (recommended to be at least 60 cm depth). After a typical five to seven night interval from dispensing the paste bait as a VTA, it would be normal practice for each bait station to be revisited and all toxic baits to be recovered and destroyed. No specific provision for the recovery of dead carcasses of target pests (eg, stoats, feral cats) is considered necessary as the residual levels of PAPP in animals are expected to be very low. The ingestion of a single bait represents 35–80 mg PAPP Paste A depending on the species and animal size. Given the proposed use pattern with bait stations, the Agency has made no quantitative assessment of risks to the aquatic environment since exposure should not occur during use of the bait. The only possible route of exposure would occur through spillage of the product (ERMA 2010).

Water solubility is about 230 mg/L at 22°C and 350 mg/L at 37°C. As PAPP is water soluble, there is a risk to waterways from its use. However, PAPP has been developed for use in bait stations, which will be placed away from waterways.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The weight of evidence indicates that PAPP is not mutagenic and is not likely to cause cancer. Studies (on rat and monkey) indicate that there are no significant or severe chronic systemic toxic or target organ effects from prolonged sub-lethal doses of PAPP, other than secondary effects of methaemoglobinaemia. Data from the literature indicates a human dose of PAPP at 10 mg/kg b.w. will not have an effect. In volunteers given 50–100 mg PAPP in water, the maximum methaemoglobin levels occurred within 1–2 hours with levels elevated for four hours. Other than elevated methaemoglobin levels and mild haemolysis at high doses, no other adverse effects were observed (ERMA 2010a).

4-Aminopropiophenone has been used as an antidote to cyanide, azide and radiation poisoning. PAPP-induced partial methaemoglobinaemia in humans protects against cyanide toxicosis. Methylene blue, which is available from veterinarians, will reverse the methaemoglobinaemia induced by PAPP and thus can be administered as an antidote.

The main concern to ERMA (2010) is from accidental exposure to PAPP baits. They derived an ARfD of 0.01 mg/kg bw, based on a NOAEL of 1 mg/kg bw. Commercial PAPP products contain a very effective anti-emetic (a substance which suppresses the vomit reflex). The substance is known to be effective in humans as it is used for this purpose as human medicine. This is likely to increase the likelihood that all the para-aminopropiophenone could be absorbed if it were to be ingested. While this increases the risk, it is not of great significance to the semi-quantitative risk assessment.

### Derivation of Maximum Acceptable Value

No MAV.

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# Paraquat

CAS No. 4685-14-7 (the cation). The IUPAC and CAS name for paraquat is 1,1`-dimethyl-4,4`-bipyridinium.

When this substance is used as a salt, its identity should be stated, for example:

* [paraquat dichloride](http://www.alanwood.net/pesticides/derivatives/paraquat%20dichloride.html) CAS 1910-42-5 the commonest
* [paraquat di](http://www.alanwood.net/pesticides/derivatives/paraquat%20dichloride.html)iodide CAS 4032-26-2
* [paraquat dimethylsulfate](http://www.alanwood.net/pesticides/derivatives/paraquat%20dimetilsulfate.html) CAS 2074-50-2.

Paraquat has also been called methyl viologen. Gramoxone is a well-known trade name.

### Maximum Acceptable Value

Paraquat is not mentioned in the DWSNZ or the WHO Guidelines.

The maximum acceptable concentration in Canada is 0.007 mg/L as the paraquat ion, 0.01 mg/L as paraquat dichloride.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.03 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; excursions above this level even for a short period are of concern, as the health-based guideline is based on an end-point that is common to both short-term and long-term effects.

Paraquat should not contain more than 0.2 percent of free 4,4′-bipyridyl, or 3 mg/kg of 2,2′:6′,2-terpyridine.

### Sources to water

Paraquat is a non-selective bipyridinium or bipyridyl, or quaternary nitrogen, contact herbicide derived from pyridine, used widely to control broadleaf weeds and grasses in clover seed crops, drains, forestry, industrial sites, lucerne, streets, waterways, pasture, strawberries, vegetables, citrus or deciduous fruit orchards and vineyards. It is also used to control barley grass and marijuana, and also used as a crop desiccant and defoliant, and as an aquatic herbicide.

Formulations containing paraquat have been registered for use in New Zealand since 1962. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). There are seven products containing paraquat that are currently (2009) registered for agricultural use in New Zealand. ERMA notes that 0.93 tonnes of paraquat were used in New Zealand in 2004, at an application rate of 2,200 grams of active ingredient per hectare.

Paraquat is often applied with other pesticides, for example with diquat, or with urea herbicides.

### Forms and fate in the environment

Paraquat is biodegraded very slowly in soil. Photolysis and volatilisation from soil is not significant. Paraquat is expected to be almost immobile in soil, as it binds to soil and organic matter extremely tightly. The estimated average field half-life of paraquat in soil is 1,000 days, long-term field studies have shown degradation rates of just  
5–10 percent per annum; no harmful metabolic or breakdown products are to be expected. However, in sandy soils with a low organic content, paraquat may be more readily released into soil water and be more bioavailable to organisms. Sunlight and alkaline conditions hasten the degradation process.

If released to water, paraquat will be completely removed from water in 8 to 12 days due to adsorption to suspended solids and sediment, and plant uptake. When paraquat was applied as an aquatic herbicide, at a normal application rate of 1 mg/L, the concentration was found to decrease to about one half of the initial level within 36 hours and to below 0.01 mg/L in less than two weeks. Phytotoxic damage to crops irrigated with treated water is unlikely to occur, if an interval of 10 days is observed between treatment of the water and its use, because of the rapid decrease of paraquat residues in the water (IPCS HSG 1991).

[Paraquat dichloride](http://www.alanwood.net/pesticides/derivatives/paraquat%20dichloride.html) is very soluble in water with a solubility of 700 g/L (70 percent). Paraquat has no measurable vapour pressure; Its log octanol-water partition coefficient is 2.44 (Health Canada 1986, edited 1991).

NPIC (1994) quotes for paraquat dichloride a soil half-life of 1,000 days, water solubility of 62 percent and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

The strong attraction to soil particles means that paraquat is not expected or considered to be a groundwater concern from normal paraquat use patterns.

Two water utilities in the US reported detecting paraquat in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00085 mg/L.

### Removal methods

Any treatment process that removes particulate matter should effectively reduce the concentration of paraquat. Activated carbon could enhance the process. Chlorine dioxide has been found to oxidise paraquat concentrations of 15 and 30 mg/L within minutes above pH 8.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Not carcinogenic; no indication of neurotoxicity (EU 2003). As at September 2008 the USEPA has classified paraquat dichloride in Group E: evidence of non-carcinogenicity for humans. Paraquat dichloride was not mutagenic in the Ames test using Salmonella typhimurium strains TA1535, TA1538, TA98, and TA100 (USEPA 2005).

USEPA (1997) reported the RfD to be 0.0045 mg/kg/d (as the paraquat cation) based on the systemic NOEL of 0.45 mg/kg/d from the one-year dog feeding study.

The EC (2003) developed an ADI of 0.004 mg/kg bw based on NOAEL from a one-year dog study, and a 100-fold safety factor; their ARfD is 0.005 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia for the paraquat cation is 0.004 mg/kg body weight, with a NOEL of 0.45 mg/kg bw from a one-year dietary study in the dog. The NOEL is based on lung lesions at 0.93 to 1.0 mg/kg bw/day. The ADI incorporates a safety factor of 100. The ARfD is 0.004 mg/kg bw based on the same NOEL and safety factor as the ADI.

The reference dose or chronic RfD (USEPA 2005/2006/2009/2011) is 0.0045 mg/kg/d based on a one-year feeding study in dogs with a NOAEL of 0.45 mg/kg-bw/day and an uncertainly factor of 100. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.2 mg/L. The acute reference dose (aRfD) for paraquat dichloride is 0.0042 mg/kg-bw/day for females 13–50 years of age and 0.0125 mg/kg-bw/day for children and the US population. The aRfD is based on a reproduction study in rats with a no observable adverse effect level (NOAEL) of 1.25 mg/kg-bw/day and an uncertainty factor of 100X. An additional FQPA safety factor of 3X was applied for females between the ages of 13 and 50 years due to a data gap for a prenatal developmental study conducted in a non-rodent species.

JMPR (2009) quotes an ADI of 0.005 mg paraquat cation/kg bw and ARfD of 0.006 mg paraquat ion/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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# Parathion

CAS No. 56-38-2. The IUPAC and CAS name for parathion is O,O-diethyl-O-(4-nitrophenyl) phosphorothioate. Has also been called diethyl para-nitrophenol thiophosphate or diethyl 4-nitrophenyl phosphorothionate, diethyl parathion, monothiophosphate or ethyl-parathion or parathion-ethyl.

The analogous dimethyl ester has the ISO common name [parathion-methyl](http://www.alanwood.net/pesticides/parathion-methyl.html) or methyl parathion (CAS 298-00-0, O,O-dimethyl O-4-nitrophenyl phosphorothioate). There is a separate datasheet for methyl parathion.

### Maximum Acceptable Value

WHO (2004) states that as the health-based value is much higher than parathion concentrations likely to be found in drinking-water, the establishment of a numerical guideline value for parathion is not deemed necessary. WHO (2011/2017) states that parathion occurs in drinking-water at concentrations well below those of health concern.

WHO (2017) derived a health-based value of 0.01 mg/L.

The maximum acceptable concentration for parathion in drinking-water in Canada is 0.05 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L (previously 0.01 mg/L); excursions above this level even for a short period are of concern as the health-based guideline is based on short-term effects.

4-Nitrophenol (paranitrophenol) is an impurity – see nitrophenols datasheet.

### Sources to water

Parathion is a non-systemic organophosphate insecticide and acaricide that controls numerous insects by contact and stomach action. It has some fumigant as well as acaricidal activity. Parathion is used as a pre-harvest soil and foliage treatment on a wide variety of crops, both outdoors and in greenhouses. The usual application rate is 0.2–1 kg/ha. Parathion is non-phytotoxic, except to some sensitive ornamentals, apples and pears.

Parathion does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 or 2017 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

There are currently (as at 2011) no registered products containing parathion in Australia, but de-registered compounds could still be detected in water.

Parathion appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

### Forms and fate in the environment

Parathion released to the environment will adsorb strongly to the top layer of soil and is not likely to leach significantly; USEPA (2000) quotes a half-life of up to 58 days. Parathion disappears from surface waters in about a week.

Parathion is degraded quite rapidly in the environment, mainly by hydrolysis (more rapidly as the pH approaches 9), but to a certain extent also by reduction of the nitro group as well as conversion to the oxon, paraoxon. Paraoxon is also called diethyl paraoxon and phosphoric acid diethyl-4-nitrophenyl ester. Paraoxon is more toxic than the parent compound. The half-life of the oxon is much shorter than that of parathion itself, and the oxon does not accumulate. The other degradation products are p‑nitrophenol (4-nitrophenol), p-aminophenol, diethyl thiophosphoric acid and diethyl phosphoric acid.

Water solubility of parathion is about 12–25 mg/L. The vapour pressure of parathion is 5.0 x 10-3 Pa at 20°C. Reported log octanol-water partition coefficients (log Kow) range from 3.40 to 3.93 (Health Canada 1986/91).

NPIC (1994) quotes for ethyl parathion a soil half-life of 14 days, water solubility of 24 mg/L and a sorption coefficient (soil Koc) of 5000. This resulted in a pesticide movement to groundwater rating of very low.

If released to soil, parathion is expected to have moderate to no mobility based upon Koc values ranging from 314 to 15,860. Volatilisation from moist and dry soil surfaces is not expected to be an important fate process based upon its Henry’s Law constant of 2.98 x 10-7 atm-cu m/mole and vapour pressure, respectively. After eight weeks of incubation in an organic and a mineral soil, <2 and 6 percent, respectively, of the applied parathion remained. Prior exposure of soils to p-nitrophenol resulted in increased mineralisation of parathion to carbon dioxide. p-Nitrophenol, diethylthiophosphoric acid and paraoxon have been identified as metabolites under oxidative conditions; under low oxygen conditions reduction to aminoparathion occurs. The half-life for photodecomposition of parathion on three soils ranged from 31 to 70 hours. If released into water, parathion is expected to adsorb to suspended solids and sediment in the water column based upon sediment Koc values ranging from 3,086 to 38,000. Parathion biodegrades in acclimated natural waters within several weeks; it completely degraded to aminoparathion within two weeks in acclimated water from Holland Marsh, Ontario. After 30 days’ incubation in non-sterile coastal river water, only 6 to 21 percent of parathion remained. Volatilisation from water surfaces is not expected to be an important fate process based on its Henry’s Law constant. BCFs ranging from 63 to 462 suggest bioconcentration in aquatic organisms is moderate to high. Reported hydrolysis half-lifes at 20°C at environmentally relevant pHs range from three weeks at pH 9 to 43 weeks at pH 5. The half-life for hydrolysis in sterile sea water has been reported to be approximately one year at 4°C. Divalent cations may catalyse hydrolysis. Twenty percent of parathion was lost by photolysis in two hours in Okeefenokee Swamp water (EAWAG accessed February 2015).

If released to soil, paraoxon is expected to have very high mobility based upon an estimated Koc of 48. Volatilisation from moist and dry soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 6.4 x 10-10 atm-cu m/mole and this compound’s vapour pressure, respectively. If released into water, paraoxon is not expected to adsorb to suspended solids and sediment in water based on the estimated Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 19 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis may be an important process under environmental conditions based upon hydrolysis half-lifes of 2.9, 144, and 173 days at pH values of 9.0, 7.4, and 5.0, respectively. Limited biodegradation data suggest biodegradation may be an important fate process in both soil and water; biodegradation products include p-nitrophenol and diethylphosphoric acid (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Parathion was not detected in 248 samples of municipal and private drinking water supplies from Prince Edward Island, Quebec, Ontario, Saskatchewan and Manitoba analysed from 1971 to 1986 (detection limits ranged from 0.000001 to 0.0002 mg/L) (Health Canada, 1986/91). The general population is not usually exposed to parathion from air or water, parathion residues in food being the main source of exposure.

One water utility in the US reported detecting parathion (ethyl) in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00063 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of parathion in turbid water. Activated carbon should reduce the concentration of by-products.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

WHO (2004) states that parathion in water may be determined by extracting into dichloromethane, drying the extract, redissolving in hexane and analysing by gas–liquid chromatography, phosphorus mode. The detection limit is 0.0001 mg/L.

### Health considerations

Ethyl parathion is among the most highly toxic chemicals registered with the USEPA. It has been placed in Acute Toxicity Category 1 (most toxic) for acute eye, skin, and inhalation effects. It is a potent plasma, red blood cell and brain acetyl cholinesterase inhibitor. It is toxic by all routes of exposure and cholinesterase inhibition occurs following acute, subchronic and chronic exposures to low doses of ethyl parathion (USEPA 2000). In man, an oral dose of 3–5 mg/kg is usually fatal. It is no longer used in the US.

In a study conducted in humans, a NOAEL of 7.5 mg/day (0.1 mg/kg of body weight per day) was determined for parathion on the basis of lack of effect on erythrocyte acetylcholinesterase.

JMPR (2000) quotes an ADI of 0.005 mg/kg bw and an acute RfD of 0.01 mg/kg/d for parathion.

An ADI of 0.004 mg/kg of body weight was established on the basis of a NOAEL of 0.4 mg/kg of body weight per day in the two-year study in rats for retinal atrophy and inhibition of brain acetylcholinesterase at the higher dose. A safety factor of 100 was used. A health-based value of 0.01 mg/L (rounded figure) can be derived based on an allocation of 10 percent of the ADI of 0.004 mg/kg of body weight to drinking-water. WHO (2004/2011/2017) states that because the health-based value is much higher than parathion concentrations likely to be found in drinking-water, the presence of parathion in drinking-water under usual conditions is unlikely to represent a hazard to human health. For this reason, the establishment of a numerical guideline value for parathion is not deemed necessary.

As at August 2015 and January 2017 ATSDR (<http://www.atsdr.cdc.gov/mrls/pdfs/atsdr_mrls.pdf>) quotes a minimal risk level (MRL) for parathion of:

* 0.009 mg/kg/day for intermediate-duration oral exposure (15–364 days).

The Acceptable Daily Intake (ADI) adopted in Australia for parathion is 0.005 mg/kg body weight, with a NOEL of 0.05 mg/kg bw based on a reduction in erythrocyte cholinesterase activity in a three-week oral toxicity study in humans. The ADI incorporates a safety factor of 10. The ARfD is 0.01 mg/kg bw based on a NOEL of 0.125 mg/kg bw/day for erythrocyte cholinesterase inhibition from a 35-day oral toxicity study in humans. The ARfD incorporates a safety factor of 10.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.00003 mg/kg/d, and an ARfD of 0.0003 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for ethyl parathion is 0.003 mg/L.

Parathion has been tested adequately for genotoxicity in a range of tests in vitro and in vivo. JMPR (2000) concluded that parathion is not genotoxic.

As at September 2008 the USEPA has classified ethyl parathion in Group C: a possible human carcinogen.

IARC (1983) stated that the available data provide no evidence that parathion is likely to present a carcinogenic risk to humans, ie, Group 3. IARC (2017) revised this: there is sufficient evidence for the carcinogenicity of parathion in experimental animals. The overall evaluation is that parathion is possibly carcinogenic to humans (Group 2B).

### Derivation of Maximum Acceptable Value

No MAV.

A health-based value of 0.01 mg/L can be calculated for parathion on the basis of an ADI of 0–0.004 mg/kg body weight based on a NOAEL of 0.4 mg/kg body weight per day in a two-year study in rats for retinal atrophy and inhibition of brain acetylcholinesterase at the next higher dose, and using an uncertainty factor of 100 for interspecies and intraspecies variation (WHO 2017).

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# Penconazole

CAS No. 66246-88-6. The IUPAC name for penconazole is (RS)‑1‑[2‑(2,4‑dichlorophenyl)pentyl]-1H-1,2,4-triazole. The CAS name is 1‑[2‑(2,4‑dichlorophenyl)pentyl]-1H-1,2,4-triazole.

### Maximum Acceptable Value

Penconazole does not have MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Penconazole is a systemic conazole (or triazole) fungicide used to control powdery mildew (on fruit and grapes in New Zealand).

Penconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Penconazole is moderately persistent, exhibiting a soil half-life of two to six months. It shows low leaching properties. Major metabolites are 1,2,4-triazole (CAS No. 288-88-0) and 2-(2,4-dichloro-phenyl)-3-[1,2,4]triazol-1-yl-propionic acid, which are stable and very soluble in water. Many metabolites belong to the 2,4-dichlorophenyl moiety.

The water solubility is about 70 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Penconazole was not carcinogenic in mice or rats, and after reviewing the available in vitro and in vivo short-term genotoxicity data, the JMPR meeting concluded that penconazole was not genotoxic (IPCS 1992). The estimate of acceptable daily intake for humans was 0.03 mg/kg bw on the basis of the NOAEL determined from the one-year study in dogs, which was supported by the NOAEL from the long-term study in rats; a safety factor of 100 was applied.

Penconazole was evaluated for toxicology by JMPR in 1992, when the meeting established an ADI of 0–0.03 mg/kg bw on the basis of a NOAEL of 3 mg/kg bw per day in a one-year study in dogs. In 2015 the ADI was reaffirmed for penconazole and an ARfD was established at 0.8 mg/kg bw (JMPR 2015/2016).

In 2008, the meeting established an ADI of 0–0.2 mg/kg bw for 1,2,4-triazole, based on a NOAEL of 16 mg/kg bw per day in a two-generation reproductive toxicity study in rats. The meeting established an ARfD of 0.3 mg/kg bw for 1,2,4-triazole, based on a NOAEL of 30 mg/kg bw per day in a developmental toxicity study in rabbits. JMPR (2015) reaffirmed these values.

In 2008, the meeting established a group ADI of 0–1.0 mg/kg bw for triazole alanine and triazole acetic acid (alone or in combination), based on a NOAEL of 100 mg/kg bw per day in a developmental toxicity study in rats on triazole alanine. The 2008 meeting concluded that it was unnecessary to establish an ARfD for triazole alanine and triazole acetic acid. The ADI was reaffirmed by JMPR (2015). However, the 2015 JMPR meeting established an ARfD of 3 mg/kg bw for triazole alanine and triazole acetic acid, based on a NOAEL of 300 mg/kg bw per day on the basis of mortality, clinical signs, reduced body weight gain and feed consumption observed early during treatment at 1,000 mg/kg bw per day in a new developmental toxicity study with triazole acetic acid in rats. A safety factor of 100 was used.

EC (2009) established an ADI of 0.03 mg/kg/d bw, and an ARfD of 0.5 mg/kg/d. Reaffirmed by EFSA (2014), and again in 2017; for 1,2,4-triazole, triazole acetic acid and triazole lactic acid the ADI is 0.02 mg/kg/d and the ARfD is 0.06 mg/kg. For triazole alanine the ADI is 0.1 mg/kg/d and the ARfD is 0.1 mg/kg (EFSA 2017). See datasheet for triazole metabolites for latest ADI and ARfD.

The Acceptable Daily Intake (ADI) adopted for penconazole in Australia is 0.007 mg/kg body weight, with a NOEL of 0.71 mg/kg bw.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

Developmental effects were observed in the teratogenicity studies, and the classification ‘Reprotoxic Category 3 R63 Possible risk of harm to the unborn child’ was proposed by the experts. Several plant metabolites were considered to be of the same or lower toxicity than penconazole (EFSA 2008).

### Derivation of Maximum Acceptable Value

No MAV.

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# Pencycuron

CAS No. 66063-05-6. The IUPAC name for pencycuron is 1-(4-chlorobenzyl)-1-cyclopentyl-3-phenylurea. The CAS name is N-[(4-chlorophenyl)methyl]-N-cyclopentyl-N′-phenylurea.

### Maximum Acceptable Value

Pencycuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Pencycuron is a non-systemic contact urea (or phenylurea) fungicide which inhibits mitosis and cell division. It is often used on seed potatoes. It has specific activity against the [plant pathogen](http://en.wikipedia.org/wiki/Plant_pathogen) [Rhizoctonia solani](http://en.wikipedia.org/wiki/Rhizoctonia_solani) for which it was developed. Sometimes used with captan (qv) or imazalil (qv).

Pencycuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Pencycuron is moderately persistent, with a half-life in soils of at least two months. The main metabolite is N-((4-chlorophenyl)-methyl)-N-cyclopentylamide, also called pencycuron-PB-amine.

Adsorption of pencycuron and metabolites is not pH dependent. The UV visible absorption spectrum of pencycuron indicated that direct soil photolysis would not be expected to be a process contributing to the degradation measured in field trials where the test substance was sprayed on the soil surface. In laboratory incubations in dark aerobic natural sediment water systems, pencycuron exhibited medium to high persistence, forming no major metabolites in the water or sediment compartments of the test systems. The test substance partitioned from the water to the sediment phase of the test system reaching its maximum in the sediment (55–79 percent AR) after 30 days (EFSA 2010).

The water solubility is about 0.3 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In subacute and chronic toxicity tests, pencycuron caused weight increase inhibition, increases in liver weight and fattening of the liver cells, but did not show carcinogenicity or mutagenicity.

The compound pencycuron-BP-amine is the main metabolite in rotational crops and in soil, and is a toxicological relevant metabolite. Pencycuron-PB-amine was also found in rat metabolism (8–10 percent recovered in faeces) so its toxicity was considered as adequately covered by the toxicological profile of the parent compound and the reference values established for pencycuron applicable for the consumer risk assessment purpose (EFSA 2010).

The Acceptable Daily Intake (ADI) adopted in Australia for pencycuron is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw.

IUPAC, quoting an EFSA source, refers to an ADI of 0.018 mg.kg bw. EFSA (2012/2017) and EC (2011) report an ADI of 0.2 mg/kg/d with no ARfD being deemed necessary.

For pencycuron-PB-amine the same toxicological reference values as established for pencycuron are applicable. For aniline (a metabolite, mainly from food processing) no ADI or ARfD value has been established at EU level. However, in the framework of a previous assessment, the CEF Panel of EFSA calculated the benchmark dose level causing a 10 percent increase in tumour incidence (BMDL10) that ranged from 29 to 35 mg/kg bw per day (EFSA 2017).

### Derivation of Maximum Acceptable Value

No MAV.

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# Pendimethalin

CAS No. 40487-42-1. The IUPAC name for pendimethalin is N-(1-ethylpropyl)-2,6-dinitro-3,4-xylidine. The CAS name is N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine. Also known as pendamethalin.

### Maximum Acceptable Value

Based on health considerations, the concentration of pendimethalin in drinking-water should not exceed 0.02 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; excursions above the health-based guideline even for a short period are of concern.

Pendimethalin should not contain more than 0.5 mg/kg of N-nitroso-diethylpropylamine, or 60 mg/kg of N-nitroso-pendimethalin.

### Sources to water

Pendimethalin may enter source waters as a result of its application as a selective dinitroaniline pre-emergence herbicide, used against broad-leaf weeds and annual grasses in cereals, maize and vegetable crops. It is also used to control suckers in tobacco. The total annual usage of pendimethalin in New Zealand in the late 1980s was 3,100 kg with the majority of this being in the North Island.

Pendimethalin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Pendimethalin was one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in carrots and oranges. By weight, it is the fourth most heavily used pesticide in the UK as at 2012.

### Forms and fate in the environment

Pendimethalin is a moderately persistent herbicide that can give rise to long lasting metabolites, mainly through photodegradation. Pendimethalin and metabolites bind tightly to soil particles and the leaching potential is negligible. It is lost through photodegradation, biodegradation and volatilisation. Half-lifes in soil range from 30 to 450 days with a recommended average half-life of 90 days. Little is known about its more polar degradation products. Two of the more important metabolites are 4‑[(1‑ethylpropyl)amino]-2-methyl-3,5-dinitrobenzyl alcohol and 3‑[(1‑ethylpropyl)amino]-6-methyl-2,4-dinitrobenzyl alcohol (USEPA 1997). USEPA (1999) states pendimethalin and its 3,5-dinitrobenzyl alcohol metabolite (CL202347) are the only residues of concern.

The field studies measuring degradation in the soil demonstrated that the degradation rate of pendimethalin is slow; the maximum DT90 was estimated being more than a year (EFSA 2013, 2014).

Half-life in water without sediment is about 7–30 days. The water solubility at pH 7 is 0.3 mg/L, and the sorption coefficient is 5,000 mL/g.

NPIC (1994) quotes for pendimethalin a soil half-life of 90 days, water solubility of 0.275 mg/L and a sorption coefficient (soil Koc) of 5,000. This resulted in a pesticide movement to groundwater rating of very low.

USGS (2006) give the following values: log Kow = 5.2; log Koc (where Koc is in mL/g) = 4.13; water solubility = 0.275 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.0899; half-life in aerobic soil = 1,300 days; half-life in water = >200 days.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of pendimethalin (limit of detection = 0.0002 mg/L) (ESR 2001).

WHO (2004) states that pendimethalin has been found rarely in drinking-water in the limited studies available (detection limit 0.00001 mg/L). Pendimethalin was found at a concentration below 0.0001 mg/L in one of 76 drinking-water supplies examined in the Veneto Region in Italy in 1987–88.

Pendimethalin has been found twice in groundwaters in Marlborough and Otago, ranging from 0.00003 to 0.000046 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Pendamethalin occurred at 0.3 µg/L, ie, 0.0003 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Pendamethalin occurred at 0.046 µg/L, ie, 0.000046 mg/L.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Pendamethalin was detected in one well at a concentration of 0.055 µg/L, ie, 0.000055 mg/L.

### Removal methods

WHO (2011/2017) states that concentrations of pendimethalin as low as 0.001 mg/L should be achievable using GAC. Binding tightly to soil particles suggests that any treatment process that removes particulate matter will reduce the concentration of pendimethalin.

### Recommended analytical techniques

#### Referee method

See EFSA (2012).

#### Some alternative methods

No alternative methods have been recommended for pendimethalin because no methods meet the required criteria. See WHO (2003) for further information. Also, the following information may be useful:

Pendimethalin can be determined in water samples by extraction with methylene chloride and analysis by gas chromatography with a nitrogen phosphorus detector (eg, Method EPA 507). Confirmation by a second capillary column with different polarity is strongly recommended. No information on a limit of quantitation is available.

### Health considerations

Pendimethalin appears to be absorbed poorly and excreted rapidly. Following oral administration, about 95 percent is excreted within 24 hours, principally in the faeces. Maximum tissue concentrations were found in the liver and kidney.

Pendimethalin is of low acute toxicity. In a short-term dietary study in rats, a variety of indications of hepatotoxicity as well as increased kidney weights in males were observed at the highest dose level. In a long-term dietary study, some toxic effects (hyperglycaemia in the mouse and hepatotoxicity in the rat) were present even at the lowest dose level.

USEPA (1997) reports a LOEL of 31 mg/kg/day and the NOEL at 10 mg/kg/day. An Uncertainty Factor of 100 was applied to account for interspecies extrapolation and intraspecies variability. The chronic RfD (and cPAD) was calculated to be 0.10 mg/kg body weight/day. The oral RfD had earlier been 0.04 mg/kg/d (USEPA 1991) based on an increase in serum alkaline phosphatase and liver weight, and hepatic lesions in a two-year dog feeding study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.03 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pendimethalin is 0.21 mg/L (no acute one-day value available.)

EC (2003) established an ADI of 0.125 mg/kg/d; an ARfD was not allocated. EFSA (2012, 2013 and 2014) reaffirmed these values.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 12.5 mg/kg bw from a long-term (two-year) dietary study in dogs. The NOEL is based on decreased bodyweight gain and evidence of mild effects on the liver. The ADI incorporates a safety factor of 100.

JMPR (2016) established an ADI of 0–0.1 mg/kg bw, derived from a NOAEL of 12.5 mg/kg bw per day from the two-year study of toxicity in dogs, on the basis of elevated alkaline phosphatase levels and histopathological findings in the liver at 50 mg/kg bw per day. A safety factor of 100 was applied. The meeting established an ARfD of 1 mg/kg bw, derived from a NOAEL of 100 mg/kg bw from an acute neurotoxicity study in rats for a number of clinical signs observed in both sexes at 300 mg/kg bw. A safety factor of 100 was applied.

EFSA (2018) recalculated the dietary risk assessment, taking into account that in the framework of the renewal of the approval EFSA suggested the setting of an acute reference dose (ARfD) of 0.3 mg/kg body weight. They did not mention the ADI.

Pendimethalin does not appear to have significant mutagenic activity. Long-term studies in mice and rats do not provide evidence of carcinogenicity. However, these studies have some important limitations. As at September 2008 the USEPA has classified pendimethalin in Group C: a possible human carcinogen.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV for pendimethalin in drinking-water. The lowest-observable-adverse-effect level used in the derivation is based on slight liver toxicity even at the lowest dose tested (5 mg/kg of body weight) in a long-term rat feeding study.

The MAV for pendimethalin in drinking-water was derived as follows:

5 mg/kg body weight/day x 70 kg x 0.1 = 0.0175 mg/L (rounded to 0.02 mg/L)

2 L/day x 1,000

where:

* lowest-observable-adverse-effect level = 5 mg/kg body weight per day for liver toxicity observed in a two-year rat study
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for the use of a LOAEL instead of a NOAEL an for limitations in the database).

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# Pentachlorophenol

CAS No. 87-86-5. The IUPAC and CAS name is pentachlorophenol. Also called PCP, chlorofen, 1-hydroxypentachlorobenzene, 2,3,4,5,6-pentachlorophenol or chlorophenasic acid.

Usually sold as the sodium salt (sodium pentachlorophenate), CAS No. 131-52-2, or CAS No. 27735-64-4 for the monohydrate salt.

Pentachloroanisole (CAS No. 1825-21-4) is a metabolite; also called methyl pentachlorophenate, pentachloromethoxybenzene or PCA.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of pentachlorophenol in drinking-water should not exceed 0.009 mg/L. Pentachlorophenol is included in the plan of work of the rolling revision of the WHO *Guidelines for Drinking-water Quality*.

The guideline value is considered provisional because of the variations in metabolism between experimental animals and humans.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.001 mg/L. USEPA (2011) lists a life-time health advisory of 0.04 mg/L.

The maximum acceptable concentration in Canada is 0.06 mg/L. Health Canada established an aesthetic objective of 0.03 mg/L, stating that levels above that would render drinking water unpalatable.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.01 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Unpurified technical pentachlorophenol, depending on the manufacturing process, usually contains other chlorophenols (particularly isomeric tetrachlorophenols) and chlorophenoxyphenols, as well as several microcontaminants, particularly polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs). Because of attempts to reduce toxic impurities, various technical preparations may be quite different both temporally and geographically. Chlorophenol preparations in various countries have varied from almost pure PCP to those in which 2,3,4,6‑tetrachlorophenol was the main component, 2,4,6-trichlorophenol concentrations were significant, and PCP accounted for as little as 5 to 10 percent (IARC 1986).

Table 3-2 in ATSDR (2002) lists 15 impurities found in three grades of PCP. Again, tetrachlorophenol was predominant, along with octachlorohydroxydiphenyl ether and nanochlorohydroxydiphenyl ether (all about or exceeding 2 percent).

Pentachlorophenol is one of the “priority pollutants” under the US Clean Water Act.

Pentachlorophenol, its salts and esters were added to the Stockholm Convention list of Persistent Organic Pollutants (POPs); see <http://chm.pops.int/>. PCP appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

Pentachlorophenol is listed as a “priority contaminant” in the Ministry for the Environment’s *Toxicological Intake Values for Priority Contaminants in Soil* (MfE 2011).

### Sources to water

Pentachlorophenol may enter source waters as the result of its use as a timber preservative (broad spectrum insecticide and fungicide), and in antisapstain treatment, often applied as sodium pentachlorophenate and pentachlorophenyl laurate. Some products contained up to 10 percent tetrachlorophenol. It has been used for this purpose during the past 30 to 40 years in New Zealand. Until mid-1988 up to 200 tonnes of pentachlorophenol was used annually, however the use of pentachlorophenol has now virtually ceased in response to environmental and occupational health concerns. The presence of dioxins and dibenzofuran impurities in pentachlorphenol has also contributed to the decline in its usage.

There are no products containing PCP that are currently (2008) approved for use in New Zealand. Although its use has been restricted in New Zealand since 1988, PCP was inadvertently transferred as a single component chemical in the Hazardous Substances (Chemicals) Transfer Notice 2006. Pentachlorophenol does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

As at 2011 there are no registered products containing pentachlorophenol in Australia, but de-registered compounds may still be detected in water.

MfE (2012) developed a national set of soil contaminant standards for 12 priority contaminants and five common land uses; PCP levels range from 55 to 360 mg/kg depending on land use.

Formation of pentachloroanisole in the environment may result from the degradation by micro-organisms of structurally related, commercially important, ubiquitous chlorinated aromatic compounds such as pentachlorophenol and pentachloronitrobenzene which are known rodent toxins or carcinogens. Pentachloroanisole has been known to taint fish flesh. Haloanisoles, including pentachloroanisole, can impart “musty” or “mouldy” off-flavours to wine, other beverages and foods. Haloanisoles are ranked among the most powerful odour compounds, with odour thresholds in the low part-per-trillion range. All haloanisoles have similar odours, but their sensory impact in wine vary with the specific compound and wine characteristics. See trichloroanisole datasheet (organic chemicals section) for more information.

#### 1. From treatment processes

No known sources.

#### 2. From the distribution system

No known sources.

### Forms and fate in the environment

Pentachlorophenol is very persistent in the environment, particularly if adsorbed to sediments. Half-lifes of pentachlorophenol in soil range from 7 to 120 days, pH being an important factor – absorption is maximal in strongly acidic soils. Leaching to groundwater has been observed at some timber treatment sites in New Zealand. Water solubility of PCP is about 80 mg/L, but the sodium salt is highly soluble.

Photolysis and biodegradation are believed to be the dominant transformation processes for pentachlorophenol in aquatic systems. Hydrolysis and oxidation are not important mechanisms for removal of the compound from surface waters. Chemical degradation of pentachlorophenol in water will occur mainly through photo-degradation. In surface water, pentachlorophenol will rapidly photo-degrade when exposed to direct sunlight, with more rapid degradation occurring with increased pH (when the compound is dissociated).

NPIC (1994) quotes for pentachlorophenol a soil half-life of 48 days, water solubility of 10 percent and a sorption coefficient (soil Koc) of 30. This resulted in a pesticide movement to groundwater rating of very high.

If released to soil, pentachlorophenol is expected to have low to no mobility based upon measured Koc values ranging from 1250 for the dissociated form to 25,000 for the undissociated form. The pKa of pentachlorophenol is 4.70, indicating that this compound will almost entirely exist in the anion form in the environment and anions generally do not adsorb more strongly to soils containing organic carbon and clay than their neutral counterparts. Volatilisation from moist soil is not expected because the acid exists as an anion and anions do not volatilise. As much as 55 percent of added pentachlorophenol was photodegraded in a sandy clay loam soil in 14 days, suggesting the photolysis of the dissociated form may be an important terrestrial fate process. Pentachlorophenol may not volatilise from dry soil surfaces based upon its vapour pressure. Screening biodegradability tests give conflicting results; pentachlorophenol does biodegrade but may require several weeks for acclimation. If released into water, pentachlorophenol is expected to adsorb to suspended solids and sediment based upon its measured Koc values. The pKa indicates pentachlorophenol will exist almost entirely in the anion form at pH values of 5 to 9 and therefore volatilisation from water surfaces is not expected to be an important fate process. BCF values from approximately 5 to 5,000 indicate that bioconcentration of pentachlorophenol in aquatic organisms is low to high, with the value being greatly influenced by environmental pH. Bioconcentration is expected to be pH dependent with greater accumulation at lower pH values. Pentachlorophenol is not expected to undergo hydrolysis in the environment due to the lack of functional groups that hydrolyse under environmental conditions. Pentachlorophenol has a pH-dependent absorption maximum of 303 nm and will photodegrade rapidly in surface water when exposed to direct sunlight with a measured half-life of 0.86 hours reported (EAWAG accessed February 2015).

Pentachloroanisole is a persistent degradate and is still found in sediments in US water systems; USGS (2006) gave the following values: log Kow = 5.66; log Koc (where Koc is in mL/g) = 4.62; water solubility = 0.2 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -2.91.

### Typical concentrations in drinking-water

Pentachlorophenol was not detected in any of 320 samples from 161 supplies in New Zealand sampled between 1988 and 1992. The detection limit was between 0.00002 and 0.00004 mg/L (0.02 and 0.04 g/L).

The P2 Chemical Determinand Identification Programme, sampled from 494 zones, did not find any detectable concentrations of pentachlorophenol (limit of detection = 0.0001 mg/L) (ESR 2001).

Concentrations in water samples are usually below 0.01 mg/L, although much higher concentrations in groundwater may be measured under certain conditions (WHO 2004).

105 water utilities in the US reported detecting pentachlorophenol in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.003 mg/L.

The odour threshold in water is 1.6 mg/L (ICPS 1989).

### Removal methods

WHO (2011/2017) states that concentrations of PCP as low as 0.0004 mg/L should be achievable using GAC.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (EPA 525.2).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (APHA 6420B; EPA 515.3).

2. Acetylation Liquid/Liquid Extraction Gas Chromatographic/Mass Spectrometric Method (EPA 1653).

### Health considerations

Food is usually the major source of exposure to PCP unless there is a specific local chlorophenol contamination of drinking-water or exposure from log homes treated with PCP.

In short-term and long-term animal studies, exposure to relatively high pentachlorophenol concentrations has been shown to reduce growth rates and serum thyroid hormone levels and to increase liver weights and liver enzyme activity. Exposure to much lower concentrations of technical pentachlorophenol formulations has been shown to decrease growth rates, increase weights of liver, lungs, kidneys and adrenal glands, increase liver enzyme activity, interfere with porphyrin metabolism and renal function, and alter haematological and biochemical parameters. Microcontaminants appear to be the principal active moieties in the non-acute toxicity of commercial pentachlorophenol.

Chronic exposure to pentachlorophenol may result in a range of adverse health effects in humans including irritation of the skin and mucous membranes, chloracne, neuraesthesia, depression, headaches and changes in kidney and liver function.

The toxicity of pure pentachlorophenol has not been evaluated in humans.

MfE (2011) states: While there appears to be reasonable evidence of carcinogenic effects in humans arising from exposure to PCP, there is weak evidence of genotoxicity and it seems more plausible a non-genotoxic mechanism is responsible for carcinogenic effects. As such, it is recommended that PCP be considered a threshold contaminant, with an additional uncertainty factor of 10 applied to the TDI derived by Baars et al (2001)[[1]](#footnote-1) to account for the observed carcinogenicity of PCP. This TDI is used, as it uses the most sensitive relevant toxicological endpoint (decreased thyroid hormones) from available data and appropriate uncertainty factors. This gives rise to a recommended tolerable daily intake of 0.3 μg/kg bw. Inhalation exposure is likely to be negligible on contaminated sites due to the low volatility of PCP. However, PCP is indicated to be readily absorbed dermally and an absorption factor of 0.24 is recommended. No data is available on food intake of PCP, and no PCP was detected in drinking water supplies. In circumstances where no data is available on background exposure, it has been agreed to allocate 5 percent of TDI allocated to background exposure; as such, background exposure is 0.02 μg/kg bw/day. These criteria (Table S1) are applicable to exposure to PCP only, and are not necessarily protective of effects associated with the contaminants of technical-grade PCP, such as the polychlorinated dibenzo-p-dioxins and polychlorinated dibenzofurans, which should be considered separately.

The reference dose or RfD (USEPA 2006/2009) was 0.03 mg/kg/d (and had been since 1987); the Drinking Water Equivalent Level or DWEL (USEPA 2006/2009) was 1 mg/L. USEPA (2010/2011) lists the RfD as 0.005 mg/L and the DWEL as 0.2 mg/L.

No acceptable daily intake (ADI) or acute reference dose (ARfD) values have been established for pentachlorphenol in Australia.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.005 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.001 mg/kg/day for intermediate-duration oral exposure (15–364 days)
* 0.001 mg/kg/day for chronic-duration oral exposure (>364 days).

Pentachlorophenol has been shown to be fetotoxic, delaying the development of rat embryos and reducing litter size, neonatal body weight and survival, and weanling growth.

Pentachlorophenol is not considered to be teratogenic, although birth defects arose as an indirect result of maternal hyperthermia in one study.

Pentachlorophenol has been shown to be immunotoxic in several animal species. At least part of this effect is caused by pentachlorophenol itself. Neurotoxic effects have also been reported, but the possibility that these are due to microcontaminants has not been excluded.

Pure pentachlorophenol has not been found to be highly mutagenic. The presence of at least one carcinogenic microcontaminant (hexachlorodibenzo-p-dioxin) suggests that the potential for technical pentachlorophenol to cause cancer in laboratory animals cannot be completely ruled out.

IARC classified PCP in Group 2B (the agent is possibly carcinogenic to humans) on the basis of inadequate evidence of carcinogenicity in humans but sufficient evidence in experimental animals. There is suggestive, although inconclusive, evidence of the carcinogenicity of PCP from epidemiological studies of populations exposed to mixtures that include PCP. Conclusive evidence of carcinogenicity has been obtained in one animal species (mice). Although there are notable variations in metabolism between experimental animals and humans, it was considered prudent to treat PCP as a potential carcinogen.

In addition, pentachlorophenol has been classified as a probable human carcinogen (Group B2, or in Group B as at September 2008) by the USEPA, for exposure via the oral route. However, human studies of high exposure groups, such as timber treatment workers, have not provided sufficient evidence of cancer. USEPA (2011) quotes a health advisory of 0.009 mg/L for pentachlorophenol, representing a 10-4 cancer risk; previously it had been 0.006 mg/L.

Pentachlorophenol appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

WHO (2003) stated: in 1990 IARC classified PCP in Group 2B (possibly carcinogenic to humans) because of inadequate evidence of carcinogenicity in humans and sufficient evidence in experimental animals. There is suggestive, although inconclusive, evidence of the carcinogenicity of PCP from epidemiological studies of populations exposed to mixtures including PCP. There is conclusive evidence of carcinogenicity in one animal species, although there are notable variations in metabolism between experimental animals and humans. It was therefore considered prudent to treat PCP as a potential carcinogen.

### Derivation of Maximum Acceptable Value (provisional)

Adequate dose-response data for carcinogenicity are available only from toxicological studies in animals. Based on multistage modelling of tumour incidence in the US NTP bioassay without incorporation of a body surface area correction, although recognising that there are interspecies differences in metabolism, the concentration of PCP associated with a 10-5 excess lifetime cancer risk is similar to the earlier WHO guideline value. Nevertheless, the WHO provisional guideline value of 0.009 mg/L was adopted in the DWSNZ (2005 and the 2008 revision) as a provisional MAV.

The 2000 and earlier DWSNZ MAVs were based on the information in the datasheet in the 1995 Guidelines, using a tolerable daily intake approach for the derivation of the PCP provisional MAV (which was based on the WHO 1993 Guidelines), as follows:

3 mg/kg body weight/day x 70 kg x 0.1 = 0.01 mg/L

2 L/day x 1,000

where:

* no observable adverse effect level = 3 mg/kg body weight per day from reproductive studies in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for potential carcinogenicity of technical PCP).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for pentachlorophenol is 0.001 mg/L.

The USEPA established an organoleptic effect criterion of 0.03 mg/L for pentachlorophenol. Source: [*Quality Criteria for Water*, 1986 (“Gold Book”)](http://nepis.epa.gov/Exe/ZyPDF.cgi?Dockey=00001MGA.txt), <http://www.epa.gov/wqc/national-recommended-water-quality-criteria-organoleptic-effects>.

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# Penthiopyrad

CAS No. 183675-82-3. The IUPAC name for penthiopyrad is (RS)-N-[2-(1,3-dimethylbutyl)-3-thienyl]-1-methyl-3-(trifluoromethyl)pyrazole-4-carboxamide. The CAS name is N-[2-(1,3-dimethylbutyl)-3-thienyl]-1-methyl-3-(trifluoromethyl)-1H-pyrazole-4-carboxamide. Penthiopyrad is a 50:50 racemic mixture of R and S enantiomers.

### Maximum Acceptable Value

Penthiopyrad does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Penthiopyrad is a broad spectrum pyrazole, carboxamide or amide fungicide, commonly used to control foliar and soil-borne fungal diseases, acting by stopping spore germination, and inhibiting mycelium growth and sporulation on a wide range of fruit and vegetable crops.

Penthiopyrad appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Penthiopyrad DT50 and DT90 in aerobic soils were 65.3 to 356 and 217 to >1,000 days, respectively. For the main metabolite (DM-PCA), the DT50 and DT90 were 36 to 168 and 121 to 558 days, respectively (APVMA 2012). These values come down to a few days in sunlight, but increased in anaerobic conditions. Penthiopyrad in water is photolytically and hydrolytically stable. In river and pond aerobic aquatic systems, penthiopyrad steadily dissipated from the water phase to the sediment.

Penthiopyrad is considered to show low mobility in soils but its metabolites show medium to high mobile so may possibly contaminate groundwater (EFSA 2013).

Water solubility (20°C) is about 2.5 mg/L at pH 4 and 1.4 mg/L at pH 7. The partition coefficient (20°C) in water is log Pow = 4.5 from pH 4 to 10. Henry’s Law constant is 4.15 x 10-4 Pa m3 mol-1 at pH4; 1.40 x 10-4 Pa m3 mol-1 at pH 5; 7.66 x 10-3 Pa m3 mol-1 at pH 7, and 6.36 x 10-3 Pa m3 mol-1 at pH 10. Penthiopyrad is hydrolytically stable over five days at 50°C in the pH range 4 to 9, and photolytically stable over 15 days at 25°C and pH 7 (JMPR 2012) – which also tabulates known metabolites.

### Removal methods

Treatment processes that removal particulate matter should reduce the concentration of penthiopyrad.

### Health considerations

Penthiopyrad is extensively and rapidly absorbed and widely distributed. Oral absorption is estimated to be greater than 83 percent. There is no evidence for accumulation. Excretion of penthiopyrad is predominantly through the bile/fecal route but with appreciable amounts excreted in urine. Low acute toxicity is observed when penthiopyrad is administered by the oral, dermal and inhalation routes to rats (EFSA 2013).

The FAO/WHO 2011 meeting established an acceptable daily intake (ADI) of  
0–0.1 mg/kg bw on the basis of a NOAEL of 11 mg/kg bw per day in the multigeneration reproduction study in rats for decreased body weight gain in F1 males and adrenal effects in F1 females (increased weight and cortical hypertrophy). A safety factor of 100 was applied. The meeting also established an acute reference dose (ARfD) of 1 mg/kg bw on the basis of a NOAEL of 125 mg/kg bw in the acute neurotoxicity study in rats for clinical signs of neurotoxicity (eg, decreased motor activity and body temperature, hunched posture, unsteady gait). A safety factor of 100 was applied.

APVMA (2012) established the ADI at 0.1 mg/kg bw/d (rounding down) using the lowest NOAEL of 11 mg/kg bw/d from a two-generation reproduction toxicity study in rats based on reduced body weight gain in F1 adult males, increased liver weight in P and F1 adult females and increased adrenal weight with increased incidence. The ARfD is established at 0.75 mg/kg bw using a default safety factor (SF) of 100 to account for potential intraspecies (SF of 10) and interspecies (SF of 10) variation. In February 2017 this ARfD was adjusted to 1 mg/kg based on acute oral neurotoxicity rat study – a NOAEL of 125 mg/kg bw was based on clinical signs (decreased motor activity, decreased body temp, hunched position and unsteady gait) at the next higher dose (<https://apvma.gov.au/>).

EFSA (2013) and EC (2013) quote the same ADI and ARfD as APVMA (2012). EFSA (2016) confirmed these values and added that for the PAM metabolite the ADI is 0.0024 mg/kg/d and the ARfD is 0.024 mg/kg/d, and for the 753-A-OH metabolite, peer review experts concluded that it is of a similar toxicity as the parent.

JPMR (2012) established an Acceptable Daily Intake (ADI) of 0–0.1 mg/kg bw/day for penthiopyrad and quotes an ARfD of 1 mg/kg bw. Reaffirmed in JMPR (2013) and FAO/WHO (2013).

USEPA (2012) quotes a chronic RfD (and cRfD) of 0.27 mg/kg/d, and an ARfD (and aPAD) of 1.25 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for penthiopyrad is 12.5 mg/L. They add that penthiopyrad shows “suggestive evidence of carcinogenicity” based on liver tumours in male mice. The dose and non-cancer endpoint selected for chronic dietary exposure (cRfD) are protective of potential cancer effects.

Penthiopyrad is not considered to be a carcinogenic hazard to humans. Penthiopyrad was not a reproductive or developmental toxicant, and tested negative in vitro and in vivo in a battery of mutagenicity and/or genotoxicity studies. Additionally, the available data was not considered to demonstrate a neurotoxic or immunotoxic potential. Metabolites are of low acute toxicity (APVMA 2012).

### Derivation of Maximum Acceptable Value

No MAV.

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# Permethrin

CAS No. 52645-53-1. The IUPAC name for permethrin is 3-phenoxybenzyl (1RS,3RS;1RS,3SR)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate, or 3‑phenoxybenzyl (1RS)-cis, trans-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate. The CAS name is (3-phenoxyphenyl)methyl 3‑(2,2‑dichloroethenyl)-2,2-dimethylcyclopropanecarboxylate. It is a mixture of four stereo-isomers.

Some subsets of isomers of this substance have their own ISO common name, eg, [biopermethrin](http://www.alanwood.net/pesticides/biopermethrin.html) and [transpermethrin](http://www.alanwood.net/pesticides/transpermethrin.html) but these do not appear to be used as such in New Zealand.

Permethrin, a Type I synthetic pyrethroid, is a mixture of four stereoisomers of the (1R, trans isomer called biopermethrin, CAS No. 51877-74-8) (1R, cis) (1S, trans isomer called transpermethrin, CAS No. 52341-32-9) and (1S, cis) configurations. In most technical products, the cis:trans ratio is about 2:3, and the 1R:1S ratio is 1:1 (racemic). The composition ratio of the above isomers is about 3:2:3:2 (IPCS, 1990). Of the four isomers, the (1R, cis) and the (1R, trans) isomers are the two esters primarily responsible for insecticidal activity. The term permethrin is used here to refer to material with a cis:trans ratio of 2:3, unless otherwise stated. JMPR (2008) refers to 40:60 cis/trans permethrin.

### Maximum Acceptable Value

WHO (17) did not establish a guideline value because permethrin is not recommended for direct addition to drinking-water as part of WHO’s policy to exclude the use of any pyrethroids for larviciding of mosquito vectors of human disease.

In DWSNZ 1995, 2000 and 2005, the provisional MAV for permethrin in drinking-water had been 0.02 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.2 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The USEPA concluded on 22 September 2009 that permethrin is known or anticipated to occur in PWSs and may require regulation. Therefore they added permethrin to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009a).

One study reported an organoleptic threshold in water of 0.2 mg/L; however, permethrin is not an aesthetic determinand.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for permethrin in water (set by an approval under Part 5 of the HSNO Act) of 0.0001 mg/L (1 µg/L).

### Sources to water

Permethrin may enter source waters as a result of its application as a contact insecticide, commonly used as a fast acting neurotoxin against mosquitoes and flies. It is used against a wide range of pests in the home, agriculture, forestry and public health, treatment of textile fibres (eg, moths), wood preservation (eg borer), and may be used to protect stored grain. With d-phenothrin, it is recommended for use in aircraft disinsection (WHO 2013); d-phenothrin (2 percent) for space spraying and permethrin (2 percent) for residual disinsection. They are used together in New Zealand and Australia as at 2014 (MPI 2014).

The total annual usage of permethrin in New Zealand in the late 1980s was 3,400 kg with the majority of use being in the North Island. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Permethrin was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in lettuce.

Concentrations of permethrin as high as 0.8 mg/L have been recorded in surface water (WHO 2005).

#### 1. From the distribution system

Permethrin had been a WHOPES recommended larvicide used to control aquatic invertebrates in water mains and containers. WHO (2011) now states that:

“adding permethrin directly to drinking-water for public health purposes is not recommended by WHO, as part of its policy to exclude the use of any pyrethroids for larviciding of mosquito vectors of human disease. This policy is based on concern over the possible accelerated development of vector resistance to synthetic pyrethroids, which, in their application to insecticide-treated mosquito nets, are crucial in the current global anti-malaria strategy”.

### Forms and fate in the environment

Permethrin is photodegraded in water and on soil surfaces. In soil permethrin binds strongly to soil; it degrades rapidly by hydrolysis and microbial degradation. The half-life in soils ranges from 6 to 105 days with a recommended average half-life of about 30–40 days. The trans isomer degraded more rapidly than the cis isomer, with ester cleavage being the major initial degradative reaction. The compounds generated by ester cleavage were then further oxidised, eventually yielding CO2 as the major terminal product. USEPA (2009) states that for tolerance expression and risk assessment, the parent (both cis-and trans-permethrin) is the only residue of concern for both plants and livestock, and drinking water exposure.

Permethrin disappears rapidly from the environment: in 6 to 24 hours from ponds and streams; in seven days from pond sediment; and in 58 days from foliage and soil in forests. Thirty percent of the compound was lost within one week from cotton leaves in a field (IPCS 1989). In water, permethrin is broken down by photolysis into 3‑phenoxybenzyl alcohol and dichlorovinyl acid (NPIC).

The water solubility of permethrin is 0.006 mg/L in some references and 0.2 mg/L in others. Studies to investigate the leaching potential of permethrin and its degradates showed that very little downward movement occurs in soils.

Octanol-Water Partition Coefficient (Kow): 6.1 at 20°C. Henry’s constant: 1.4 x 10-6 atm·m3/mol; 5.1 x 10-13 atm mole/m3. Soil Sorption Coefficient (Koc): 1 x 105.

NPIC (1994) quotes for permethrin a soil half-life of 30 days, water solubility of 0.006 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

If released to soil, permethrin is expected to have no mobility based upon a Koc range from 10,471 to 86,000. Volatilisation from moist soil surfaces is possible based upon an estimated Henry’s Law constant of 2.4 x 10-6 atm-cu m/mole. However, adsorption to soil is expected to attenuate soil volatilisation. Permethrin degrades in soil through biodegradation and abiotic hydrolysis. Direct photolysis can occur on soil surfaces exposed to sunlight. Trans-permethrin has been shown to degrade faster in soil and sediment than the cis-isomer. Field dissipation half-lifes for permethrin generally fall in the range from 6 to 106 days. Under aerobic conditions, the field dissipation half-life is roughly 30 days (4 to 40-day range) and under anaerobic conditions, the field dissipation half-life is roughly 108 days (3 to 204-day range). If released into water, permethrin is expected to adsorb to suspended solids and sediment based upon its Koc values. Volatilisation from water surfaces is possible based on its estimated Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 39 days and 289 days, respectively. However, volatilisation from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. BCF values for rainbow trout and sheepshead minnow of approximately 560 and 480, respectively, suggest bioconcentration in aquatic organisms is high. At pH 4, pH 5 and pH 7 (25°C), permethrin is stable towards abiotic hydrolysis; at pH 9, the abiotic hydrolysis half-life is in the range of 37 to 50 days. The direct photolysis half-life in water is about 23 to 37 days. Reaction with photo-oxidant species in natural waters can decrease the photodegradation half-life. The biodegradation half-life of permethrin in a sediment-seawater solution was less than 2.5 days (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of permethrin (limit of detection = 0.0002 mg/L) (ESR 2001).

When permethrin is used to control aquatic invertebrates in water mains, concentrations of about 0.01 mg/L will be present in the water for short periods.

### Removal methods

Because it is strongly attracted to particles, coagulation and many filtration processes should remove permethrin readily. Under normal disinfection conditions, chlorine does not react with either isomer.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

#### Some alternative methods

Gas–liquid chromatography with a flame ionisation detector.

### Health considerations

Exposure of the general population to permethrin is mainly via the diet.

Permethrin is absorbed readily when given orally. Distribution occurs rapidly in the body, mostly to adipose tissue, followed by liver, kidney and brain. Permethrin administered to mammals is almost completely eliminated from the body within several days.

Permethrin has a low acute oral toxicity in mammals. The cis-isomer is the more toxic form. Oral toxicities of the major metabolites of permethrin are lower than those of the parent compound. The major signs of acute intoxication are effects on the central nervous system, consisting of uncoordinated movements, whole body tremors, and loss of balance. Overt signs of toxicity do not appear until near-lethal doses.

Forestry workers using permethrin reported symptoms including itching and burning of the skin and itching and irritation of the eyes. Paraesthesia (sensation abnormality) was induced in volunteers about 30 minutes after the application of permethrin solution (total 0.5 mg) to the earlobe. Of 10 volunteers treated with 15–40 mL of a permethrin (1:3) (1 percent) head louse solution, three developed mild, patchy erythema (skin reddening), which faded 4–7 days later.

The cis:trans isomer ratio of permethrin can influence certain hazard characteristics. For example, the acute oral LD50 of 80:20 cis:trans permethrin to rats (220 mg/kg bw) is lower than that of 20:80 cis:trans permethrin (6,000 mg/kg bw), although the acute RfD and ADI apply to all ratios of permethrin isomers (JMPR 2008). The ADI of  
0–0.05 mg/kg bw, previously set by the JMPR in 1987 was extended from 40:60 permethrin to include 25:75 permethrin, and an acute RfD of 1.5 mg/kg bw was subsequently allocated.

USEPA (2009) quotes a chronic dietary RfD of 0.25 mg/kg/d based on an oral NOAEL of 25 mg/kg/d. The oral RfD had earlier been 0.05 mg/kg/d (USEPA 1992). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.25 mg/kg/d, and an ARfD of 0.25 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for permethrin is 2.50 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw from a two-year dietary study in rats and a one-year oral dosing study in dogs. This NOEL is based on neurotoxic effects including tremors, incoordination and convulsions. The ADI incorporates a safety factor of 100. WHO (2013) repeats these values.

Dietary permethrin does not appear to affect reproduction adversely in rats or mice.

ECHA (2014) discussed two relevant metabolites: 3-(2,2-dichlorovinyl)-2,2-dimethyl-(1-cyclopropane)carboxylate (DCVA) and 3-phenoxybenzoic acid (PBA), concluding that any risk identified is significantly lower than that due to permethrin itself.

Permethrin has not exhibited mutagenic activity in a range of short-term mutagenicity assays. JMPR concluded that technical-grade permethrin is not a reproductive or developmental toxin.

The International Agency for Research on Cancer has classified permethrin in Group 3 (not classifiable as to its carcinogenicity to humans), as there are no human data and only limited data from animal studies. Permethrin is not genotoxic. As at May 2002 the USEPA had classified permethrin in Group C: a possible human carcinogen, but in September 2008 they described it as “likely to be carcinogenic to humans”.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.3 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.2 mg/kg/day for intermediate-duration oral exposure (15–364 days).

USEPA (2015) found that based on the available in vitro and mammalian in vivo data, there appears to be a potential interaction with permethrin and the androgen pathway in mammals. There is no convincing evidence of potential interaction with the estrogen or thyroid pathways in mammals or wildlife.

### Derivation of Maximum Acceptable Value

WHO (2005) stated that concentrations of permethrin in drinking-water are usually far below levels of health concern. It is therefore not considered necessary to derive a health-based guideline value where permethrin is not added directly to water as a larvicide.

For guidance purposes, a health-based value can be determined from the ADI of  
0–0.05 mg/kg of body weight, established for technical-grade permethrin with cis:trans ratios of 25:75 to 40:60 on the basis of a NOAEL of 5 mg/kg body weight per day in a two-year dietary study in rats, which was based on clinical signs and changes in body and organ weights and blood chemistry at the next higher dose, and a NOAEL of 5 mg/kg body weight per day in a one-year study in dogs, based on reduced body weight at 100 mg/kg body weight per day, and applying an uncertainty factor of 100 for interspecies and intraspecies variation. Assuming a 60 kg adult drinking two litres of water per day and allocating 20 percent of the upper limit of the ADI to drinking-water, a health-based value of 0.3 mg/L can be derived (WHO 2011a/2017).

In the 1995, 2000 and 2005 DWSNZ, the provisional MAV had been derived as follows:

A tolerable daily intake approach has been used for the derivation of a MAV for permethrin in drinking-water. In 1987, Joint FAO/WHO Meetings on Pesticide Residues (JMPR) recommended an acceptable daily intake for 2:3 and 1:3 cis:trans-permethrin which has been used in the derivation of the MAV given below. It is based on a two-year dietary study in rats that observed clinical signs and changes in body and organ weights and blood chemistry, and from a one-year study in dogs, based on reduced body weight.

5 mg/kg body weight/day x 70 kg x 0.01 = 0.0175 mg/L (rounded to 0.02 mg/L)

2 L/day x 100

where:

* no observable adverse effect level = 5 mg/kg body weight per day for obtained in a two-year rat study
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.01
* uncertainty factor = 100 (for inter and intra-species variation).

If permethrin is to be used for short periods as a larvicide for the control of mosquitos and other insects of health significance in drinking-water sources, the share of the ADI allocated to drinking-water may be increased to 20 percent. In such cases, the guideline value would be 0.3 mg/L (0.4 mg/L for 70 kg body weight).

Adding permethrin directly to drinking-water for public health purposes is not recommended by WHO, as part of its policy to exclude the use of any pyrethroids for larviciding of mosquito vectors of human disease. This policy is based on concern over the possible accelerated development of vector resistance to synthetic pyrethroids, which, in their application to insecticide-treated mosquito nets, are crucial in the current global malaria strategy.

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# Phenmedipham

CAS No. 13684-63-4. The IUPAC name for phenmedipham is methyl 3‑(3‑methylcarbaniloyloxy)carbanilate or 3-methoxycarbonylaminophenyl 3‑methylcarbanilate. The CAS name is 3-[(methoxycarbonyl)amino]phenyl (3‑methylphenyl)carbamate. Also called methyl-m-hydroxycarbanilate-m-methylcarbanilate.

### Maximum Acceptable Value

Phenmedipham does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Phenmedipham is a non-systemic selective post-emergence contact carbanilate (carbamate) herbicide, mainly used on beets to control annual broadleaf weeds and annual grasses. Toluene with maximum content of 2 g/kg, 3-methylaniline and 3‑aminophenol with a maximum content of 1 g/kg each are considered relevant impurities. It seems to be sold in New Zealand as a mixture with desmedipham (qv).

Phenmedipham appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Form and fate in the environment

In soil, 71–86 percent of the amount determined one day after treatment was degraded in 90 days, mainly to methyl-3-hydroxycarbanilate. Phenmedipham remains in the top layers of soil (0 to 2 inches) after application. The half-life of phenmedipham in various soils ranges from 6 to 40 days. No groundwater contamination is expected. EFSA (2014) states that the soil degradation rate of phenmedipham is moderate: the maximum DT90 was 133 days; metabolites MHPC and APMP [m-aminophenyl-N-(3-methylphenyl) carbamate] are 121 and 231 days respectively.

The half-life in water is usually measured at less than one day. The main degradation product is MHPC (methyl-3-hydroxyphenyl carbamate – CAS No. 13686-89-1). Other degradation products include 3-aminophenol and 3-methoxycarbonylaminophenol (CAS No. 13683-89-1). For others, see EFSA (2014).

Water solubility is about 2–5 mg/L at pH 3 or 4; it decomposes at a neutral or alkaline pH.

NPIC (1994) quotes for phenmedipham a soil half-life of 30 days, water solubility of 4.7 mg/L and a sorption coefficient (soil Koc) of 2,400. This resulted in a pesticide movement to groundwater rating of very low.

### Analytical methods

#### Referee method

No MAV in the DWSNZ.

### Health considerations

Phenmedipham distributes widely through the body with highest residues found in the blood. The metabolites 3-aminophenol and 3-aminotoluene may be of special toxicological concern. Phenmedipham shows no indication of carcinogenicity. Although phenmedipham is a carbamate, it is not a cholinesterase inhibitor.

The ADI derived by the EC (2004) is 0.03 mg/kg bw; an ARfD was considered to be unnecessary. EFSA (2014, 2018) reaffirmed these values.

The RfD is 0.25 mg/kg bw based on a NOAEL of 25 mg/kg/d dervided from a two-year feeding and carcinogenicity study using rats, and an uncertainty factor of 100 (USEPA 1990). USEPA (2005) quotes a chronic RfD of 0.24 mg/kg/d based on a NOAEL of 24 mg/kg/d from a combined chronic toxicity/cancer study on the rat, observing hemolytic anemia in both sexes, decreased body weight/body weight gain and food efficiency in females, increased renal pelvic epithelial hyperplasia and mineralisation in males. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.24 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for phenmedipham is 1.68 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia (as at December 2008) for phenmedipham was 0.01 mg/kg body weight, with a NOEL of 1.5 mg/kg bw. By 2011 this was changed to 0.03 mg/kg body weight, with a NOEL of 3.4 mg/kg bw. An ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose.

### Derivation of Maximum Acceptable Value

No MAV.

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# d-Phenothrin

CAS No. for racemic phenothrin is 26002-80-2; no CAS No. allocated for d-phenothrin. The IUPAC name is 3-phenoxybenzyl (1RS,3RS;1RS,3SR)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate, or 3-phenoxybenzyl (1RS)-cis-trans-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate, or 3-phenoxybenzyl (±)-cis-trans-chrysanthemate. The CAS name is (3-phenoxyphenyl)methyl 2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate.

Phenothrin is normally sold as d-phenothrin, which is a mixture of the two isomers (from the total of four) that have the highest activity. The CAS No. for the (1 R)‑cis‑isomer is 51186-88-0. The CAS No. for the (1 R)-trans-isomer is 26046-85-5. Racemic phenothrin is no longer produced.

Refer also to the pyrethrin and pyrethroids datasheet.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for d-phenothrin in water (set by an approval under Part 5 of the HSNO Act) of 0.3 ng/L (0.0003 µg/L).

### Sources to water

Despite the preceding paragraph, d-phenothrin does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

d-Phenothrin is recommended for use in aircraft disinsection (WHO 2013); d‑phenothrin (2 percent) for space spraying and permethrin (2 percent) for residual disinsection.

### Forms and fate in the environment

Phenothrin is one of the least persistent pyrethroids. d-Phenothrin is degraded in the environment primarily through UV light reactions. In upland conditions, the half-life of d-phenothrin in the soil is 1–2 days. In flood conditions, the half-life of d-phenothrin in the soil ranged from two weeks up to two months. d-Phenothrin has low water solubility (2 mg/L) and binds tightly to soil. Based on these properties, d-phenothrin is relatively immobile in soil and its potential to contaminate groundwater is low. In anaerobic conditions, d-phenothrin is stable to hydrolysis at all pH values with an anaerobic aquatic half-life of 173 days. With exposure to sunlight, such as in clear shallow water, d-phenothrin is readily degraded through aqueous photolysis with a half-life of 6.5 days (NPIC). Octanol-Water Partition Coefficient (log Kow): 6.0. Henry’s constant: 6.8 x 10-6 atm·m3/mol. Soil Sorption Coefficient (Koc): 1.25 to 1.4 x 105.

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The JMPR concluded that: “Data presented indicate the similarity in metabolism and toxicity of phenothrin and d-phenothrin, thus indicating that data for phenothrin can be used to support the toxicological data base for d-phenothrin”.

NPIC quotes an acute RfD of 0.03 mg/kg/d for d-phenothrin, and 0.007 mg/kg/d chronic RfD.

The Acceptable Daily Intake (ADI) adopted in Australia for phenothrin is 0.02 mg/kg body weight, with a NOEL of 2.5 mg/kg bw. The ADI adopted by JMPR for d‑phenothrin is 0.05 mg/kg/d. ARfDs were not allocated.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.007 mg/kg/d, and an ARfD of 0.03 mg/kg/d for d-phenothrin. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for d-phenothrin is 0.99 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

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# Phenylphenol

CAS No. 90-43-7. The IUPAC name for phenylphenol is biphenyl-2-ol. The CAS name is [1,1′-biphenyl]-2-ol. Also called 2-phenylphenol, orthophenyl phenol, ortho-xenol, 2‑hydroxybiphenyl, 2-hydroxy-1,1′-biphenyl, 2-biphenylol, biphenyl-2-ol and OPP.

The sodium salt is called sodium o-phenylphenate, CAS No. 132-27-4; sometimes abbreviated to SOPP.

### Maximum Acceptable Value

WHO 2004/2011/2017 states that phenylphenol occurs in drinking-water at concentrations well below those at which toxic effects are observed.

WHO (2017) derived a health-based value of 1 mg/L.

In DWSNZ 2005, the provisional MAV for phenylphenol in drinking-water had been 1.4 mg/L.

### Sources to water

2-Phenylphenol is used as a disinfectant, bactericide, fungicide and virucide. In agriculture, it is used in disinfecting fruits, vegetables and eggs. It is also used as a general surface disinfectant in hospitals (eg, in antibacterial soaps), nursing homes, veterinary hospitals, poultry farms, dairy farms, piggeries, commercial laundries, barbershops, seed boxes and food processing plants. Phenylphenol is also used as an intermediate for dyes, resins and rubber chemicals.

Orthophenyl phenol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Form and fate in the environment

Orthophenylphenol (and its salts, collectively) is stable and persistent in abiotic aqueous media at pHs 5, 7 and 9. When exposed to sunlight in neutral aqueous medium, it degrades with a half-life of 14 days. Photolytically, therefore, it is not stable. Exposure to UV light (at 253.7 nm), results in the degradation products: phenyl benzoquinone, phenylhydroquinone, and 2-hydroxy benzofuran. 2-Methoxybiphenyl is another metabolite. The major degradation route appears to be through biodegradation in aerobic and anaerobic environments. The observed half-life values vary from three hours to three weeks, depending on the exposure site (holding pond to open river etc) (USEPA 2006).

Groundwater contamination does not seem likely. 2-Phenylphenol is degraded readily in surface waters, with a half-life of about 1 week in river water. Water solubility of phenylphenol is about 700 mg/L; the solubility of sodium o-phenylphenate is about 53 percent.

EC (2002) quotes an octanol-water partition coefficient (log Kow) of 3.18, an organic carbon water partition coefficient (Koc) of 2.5, and Henry’s Law Constant of 4.35 x 10-4 to 4.24 x 10-3 Pa-m3 mol-1 (4.41 x 10-9 to 4.3 x 10-8 atm-m3 mol-1).

If released to soil, o-phenylphenol is expected to be immobile based upon an estimated Koc of 6,700. Volatilisation from moist soil surfaces may be an important fate process based upon a Henry’s Law constant of 1.5 x 10-6 atm-cu m/mole. o‑Phenylphenol is not expected to volatilise from dry soil surfaces based upon its vapour pressure. Utilising the Japanese MITI test, o-phenylphenol reached 47 to 86 percent of its theoretical BOD in two weeks indicating that biodegradation may be an important environmental fate process. If released into water, o-phenylphenol is expected to adsorb to sediment and suspended solids in water based upon the estimated Koc. Biodegradation in water is expected based on a 50 percent reduction of o-phenylphenol concentration within one week in river water. Volatilisation from water surfaces may occur based on its Henry’s Law constant. However, volatilisation from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. An estimated BCF of 51 suggests the potential for bioconcentration in aquatic organisms is moderate. Hydrolysis is not expected to occur due to the lack of hydrolysable functional groups (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Phenylphenol has been found in Marlborough groundwater at 0.0001 mg/L (MAF 2006, who added that phenylphenol is a general breakdown product).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Phenylphenol occurred at 0.1 µg/L ie at 0.0001 mg/L.

### Analytical methods

#### Referee method

None in DWSNZ.

#### Some alternative methods

See WHO (2003) for further information.

### Health considerations

2-Phenylphenol has been determined to be of low toxicity.

The 1999 JMPR decided that an acute RfD is unnecessary. JMPR (2002) quotes an ADI of 0.4 mg/kg bw.

USEPA (2006) quotes a chronic RfD of 0.39 mg/kg/d based on a NOAEL of 39 mg/kg/d from combined oral toxicity/carcinogenicity study in rats; the study indicated decreased body weight, body weight gain, food consumption and food efficiency, increased clinical and gross pathological signs of toxicity at the LOAEL of 200 mg/kg/day.

The Acceptable Daily Intake (ADI) adopted in Australia for ortho-phenylphenol is 0.4 mg/kg body weight. An ARfD was considered unnecessary.

EC (2010) established an ADI of 0.4 mg/kg/d and considered that an ARfD was unnecessary. EFSA (2017) reaffirmed the ADI, and also deemed an acute reference dose (ARfD) was not necessary.

Both 2-phenylphenol and its sodium salt are carcinogenic in male rats, and 2‑phenylphenol is carcinogenic in male mice. However, urinary bladder tumours observed in male rats and liver tumours observed in male mice exposed to 2‑phenylphenol appear to be threshold phenomena that are species- and sex-specific. The IARC concluded that there is limited evidence in experimental animals for the carcinogenicity of ortho-phenylphenol, but there is sufficient evidence in experimental animals for the carcinogenicity of sodium ortho-phenylphenate. JMPR has concluded that 2-phenylphenol is unlikely to represent a carcinogenic risk to humans. Although a working group convened by IARC has classified the sodium salt of 2-phenylphenol in Group 2B (possibly carcinogenic to humans) and 2-phenylphenol in Group 3 (not classifiable as to its carcinogenicity to humans), JMPR noted that the IARC classification is based on hazard identification, not risk assessment, and is furthermore limited to published literature, excluding unpublished studies on toxicity and carcinogenicity. JMPR also concluded that there are unresolved questions about the genotoxic potential of 2-phenylphenol.

This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008. However, ECHA (2015) states that biphenyl-2-ol is not genotoxic, mutagenic, reproductive or a developmental toxicant.

USEPA (2015) found that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for o-phenylphenol since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

Phenylphenol is on the EC List (Annex 15) of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2002).

### Derivation of Maximum Acceptable Value

WHO (2017) stated that a health-based value of 1 mg/L can be calculated for 2‑phenylphenol on the basis of an ADI of 0–0.4 mg/kg body weight, based on a NOAEL of 39 mg/kg body weight per day in a two-year toxicity study on the basis of decreased body weight gain and hyperplasia of the urinary bladder and carcinogenicity of the urinary bladder in male rats, using an uncertainty factor of 100 for interspecies and intraspecies variation. Because of its low toxicity, however, the health-based value derived for 2-phenylphenol is much higher than concentrations of 2-phenylphenol likely to be found in drinking-water. Under usual conditions, therefore, the presence of 2-phenylphenol in drinking-water is unlikely to represent a hazard to human health. For this reason, the establishment of a formal guideline value for 2-phenylphenol is not deemed necessary.

The MAV (provisional) for phenylphenol in drinking-water had been derived in the DWSNZ (2005) as follows; WHO (2011) now calls this a health-based value:

39 mg/kg body weight per day x 70 kg x 0.1 = 1.365 mg/L (rounded to 1.4 mg/L)

2 L x 100

where:

* no observable adverse effect level = 39 mg/kg body weight per day in a two-year toxicity study for decreased body weight gain and hyperplasia of the urinary bladder and carcinogenicity of the urinary bladder in male rats
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult per day = 2 L
* uncertainty factor = 100 for intra- and interspecies variation.

WHO (2004) states that because of its low toxicity, the health-based value derived for 2-phenylphenol is much higher than 2-phenylphenol concentrations likely to be found in drinking-water. Under usual conditions, therefore, the presence of 2-phenylphenol in drinking-water is unlikely to represent a hazard to human health. For this reason, the establishment of a guideline value for 2-phenylphenol is not deemed necessary.

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# Phorate

CAS No. 298-02-2. The IUPAC and CAS name for phorate is O,O-diethyl S‑ethylthiomethyl phosphorodithioate. Also called 5-phosphane and thimet (a trade name).

### Maximum Acceptable Value

WHO (2004 and 2011) states that phorate is unlikely to occur in drinking-water, so did not develop a guideline value for drinking-water.

The maximum acceptable concentration for phorate in Canada is 0.002 mg/L.

### Sources to water

Phorate, an organophosphorus compound, is a broad spectrum insecticide, nematicide and acaricide that controls pests by systemic, contact, and fumigant action. It is used against sucking and chewing insects, leafhoppers, leafminers, mites, some nematodes and rootworms. Phorate is used in pine forests and on root and field crops, including corn, cotton, coffee, some ornamental and herbaceous plants and bulbs, usually at the time of planting.

Phorate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 6.3 tonnes of phorate were used in New Zealand in 2004, at an application rate of 2,200 grams of active ingredient per hectare. After 1 July 2016 phorate was no longer able to be manufactured in or imported into New Zealand.

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Phorate should not contain more than 2 g/kg of sulfotep.

### Forms and fate in the environment

In the environment, phorate is degraded by micro-organisms and interaction with water. Phorate itself is not persistent in plants. However, phorate protects plants for a long time because its breakdown product persists in plants and soils.

Phorate binds to soil organic matter and clay particles and is almost immobile in soils. Thus, it does not leach easily and is transported mainly with run-off via sediment and water. Phorate has some potential, though minimal, to leach through the soil and contaminate groundwater, particularly where soils are sandy and aquifers are shallow.

Phorate is moderately persistent in the soil. Its half-life under aerobic laboratory conditions is 82 days, while a field study noted a half-life of 7.5 days. It is least persistent in clay soil, while it is slowly released from peat/sand and sandy soils. Phorate disappears almost completely from sand/muck soils within one year.

Based on environmental fate data, hydrolysis and microbial degradation appear to be the most important means of phorate dissipation in the environment. Phorate is very unstable to photolysis in water, but photolysis in the field may not be important since phorate degrades rapidly by hydrolysis and aerobic soil metabolism. Phorate rapidly photolyses in water to form formaldehyde and phorate sulfoxide (CAS No. 2588-03-6). Parent phorate degrades in water with half-lifes of three days at pHs 5, 7, and 9. Parent phorate is very mobile to essentially immobile in soil depending on the soil organic carbon content, but is not persistent in aerobic soil. In soil, parent phorate degrades into the oxidised metabolites phorate sulfoxide and phorate sulfone (CAS No. 2588‑04‑7). These degradates are more persistent and mobile than parent phorate, so are more likely to be present in water resources than the parent (USEPA 2006).

If released to soil, phorate is expected to have low to slight mobility based upon Koc values ranging from 543 to 3,200. Volatilisation from moist soil surfaces is expected based upon a Henry’s Law constant of 4.37 x 10-6 atm-cu m/mole. However, adsorption to soil is expected to attenuate volatilisation. Biodegradation studies suggest phorate will biodegrade in soils (half-lifes ranging from 5 to 68 days) and in the water column (half-lifes ranging from 1 to 1.5 days). If released into water, phorate is expected to adsorb to suspended solids and sediment based upon the Koc values. Volatilisation from water surfaces is expected based on its Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 14 and 105 days, respectively. However, volatilisation from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. A BCF of 90 for juvenile sheepshead minnows suggests bioconcentration in aquatic organisms is moderate. Half-lifes for the hydrolysis of phorate at pH 5.7, 8.5, 9.4, and 10.25, were 52, 61, 62, and 33 days, respectively, producing diethyl disulfide, hydrogen sulfide, and formaldehyde under alkaline conditions (EAWAG accessed February 2015).

The solubility of phorate in water is about 30–50 mg/L, but it is unstable in water, especially under alkaline (basic) conditions. As it breaks down in water, non-toxic, water-soluble products are formed. Phorate has a vapour pressure of 0.11 Pa at 20°C, reported log octanol-water partition coefficients range from 2.92 to 4.26 (Health Canada 1986).

NPIC (1994) quotes for phorate a soil half-life of 60 days, water solubility of 22 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

Phorate was not detected in 24 samples of municipal and private drinking water supplies in two cities (Harrow 1985, and Toronto 1971 to 1982) in Ontario (detection limit 0.00002 mg/L). It was found in one of seven samples from Prince Edward Island at a level of 0.15 mg/L. It was not detected in 949 stream water samples from 11 agricultural watersheds in southern Ontario from 1975 to 1977 (detection limit not reported) or in 446 samples from three Ontario river basins surveyed from 1981 to 1985 in which more than 1,200 kg of phorate were applied annually (detection limit 0.0001 mg/L) (Health Canada 1986).

### Removal methods

Because phorate is attracted to soil particles and organic matter, coagulation processes should reduce its concentration. No information is available on processes that can be used to remove phorate degradation products from water.

### Analytical methods

#### Referee method

A referee method cannot be selected for phorate because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for phorate for the above reason.

### Health considerations

The oral LD50 for rats is 1.0 mg/kg. The oral LD50 for mice ranges from 3.5 to 6.59 mg/kg. Guinea pigs have an oral LD50 of 20 mg/kg.

JMPR conducted the toxicological review in 2004, which established an ADI of  
0–0.0007 mg/kg bw and an ARfD of 0.003 mg/kg bw. These values were reaffirmed in JMPR (2012).

USEPA (2006) quotes a chronic RfD of 0.0005 mg/kg/d, based on a NOAEL of 0.05 mg/kg/d from observing red blood cell and brain cholinesterase inhibition in dog studies. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0005 mg/kg/d, and an ARfD of 0.0025 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for phorate is 0.025 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand for phorate is 0.0005 mg/kg body weight, with a NOEL of 0.05 mg/kg bw.

Long-term studies of mice fed high doses of 98.7 percent pure phorate showed no effects on fertility, gestation, and viability. This suggests that phorate is unlikely to cause reproductive effects in humans.

No birth defects were found in two studies on the rat. This suggests that phorate does not cause birth defects. There was some maternal and embryo toxicity at relatively low doses (0.5 mg/kg).

Available mutagenicity studies involving microbial and mammalian cells have shown no adverse effects on genes or chromosomes. Thus it appears that phorate does not cause mutations. Valid studies on the carcinogenicity of phorate are not available. As at September 2008 the USEPA has classified phorate in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

There are limited and insufficient data on phorate on which to propose a MAV for drinking-water.

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# Phosphine

CAS No. 7803-51-2. The IUPAC name for phosphine is now phosphane. Also called phosphorus trihydride, hydrogen phosphide, phosphamine and once upon a time phosphoretted hydrogen.

### Maximum Acceptable Value

Phosphine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Phosphine is extremely rare in nature. It occurs transiently in marsh gas and other sites of anaerobic degradation of phosphorus-containing matter.

Phosphine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is registered as an insecticide.

Aluminium phosphide (CAS No. 20859-73-8) and magnesium phosphide (CAS No. 12057-74-8) also appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM), as insecticides and vertebrate toxic agents. Contact of the solid material with moisture in the air, or with water or acids, releases phosphine. Zinc phosphide (CAS No. 1314-84-7) does not appear.

Phosphine is replacing methyl bromide in several countries as a fumigant against insects and rodents, although there are reports of some pests developing resistance. Plant and Food (2009) summarised research into use of phosphine for fumigating export logs and timber.

In the US it is registered for control of certain insects in the following non-food commodities: animal hide; processed or unprocessed cotton, wool and other natural fibres or cloth; clothing, feathers, furs, human hair, rubberized hair, vulcanized hair, mohair, leather products; tobacco; wood, cut trees, wood chips and wood and bamboo products; paper and paper products; non-food flour; dunage; non-food starch; dried plants and flowers. Such dedicated lots may be fumigated in transport vehicles (truck trailers, railcars, and containers) prior to shipment (PMEP).

The technical grade of phosphine may contain impurities of higher phosphines (diphosphine) and substituted phosphines, which are responsible for the characteristic foul odour of phosphine which is often described as “fishy” or “garlicky”; when pure it has no odour.

### Forms and fate in the environment

Phosphides react with moisture or water to release phosphine gas, which eventually dissipates into the atmosphere. Studies suggest that phosphine below the soil surface is quickly adsorbed and degraded by micro‑organisms. The interaction of phosphine with soil appears to be mixed chemisorption (irreversible) and physisorption (reversible), with the extent of each dependent on soil type. The resulting material from the reaction is aluminium (or magnesium) hydroxide. Any phosphine that remains in the soils or water will form relatively harmless inorganic compounds such as phosphoric acid.

Because of its high vapour pressure (40 mm Hg at -129.4°C) and Henry’s Law Constant (0.1 atm m3/mol), phosphine at the soil surface is expected to rapidly dissipate into the atmosphere. The half-life of phosphine in air is about five hours with the mechanism of degradation being photoreaction with hydroxy radicals. The dark half-life is approximately 28 hours. The expected reaction products of phosphine in air are oxyacids of phosphorus and inorganic phosphate which are non-volatile.

Water solubility of phosphine is about 300–400 mg/L (Plant and Food quotes 368.4 mg/L), or about 220 mL per litre.

### Health considerations

Phosphine is a highly toxic respiratory poison.

The USEPA’s Office of Pesticide Programs (OPP) established a reference dose (RfD) of 0.0113 milligrams per kilogram body weight per day (mg/kg/day) for phosphine based on the NOEL of 3 ppm (4 mg/m3) converted to 1.13 mg/kg/day from the chronic inhalation study in rats and the uncertainty factor of 100. This RfD has not yet been adopted by the USEPA’s *Integrated Risk Information System (IRIS)* which lists the RfD for this chemical as 0.0003 mg/kg/day based on a NOEL (0.026 mg/kg/day, the only dose tested) from a two-year rat feeding study and an uncertainty factor of 100 (USEPA 1993). The OPP, however, has indicated that phosphine in the diet is difficult to measure because of volatilisation and “therefore, the actual dosages in this study are unknown” (*Federal Register* 64: 30939–49, 9 June). See PMEP.

INCHEM, quoting WHO (1988), states: the acceptable daily intake of phosphine/phosphide residues could be extrapolated as 0.01 mg/kg or less.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0113 mg/kg/d, and an ARfD of 0.018 mg/kg/d for aluminium phosphide.

EFSA (2015) quotes an ADI of 0.011 mg/kg/d for phosphane (based on the median residue levels in the raw agricultural commodities), and an ARfD of 0.019 mg/kg bw (based on the highest residue levels in the raw agricultural commodities).

Phosphine did not cause oncogenic effects in either the rat chronic feeding or chronic inhalation studies. Genotoxicity studies have equivocal results overall, with some being negative and others positive. The USEPA classifies phosphine as a group D (not classifiable as to human carcinogenicity) carcinogen. The USEPA does not believe that aluminium and magnesium phosphide pose a carcinogenic concern.

### Derivation of Maximum Acceptable Value

No MAV.

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# Phoxim

CAS No. 14816-18-3. The IUPAC name for phoxim is O,O-diethyl α‑cyanobenzylideneaminooxyphosphonothioate, or (EZ)‑2‑(diethoxyphosphinothioyloxyimino)-2-phenylacetonitrile. The CAS name is 4‑ethoxy-7-phenyl-3,5-dioxa-6-aza-4-phosphaoct-6-ene-8-nitrile 4-sulfide.

Phoxim is a diethyl ester; the dimethyl ester is called phoxim-methyl, CAS No. 14816‑16-1. Chlorophoxim may be encountered too: CAS No. 14816-20-7.

### Maximum Acceptable Value

Phoxim does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Phoxim is a non-systemic [oxime organothiophosphate insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#oxime_organothiophosphate_insecticides) and acaricide.

Phoxim does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides). Since 2014 phoxim is no longer able to be manufactured in or imported into New Zealand.

Phoxim has been dosed to soil to control pests such as wireworm, and used to protect stored products from insect damage. Phoxim has been banned for use on crops in the [European Union](http://en.wikipedia.org/wiki/European_Union) since 22 December 2007; it is used in veterinary medicine to treat [ectoparasitic](http://en.wikipedia.org/wiki/Ectoparasite) [acarids](http://en.wikipedia.org/wiki/Acarid), eg, sheep dip. Phoxim has been used overseas to protect wood from termites. WHO (1978) states that it is a useful larvicide recommended for use in outdoor surface water.

### Forms and fate in the environment

Phoxim is not persistent in soil or water, soil-half-life about six days, and it not likely to leach to groundwater (IUPAC). Phoxim is unstable in alkaline water, otherwise it is reasonably stable. Hydrolysis rather than photodegradation is probably the main degradation path for phoxim in aqueous conditions.

Water solubility is about 2 mg/L.

### Recommended analytical techniques

#### Some alternative methods

See WHO (1999).

### Health considerations

Phoxim is an insecticide with selective properties: it is toxic to insects but virtually non-toxic to mammals.

The JMPR 1984 Joint Meeting established an ADI of 0–0.001 mg/kg bw on the basis of inhibition of plasma cholinesterase activity. This was revised to 0.004 mg/kg on the basis of the NOEL of 0.38 mg/kg bw per day for effects on the liver and inhibition of brain acetylcholinesterase activity in the two-year study of toxicity in dogs and a safety factor of 100 (IPCS 2000).

EMEA (2000) quotes an overall oral NOEL of 0.375 mg/kg/d based on effects on the liver and a reduction of the acetylcholinesterase activity in the brain observed in a two-year study on dogs, applying a safety factor of 100 to an ADI of 0.00375 mg/kg bw, ie, the same study as above, but without rounding-off.

The Acceptable Daily Intake (ADI) adopted in Australia for phoxim is 0.00025 mg/kg body weight, with a NOEL of 0.025 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

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EMEA. 2000. *Committee for Veterinary Medicinal Products: Phoxim, summary report – extension to sheep*. EMEA/MRL 756/00-FINAL. See www.emea.europa.eu/pdfs/vet/mrls/075600en.pdf

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# Picloram

CAS No. 1918-02-1. The IUPAC name for picloram is 4-amino-3,5,6-trichloropyridine-2-carboxylic acid, or 4-amino-3,5,6-trichloropicolinic acid. The CAS name is 4-amino-3,5,6-trichloro-2-pyridinecarboxylic acid. Can be called 3,5,6-trichloro-4-aminopicolinic acid or ATPC.

When this substance is used as an ester or a salt, its identity should be stated, for example [picloram-2-ethylhexyl](http://www.alanwood.net/pesticides/derivatives/picloram-2-ethylhexyl.html) [CAS No. 36374-99-9], [picloram-isoctyl](http://www.alanwood.net/pesticides/derivatives/picloram-isoctyl.html) [CAS No. 26952-20-5], [picloram-methyl](http://www.alanwood.net/pesticides/derivatives/picloram-methyl.html) [CAS No. 14143-55-6], [picloram-olamine](http://www.alanwood.net/pesticides/derivatives/picloram-olamine.html) [CAS No. 55871-00-6], [picloram-potassium](http://www.alanwood.net/pesticides/derivatives/picloram-potassium.html) [CAS No. 2545-60-0], [picloram-triethylammonium](http://www.alanwood.net/pesticides/derivatives/picloram-triethylammonium.html) [CAS No. 35832-11-2], [picloram-tris(2-hydroxypropyl)ammonium](http://www.alanwood.net/pesticides/derivatives/picloram-tris(2-hydroxypropyl)ammonium.html) [CAS No. 6753-47-5].

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of picloram in drinking-water should not exceed 0.2 mg/L (200 μg/L). Picloram is not mentioned in the WHO Guidelines.

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.5 mg/L. The maximum acceptable concentration for picloram in Canada is 0.19 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.3 mg/L; excursions above this level over a short to medium period are of concern, because the health-based guideline is based on effects observed in a three-month study.

The USEPA limited the level of hexachlorobenzene in technical-grade picloram to a maximum of 200 mg/kg (0.02 percent); JMPR (2005) has a maximum content of 0.005 percent. The manufacturer (USEPA 1995) certifies that hexachlorobenzene is <100 mg/L and nitrosamines <1 mg/L.

EPA established an environmental exposure limit of 0.029 mg/L (29 µg/L) for picloram in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Picloram, a pyridine-based (or picolinic acid or chloropicolinic acid) systemic herbicide, is used as a post-emergent systemic herbicide for the control of deeply rooted and woody plants and a wide range of broadleaf weeds; however many grasses show resistance to its effects.

Picloram appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is available in a variety of formulations (esters and salts), some of which contain other active ingredients: eg, clopyralid, 2,4-D or triclopyr. Trade names include: Radiate, Tordon 2G and 50-D, Tordon Brushkiller and Tordon Gold Herbicide, Vigilant and Grazon.

ERMA notes that 11.1 tonnes of picloram were used in New Zealand in 2004, at an application rate of 1,200 grams of active ingredient per hectare.

Picloram was found in 420 of 744 surface water samples collected from 135 locations and in three of 64 groundwater samples collected from 30 locations in seven states of the USA. Maximum levels were 0.005 mg/L in surface water 0.0002 mg/L in groundwater.

### Forms and fate in the environment

If released to water, picloram is not expected to adsorb to suspended solids or sediment based on its Koc values. The principal environmental risks of picloram relate to contamination of surface water and groundwater, and damage to non-target terrestrial plants including crops adjacent to areas of application via run-off or drift. Picloram is among the most mobile (Koc values measured at 0.026 to 100) of currently [USEPA] registered pesticides and eventual contamination of groundwater is virtually certain in areas where picloram residues persist in the overlying soil (USEPA 1995). Picloram was considered a Priority A chemical for potential groundwater contamination by the USEPA and ranked first of 52 chemicals in the Agriculture Canada priority scheme for potential groundwater contaminants.

Picloram is resistant to biotic and abiotic degradation processes and in some soils (acidic and basic) it is nearly recalcitrant to all degradation processes. The pKa of picloram is 2.3, indicating that this compound will exist almost entirely in anion form in the environment; anions generally do not adsorb to particulate matter. It is stable to hydrolysis, volatilisation and anaerobic degradation, and degrades very slowly with half-lifes ranging from 150 to 500 days. It is degraded by ultraviolet light and sunlight on soil surfaces or in shallow aqueous solutions within a few days to a few weeks.

Picloram is extremely mobile. Nearly 100 percent of the chemical leached but none of it degraded over a three-year period in a University of Arkansas study. It does not adhere to soil and so may leach to groundwater, and has in fact been detected there. Given its high persistence, it appears unlikely that picloram will degrade once it reaches groundwater, even over a period of several years (USEPA 1995).

USEPA classified picloram as a Restricted Use pesticide in 1978 as a result of recurring reports of phytotoxicity to economically important crops caused by contamination of water supplies (USEPA 1995).

Studies of mobility and degradation in New Zealand soils have reported mobilities (as Koc) ranging from 19 to 47, which suggest a moderate level of adsorption to organic soils(Close et al 2001). In New Zealand, within 12‑months after aerial application of 1.1 kg/ha picloram, residues in soil had fallen to ‘safe levels’ in 65 percent of locations sampled; the figure rose to 75 percent after 14 months (MacDiarmid 1975).

EFSA (2013) states that soil studies demonstrated the degradation rate of picloram is moderate; the maximum field DT90 (considered only valid for application rates up 52 g/ha) was 163 days.

Picloram is very soluble in water: 430 mg/L (Merck & Co 1996). JMPR quotes 560 mg/L for the acid, 53 percent for the potassium salt and >67 percent for the tri-iso-propanolamine salt.

Health Canada (1988, edited 1990) states that its vapour pressure is very low, 8.3 × 10-5 Pa at 35°C, and its log octanol-water partition coefficient is very low; it is not bioconcentrated in animals.

NPIC (1994) quotes for picloram salt a soil half-life of 90 days, water solubility of 20 percent and a sorption coefficient (soil Koc) of 16. This resulted in a pesticide movement to groundwater rating of very high.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included picloram, so typical concentrations in New Zealand drinking-waters are unknown.

Picloram has been found four times in groundwaters in Waikato and Canterbury, ranging from 0.00002 to 0.0028 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Picloram occurred at 0.3 µg/L, ie, 0.0003 mg/L.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Picloram was detected in one well at a concentration of 0.36 µg/L, ie, 0.00036 mg/L.

Pesticide monitoring by Environment Canterbury has detected picloram twice in groundwater from one location (concentrations 0.00018 and 0.0003 mg/L) in and close to the Level Plain area in South Canterbury(Close et al 2001). Additionally, picloram has been detected at three sites in the Waikato region in pesticide monitoring of groundwater conducted by Environment Waikato. Concentrations ranged from 0.00002–0.0028 mg/L (Hadfield and Smith, p12).

The USEPA Office of Drinking Water’s STORET database indicates that picloram has been reported in 420 of 744 surface water samples (USEPA 1995). However, despite its persistence and mobility in soils, picloram has been detected infrequently in surface water and groundwater in four provinces in Canada (Hiebsch 1988, cited in Health Canada 1988/90). Picloram was not detected (detection limit 0.0001 mg/L) in raw or treated water from 13 municipalities in Ontario during 1985. In one shallow well, the concentration rose from 0 to 0.0015 mg/L 287 days after use in a field some distance from the well. A maximum concentration of 0.011 mg/L was reached 333 days after use.

Forty-eight water utilities in the US reported detecting picloram in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0094 mg/L.

### Removal methods

Although many reports state that picloram is very mobile, others suggest that it adsorbs to soil – this will depend on the picloram formulation and soil type. Therefore treatment processes that remove particulate matter may be effective at reducing the concentration of picloram in some situations.

Picloram is oxidised by ozone (Haag and Yao 1992). This is achieved most effectively at higher pH values which favour hydroxyl radical formation. Some newer advanced oxidation processes may be more effective.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of picloram, although a guide to the efficiency of the process cannot be provided. Picloram is strongly adsorbed on acid organic substances such as peat moss and on activated charcoal, so it is likely that a useful method could be derived for its removal from water supplies.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Recommended analytical techniques

#### Referee method

Liquid/liquid extraction/gas chromatography-electron capture detector (APHA 6640B; EPA 515.3).

#### Some alternative methods

High pressure liquid chromatography/photodiode array ultraviolet detector (EPA 555).

### Health considerations

There is no information available regarding the greatest source of exposure to picloram for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

Absorption of picloram through the gastrointestinal tract is rapid and almost complete. In human volunteers, the absorption half-time was 20 minutes. After oral administration of 5 and 0.5 mg/kg body weight radiolabelled doses, concentrations in the blood were proportional to the dose administered and were highest during the first hour. Picloram was excreted rapidly and unchanged in the urine. Most of the dose (77 to 86 percent) was excreted within the first six hours, and 94 percent of the dose was recovered after 72 hours (Nolan et al 1984, cited in Health Canada 1998).

#### Acute exposure

In studies using laboratory animals, picloram generally has been shown to be of moderate to low acute toxicity with oral LD50 values in the range of 2,000 to 8,000 mg/kg body weight for the rabbit, mouse, guinea pig and rat (NRC 1974, cited in Health Canada 1988). These levels suggest a low/variable acute oral toxicity when compared with other pesticides. It has been shown to potentially cause the following health effects from acute exposures: damage to central nervous system, weakness, diarrhoea and weight loss. Picloram and its derivatives are only slightly toxic by the oral routes and USEPA have placed it in Toxicity Category III (the second lowest of four categories) for this effect.

#### Chronic exposure

In a subchronic toxicity study using rats, picloram caused changes in the liver. A dog dietary study resulted in decreases in body weight gain, food consumption, liver weights and several enzymes.

The USEPA in 1995 and 1998 stated that the chronic reference dose (RfD) for picloram was calculated to be 0.20 mg/kg/day based on a NOEL of 20 mg/kg/day body-weight per day from a two-year rat chronic feeding study. An uncertainty factor of 100 was used to account for the inter-species extrapolation and intraspecies variability. The oral RfD had earlier been 0.07 mg/kg/d (USEPA 1992) based on increased liver weight in a six-month dog feeding study.

Later (USEPA 2006/2009/2011) the reference dose or RfD is 0.02 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.7 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.07 mg/kg body weight, with a NOEL of 7 mg/kg bw from a short-term (three-month) dietary study in dogs. The NOEL is based on increased liver weight. The ADI incorporates a safety factor of 100.

EC (2010) established an ADI and ARfD of 0.3 mg/kg/d. Reaffirmed in EFSA (2013).

Chronic exposure to picloram has the potential to cause liver damage. A chronic toxicity study using dogs resulted in increased liver weight. A chronic/carcinogenicity study using rats resulted in chronic toxicity in males only and no evidence of carcinogenicity. Based on these studies, picloram was classified as a Group E chemical, one showing evidence of non-carcinogenicity for humans (USEPA 1995). USEPA (1998) states that picloram acid was evaluated in the Ames test; the test substance did not produce a mutagenic response either in the presence or absence of activation.

Picloram is classified by the International Agency for Research on Cancer (IARC) as Group 3: Unclassifiable as to carcinogenicity to humans. As at September 2008 the USEPA has classified picloram (the acid, ester and salt) in Group E: evidence of non‑carcinogenicity for humans. One form of picloram, isooctyl/ethylhexyl picloram (IOE), bears structural similarity to di(2-ethylhexyl)phthalate (DEHP) in that both possess a 2-ethylhexyl moiety. DEHP and certain other substances containing the 2‑ethylhexyl moiety have been found to be carcinogenic in rodents. The USEPA (1995) performed a cancer risk assessment for workers and found that the risk associated with post-application exposure is not a major concern.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for picloram in drinking-water, as follows:

0.07 mg/kg body weight per day x 70 kg x 0.1 = 0.245 mg/L (rounded to 0.2 mg/L)

2 L

where:

* tolerable daily intake = 0.07 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for picloram is 0.5 mg/L.

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# Picoxystrobin

CAS No. 117428-22-5. The IUPAC name for picoxystrobin is methyl (2E)-3-methoxy-2-{2-[6-(trifluoromethyl)-2-pyridyloxymethyl]phenyl}acrylate. The CAS name is methyl (αE)-α-(methoxymethylene)-2-[[[6-(trifluoromethyl)-2-pyridinyl]oxy]methyl]benzeneacetate.

### Maximum Acceptable Value

Picoxystrobin is not mentioned in the DWSNZ, or in the WHO Guidelines.

EPA established an environmental exposure limit of 0.8 mg/L for picoxystrobin in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Picoxystrobin is a [methoxyacrylate strobilurin fungicide](http://www.alanwood.net/pesticides/class_fungicides.html#methoxyacrylate_strobilurin_fungicides), and appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Picoxystrobin was the fourth strobilurin to come to market when it was launched in 2001.

As with other strobilurin analogues, picoxystrobin inhibits fungal respiration and has both preventative and curative properties. Picoxystrobin is commonly used on cereal crops to control brown rust, tan spot, powdery mildew, and net blotch in cereals, pulses and oilseeds.

### Forms and fate in the environment

Sterile solutions of picoxystrobin were irradiated with artificial light for a time period equivalent of up to 30 days natural summer sunlight at a latitude 50°N. Under the conditions of the study the half-life of picoxystrobin is estimated to be in the range 17 to 25 days (EC 2003). There is no significant hydrolysis in water, pH 4 to 9. The half-life in water sediment systems was measured at about 10 to 100 days, with 20 days being typical. It is not particularly mobile in soil so should not be a threat to groundwater. See EFSA (2011) and JMPR (2012) for a list of metabolites.

EFSA (2014) states that the degradation rate of picoxystrobin is slow in the soil and the DT90 value exceeds 100 days. JMPR (2012) reports DT50 values for picoxystrobin determined using a first-order multi-compartmental model ranged from 16 to 38 days, while the DT90 values ranged from 76–337 days.

Water solubility about 3.1 mg/L at 20°C. The octanol/water partition coefficient = logKow = 3.68 at 20°C. Photolysis in sterile water at 25°C and pH 7 is reported between 6 and 60 days. Henry’s Law constant = about 5 x 10-4 Pa m3 mol-1 (20°C) (JMPR 2012).

### Removal methods

Being not particularly mobile in soil suggests that treatment systems that remove particulate matter should help reduce the concentration of picoxystrobin in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The toxicological studies were performed on picoxystrobin; it is noted that no toxicological data are available on the Z-isomer of picoxystrobin (EFSA 2011).

The lowest relevant short-term oral NOAEL/NOEL is 4.3 mg/kg bw/d in the dog. EC (2003) also reports that picoxystrobin is not genotoxic and there is no evidence of carcinogenicity. EC (2003) established an ADI of 0.043 mg/kg/d, adding that an ARfD was not allocated because no relevant acute effects were noted. EFSA (2011/2014) quote an ADI of 0.042 mg/kg/d. No ARfD was deemed necessary at the time of evaluation in 2003 (EFSA 2014).

The FAO/WHO 2012 meeting established an acceptable daily intake (ADI) of  
0–0.09 mg/kg bw on the basis of the overall NOAEL of 8.5 mg/kg bw per day in the 90‑day and one-year dog studies, based on body weight loss, reduced feed consumption and clinical signs at 16 mg/kg bw per day. A safety factor of 100 was applied.

The JMPR meeting established an acute reference dose (ARfD) of 0.09 mg/kg bw on the basis of the overall NOAEL of 8.5 mg/kg bw per day in the 90-day and one-year dog studies, based on body weight loss and reduced feed consumption at the beginning of the study at 16 mg/kg bw per day. A safety factor of 100 was applied. This value is supported by a BMD analysis of the motor activity changes seen at the lowest dose in the acute neurotoxicity study. The meeting noted that this ARfD is possibly conservative and that it might be possible to refine it (FAO/WHO 2012).

### Derivation of Maximum Acceptable Value

No MAV.

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# Pindone

CAS No. 83-26-1. The IUPAC name for pindone is 2-pivaloylindan-1,3-dione or 2‑(2,2‑dimethylpropanoyl)-1H-indene-1,3(2H)-dione. The CAS name is 2-(2,2-dimethyl-1-oxopropyl)-1H-indene-1,3(2H)-dione. It is also marketed as the sodium salt (CAS No. 6120-20-3). Also called pival (the calcium salt) and pivalyn (the sodium salt).

### Maximum Acceptable Value

Pindone is not mentioned in the DWSNZ or in the WHO Guidelines.

### Sources to water

Pindone is a ‘first generation\*’ indandione anticoagulant rodenticide, and appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). It is pharmacologically analogous to warfarin, and is used in New Zealand for rabbit control on pasture and sometimes for predator control in bush, usually distributed in cereal and carrots. Pindone is often used to control pests in areas where the alternative poison, sodium fluoroacetate (1080), cannot be used because of risk to domestic animals. It does not appear to be used in North America or Europe; more is used in New Zealand than in Australia. More than 100 tonnes of pindone pellets were sold for rabbit control in New Zealand in 1993 (NRA 2002).

\* ‘First generation’ products have largely been superseded by ‘second generation’ anticoagulants such as brodifacoum (see datasheet). These newer compounds were needed because the efficacy of some ‘first generation’ products has been reduced by the development of resistance.

### Forms and fate in the environment

Very few data are available for the first generation anticoagulants. The available database for pindone is particularly meagre, and the compound has been declared ineligible for reregistration in the US after the registrant failed to respond to a data call in the early 1990s.

If released to soil, pindone is expected to have low mobility based upon an estimated Koc of 900. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 9.3 x 10-12 atm-cu m/mole. If released into water, pindone is expected to adsorb to suspended solids and sediment based upon the estimated Koc. Volatilisation from water surfaces is not expected to be an important fate process based upon this compound’s estimated Henry’s Law constant. An estimated BCF of 120 suggests the potential for bioconcentration in aquatic organisms is high (NIH TOXNET). Pindone residues were found in the soil of an airstrip six months after it was used in an aerial baiting programme (from NSW Government 2013).

Analysis has revealed that the concentration of pindone sodium in water declined linearly with time, with extrapolated half-lifes of 370 weeks at 8.5°C, and 27 weeks at 30.5°C (NRA 2002). Water solubility is about 20 mg/L.

### Removal methods

No information available.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

Refer to Landcare Research New Zealand.

### Health considerations

Broadcast application of these pellets in New Zealand by hand or aircraft to control possums requires a controlled substances licence.

For accidental intake, an antidote to pindone is vitamin K.

### Derivation of Maximum Acceptable Value

No MAV.

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# Pinoxaden

CAS No. 243973-20-8. The IUPAC name for pinoxaden is 8-(2,6-diethyl-p-tolyl)-1,2,4,5-tetrahydro-7-oxo-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-9-yl 2,2-dimethylpropionate. The CAS name is 8-(2,6-diethyl-4-methylphenyl)-1,2,4,5-tetrahydro-7-oxo-7H-pyrazolo[1,2-d][1,4,5]oxadiazepin-9-yl 2,2-dimethylpropanoate.

### Maximum Acceptable Value

Pinoxaden is not mentioned in the DWSNZ, or in the WHO Guidelines.

### Sources to water

Pinoxaden is a phenylpyrazole or phenylpyrazolin herbicide, for post emergence control of grass weeds, commonly used on wheat and barley. It is always used with the adjuvant coded A-12127R. Toluene was considered as a relevant impurity and its maximum value in the specification is set at 1 g/kg.

Pinoxaden appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The fate and disposition of pinoxaden in the environment suggest that it is persistent and mobile, stable to hydrolysis, and has the potential to reach aquatic environments.

Hydrolysis of pinoxaden is pH dependent and occurs faster under basic (high pH) conditions. In soil, photolysis is also not a significant pathway for degradation for pinoxaden without hydrolytic degradation. Pinoxaden degrades rapidly under aerobic soil metabolism conditions with half-lifes ranging from two to three days.

Aqueous photolysis of pinoxaden is not a major dissipation route when exposed to sunlight. Under aerobic aquatic conditions, more than 86 percent of applied activity remains (in total system) in the form of the major degradate M2. Volatility is not a significant route of dissipation. The major degradates of pinoxaden (M2 and M3) are considered to be mobile. The groundwater metabolites M2, M3, M11, M52, M54 M55 and M56 are considered relevant (EFSA 2013).

Water solubility is about 200 mg/L, without dissociation. Henry’s Law constant = 9.2 x 10-7 Pa m3 mol-1 at 25ºC. Partition coefficient = Log Pow = 3.2 at 25ºC.

### Removal methods

No information available.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2013).

### Health considerations

Pinoxaden is rapidly and extensively absorbed after oral administration, widely distributed and almost completely excreted after 72 hours. It is not acutely toxic via oral and dermal route.

USEPA (2005) adopted both acute and chronic RfDs of 0.30 mg/kg/d, however, the acute RfD applies to females only, there is no acute RfD for the general population. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0006 mg/kg/d, and an ARfD of 0.00356 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pinoxaden is 0.118 mg/L.

Although an acceptable cancer study in rats was submitted, the dietary cancer study in the mouse was found to be unacceptable due to the failure to test at high enough doses. Nonetheless, based on the weight-of-evidence, a repeat carcinogenicity study in mice is not required at this time (USEPA 2005).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw, and the ARfD is 0.3 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EFSA (2013) quotes an ADI and ARfD of 0.1 mg/kg/d, as does EC (2016).

JMPR (2016) established an ADI for pinoxaden of 0–0.1 mg/kg bw, based on a NOAEL of 10 mg/kg bw per day for histopathological changes in the kidneys and associated changes in water intake and urine volume in a two-year rat toxicity and carcinogenicity study and using a safety factor of 100. This ADI provides a margin of about 5,000 for the LOAEL for equivocal carcinogenic effects in rats. The meeting established an ARfD of 0.3 mg/kg bw, based on a NOAEL of 30 mg/kg bw per day for reduced maternal body weight, body weight gain and feed consumption and embryo/fetal toxicity in a developmental toxicity study in rabbits and using a safety factor of 100. The ADI and ARfD can be applied to the metabolites M3, M4, M6 and M10, which are of no greater toxicity than pinoxaden.

### Derivation of Maximum Acceptable Value

No MAV.

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# Piperonyl butoxide

CAS No. 51-03-6. The IUPAC name for piperonyl butoxide is 5‑[2‑(2‑butoxyethoxy)ethoxymethyl]-6-propyl-1,3-benzodioxole or 2‑(2‑butoxyethoxy)ethyl 6-propylpiperonyl ether. The CAS name is 5‑[[2‑(2‑butoxyethoxy)ethoxy]methyl]-6-propyl-1,3-benzodioxole. Sometimes called PBO, or α-[2-(2-butoxyethoxy)ethoxy]-4,5-(methylenedioxy)-2-propyltoluene.

### Maximum Acceptable Value

Piperonyl butoxide is not mentioned in the DWSNZ, or in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.6 mg/L; minor excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

Dihydrosafrole, also called 5-propyl-1,3-benzodioxole (CAS No. 94-58-6) is a relevant impurity if >0.1 g/kg (WHO 2011).

### Sources to water

Piperonyl butoxide, a safrole derivative, is a [pesticide](http://en.wikipedia.org/wiki/Pesticide) [synergist](http://en.wikipedia.org/wiki/Synergy). It does not, by itself have pesticidal properties. However, when added to insecticide and parasiticide mixtures, typically allethrin, [pyrethrin](http://en.wikipedia.org/wiki/Pyrethrin), [pyrethroid](http://en.wikipedia.org/wiki/Pyrethroid), rotenone and [carbamate](http://en.wikipedia.org/wiki/Carbamate) [insecticides](http://en.wikipedia.org/wiki/Insecticide), their potency is increased considerably. This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Piperonyl butoxide degrades rapidly (8.4 hour half-life) in the water environment by photolysis, and is metabolised by soil micro-organisms (half-life 1–5 days). Other tested routes of degradation, such as hydrolysis, aerobic and anaerobic aqueous metabolism, are very slow or have questionable rates due to experimental difficulties, as in the case of soil photodegradation. The degradation products are believed to present no more problems than the parent compound. The water solubility of piperonyl butoxide is about 15 to 30 mg/L, and has a moderate to low leaching potential. The octanol/water partition coefficient is log POW = 4.8 at 20°C at pH 6.5. The photolysis half-life is 8.4 hours at 25°C at pH 7 when exposed to natural sunlight.

### Removal methods

No information available. Its low half-life suggests the concentration of piperonyl butoxide is unlikely to be found at nuisance concentrations after water treatment.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

JMPR developed an acceptable daily intake for humans of 0.03 mg/kg bw (IPCS 1972). This was revised to 0.2 mg/kg on the basis of the lowest NOAEL of 16 mg/kg bw/day (IPCS 1995). The 2001 JMPR concluded that an acute RfD for piperonyl butoxide was unnecessary.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 (0.03 pre-1997) mg/kg body weight, with a NOEL of 16 mg/kg bw from a long-term study (one-year dietary study) in dogs. The NOEL is based on increased liver weight and associated hepatocellular hypertrophy, increased serum ALP activity, and increased thyroid weight. The ADI incorporates a safety factor of 100.

IARC (1983) stated that the available data provide no evidence that piperonyl butoxide is likely to present a carcinogenic risk to humans, ie, Group 3. It is generally believed that the other ingredients present more health effects than piperonyl butoxide (JMPR 1983). As at September 2008 the USEPA has classified piperonyl butoxide in Group C: a possible human carcinogen.

Piperonyl butoxide has low oral toxicity. The liver is the target organ; increased liver weights appear to be dose dependent. The USEPA has classified piperonyl butoxide in Group C: a possible human carcinogen, and as a possible endocrine disruptor.

Acute and chronic drinking-water levels of concern (DWLOCs) were calculated based on dietary exposure estimates, default body weight and water consumption figures. However, the estimated drinking-water concentrations (EDWCs) for both surface water and groundwater are well below both the acute and chronic DWLOCs indicating that combined exposure to PBO in food and water is not a concern (USEPA 2006). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.155 mg/kg/d, and an ARfD of 6.3 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for piperonyl butoxide is 63 mg/L.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for piperonyl butoxide since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Pirimicarb

CAS No. 23103-98-2. The IUPAC name for pirimicarb is 2-dimethylamino-5,6-dimethylpyrimidin-4-yl dimethylcarbamate. The CAS name is 2-(dimethylamino)-5,6-dimethyl-4-pyrimidinyl dimethylcarbamate.

### Maximum Acceptable Value

Pirimicarb is not mentioned in the DWSNZ or in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L (previously 0.005 mg/L); excursions above this level even for a relatively short period are of concern, as the health-based guideline is based on short- to medium-term effects.

### Sources to water

Pirimicarb is a post-emergence dimethyl [carbamate](http://en.wikipedia.org/wiki/Carbamate) [insecticide](http://en.wikipedia.org/wiki/Insecticide) used to control [aphids](http://en.wikipedia.org/wiki/Aphid) on vegetable, cereal and orchard crops by inhibiting [acetylcholinesterase](http://en.wikipedia.org/wiki/Acetylcholinesterase) activity. Pirimicarb residues have often been found in lettuce during the Food Residue Surveillance Programme: refer NZFSA (<http://www.nzfsa.govt.nz/>).

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Pirimicarb was rapidly degraded by photolysis in aqueous solution with DT50 values of 3.2 hours and 2.28 hours at pH 5 and 7, respectively. After a period equivalent to 31 hours in summer sunlight, only 1.2 percent and 1.4 percent of the total applied parent remained at pH 5 and 7.

USEPA (1999) states that pirimicarb is rapidly dissipated under field conditions by both photolysis and microbial metabolism leading to significantly less persistence than demonstrated under conditions of laboratory soil degradation studies. This rapid dissipation under field conditions is independent of soil pH. Pirimicarb, therefore, does not leach and is unlikely to enter surface water under the conditions of the recommended label use patterns.

“This rapid dissipation under field conditions” is not supported by EFSA (2014) which states: the available field studies indicate that the DT90 value for pirimicarb amounts for a maximum of 190 days. Laboratory studies (aerobic) also indicate that DT90 values are 288 days for desmethyl pirimicarb, 632 days for metabolite R31805 and more than 398 days for R34865.

JMPR (2006) refers to soil metabolites: carbamate metabolites (demethyl pirimicarb and demethyl formamido pirimicarb and R35140). Other identified compounds were hydroxypyrimidines and guanidine.

Its solubility in water is about 3,000 mg/L.

NPIC (1994) quotes for pirimicarb a soil half-life of 10 days, water solubility of 2,700 mg/L and a sorption coefficient (soil Koc) of 60. This resulted in a pesticide movement to groundwater rating of moderate.

### Removal methods

Its high degradation rate suggests that pirimicarb is unlikely to reach nuisance levels in source water. Some newer advanced oxidation processes and biological activated carbon should be effective at breaking down most of the pirimcarb.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

USEPA (1999) proposed an acute RfD of 0.1 mg/kg/day, based on clinical signs of systemic toxicity seen at 40 mg/kg/day in the rat acute neurotoxicity study and application of a standard 100-fold uncertainty factor to the NOAEL of 10 mg/kg. The chronic RfD is 0.035 mg/kg/day, based on haematological effects noted in the chronic dog studies at 4 mg/kg/day and application of a standard 100-fold uncertainty factor to the NOAEL of 3.5 mg/kg/day.

The JMPR toxicological review was conducted in 2004, when an ADI of 0–0.02 mg/kg bw and an ARfD of 0.1 mg/kg bw were established.

With regard to residues, the review (EC 2006) established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is 2 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems. The EC established an ADI of 0.035 mg/kg/d and an ARfD of 0.1 mg/kg/d. These values were reaffirmed in EFSA (2014) These toxicological reference values can be applied to desmethyl pirimicarb, desmethyl formamido pirimicarb and hydroxypyrimidine metabolites.

The Acceptable Daily Intake (ADI) adopted in Australia for pirimicarb is 0.002 mg/kg body weight, with a NOEL of 0.4 mg/kg bw from a short-term (90-day dietary) study in dogs. The LOEL is based on haemotoxicity. The ADI incorporates a safety factor of 200.

The ADI for New Zealand is 0.035 mg/kg/d.

The USEPA (2005) concluded that pirimicarb is “likely to be carcinogenic to humans”. This classification was based on malignant and benign tumours in male (liver, lung) and female (liver, lung, mammary gland, ovary) mice of one strain and on benign lung tumours in a second strain of female mice. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

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# Pirimiphos methyl

CAS No. 29232-93-7. The IUPAC name for pirimiphos methyl is O-2-diethylamino-6-methylpirimidin-4-yl O,O-dimethyl phosphorothioate. The CAS name is O‑[2‑(diethylamino)-6-methyl-4-pyrimidinyl] O,O-dimethyl phosphorothioate. Sometimes spelt pirimiphos-methyl and pyrimiphos-methyl.

The analogous diethyl ester has the ISO common name [pirimiphos-ethyl](http://www.alanwood.net/pesticides/pirimiphos-ethyl.html) (CAS No. 23505-41-1).

### Maximum Acceptable Value (provisional)

WHO (2017) states that pirimiphos methyl is not recommended for direct application to drinking-water unless no other effective and safe treatments are available.

Earlier they had said based on health considerations, the concentration of pirimiphos methyl in drinking-water should not exceed 0.1 mg/L.

Pirimiphos methyl was not mentioned in WHO 2004. In 2008 WHO prepared a factsheet: “Pirimiphos-methyl in Drinking-water: Use for Vector Control in Drinking-water Sources and Containers”. This assesses pirimiphos-methyl for use as a mosquito larvicide in drinking-water in containers, particularly to control dengue fever. The WHO Guidelines 3rd addendum (2008) states that a guideline value is not considered appropriate for pesticides used for vector control in drinking-water. WHO (2011) states that “the manufacturer recommends the direct addition of 1 mg/L to water. Based on the above calculations, pirimiphos-methyl is not recommended for direct application to drinking-water unless no other effective and safe treatments are available”.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.09 mg/L; excursions above this level even for a relatively short period are of concern, as the health-based guideline is based on short- to medium-term effects.

JMPR (2007) reports that pirimiphos methyl should contain no more than 5 g/kg of O,O-dimethyl phosphorochloridothioate (DMPCT), O,O,S-trimethyl phosphorodithioate. O,O,S-trimethyl phosphorothioate, O,O,O-trimethyl phosphorothioate and O-2-diethylamino-6-methylpyrimidin-4-yl-O,S-dimethyl phosphorothioate; these are as toxic or more toxic than pirimiphos methyl.

### Sources to water

Pirimiphos methyl may enter source waters as a result of its application as a broad spectrum post-harvest, non-cumulative organophosphorus (or organothiophoshorus) insecticide and acaricide for grain and seed storage insect pests and for industrial and domestic fly control. It is a fast acting fumigant with contact, and stomach action. It targets pests such as bugs, flies, beetles and weevils.

Pirimiphos methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The total annual New Zealand usage of pirimiphos methyl in the late 1980s was 19,800 kg. ERMA notes that 7.5 tonnes of pirimiphos methyl were used in New Zealand in 2004, in greenhouses and storage areas only. From 1 July 2015, only approved handlers will be able to apply pirimiphos methyl.

Pirimiphos-ethyl does not seem to be used in New Zealand. Pirimiphos-ethyl appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Pirimiphos methyl was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in celery.

Pirimiphos-methyl was being considered by WHO for addition to potable water in containers as a mosquito larvicide treatment, particularly to control dengue fever. The manufacturer recommended the direct addition of 1 mg/L to water (WHO 2017).

### Forms and fate in the environment

The water solubility of pirimiphos methyl is about 5–10 mg/L and the sorption coefficient is 1,000 mL/g (estimate).

Pirimiphos-methyl is fairly rapidly degraded in the environment, with a dissipation half-life measured in days. The mechanisms are volatilisation and photodegradation initially, with biodegradation and chemical hydrolysis considered to be more important after about 24 hours.

Pirimiphos-methyl hydrolyses rapidly at acidic pHs and is relatively stable at neutral and alkaline pH; calculated half-lifes were 7.3 days at pH 5, 79 days at pH 7, and  
54–62 days at pH 9. The main hydrolysis degradate recovered from all three pHs was 2‑(diethylamino)-4-hydroxy-6-methyl pyrimidine which did not retain the organophosphate moiety. A second degradate, O-2-diethylamino-6-methylpyrimidin-4-yl o-methyl-phosphorothioate, was recovered at significant amounts in the pH 7 and nine solutions and did still contain the organophosphate moiety, and therefore, may still have significant toxicological activity.

NPIC (1994) quotes for pirimiphos-methyl a soil half-life of 10 days, water solubility of 9 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

NPIC (1994) quotes for pirimiphos-ethyl a soil half-life of 45 days, water solubility of 93 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 342 zones, did not find any detectable concentrations of pirimiphos methyl (limit of detection = 0.0002 mg/L) (ESR 2001).

Pirimiphos methyl has been found in groundwaters in Waikato, Wellington and Nelson, ranging from 0.00001 to 0.00006 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Pirimiphos methyl occurred at 0.01 µg/L, ie, 0.00001 mg/L.

Pirimiphos methyl was found in one bore during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration was 0.000053 mg/L. The bore was in the Bay of Plenty region.

### Removal methods

No information available. However, some newer advanced oxidation processes may be effective, and activated carbon treatment has been shown to be effective.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector or Flame Photometric Detector (Organophosphorus pesticides in river and drinking-water, tentative method 1980; and Organophosphorus pesticides in sewage sludge: organophosphorus pesticides in river and drinking-water: an addition, 1985) (HMSO 1986).

#### Some alternative methods

No alternative methods have been recommended for pirimiphos methyl because no methods meet the required criteria. See WHO (2008) for further information.

### Health considerations

No specific information available, but as an organophosphate, it may be expected to show characteristic effects including inhibition of acetyl cholinesterase and central nervous system depression. Organophosphates are absorbed readily through the skin, and through the respiratory and gastrointestinal tracts.

The oral toxicity of pirimiphos-methyl is low. The only biochemical effect consistently observed with pirimiphos-methyl in acute, short-term or long-term studies is cholinesterase inhibition. In human studies, no cholinesterase inhibition was seen at 0.25 mg/kg body weight per day (the highest dose tested).

WHO (1992) has classified the compound as slightly hazardous. In two experimental studies with human volunteers of 28 and 56 days, the highest dose tested in both studies (0.25 mg/kg of body weight per day) failed to induce erythrocyte cholinesterase inhibition in either study.

The toxicology of pirimiphos-methyl was evaluated by the FAO/WHO JMPR in 1974, 1976 and 1992, the 1992 JMPR establishing an acceptable daily intake (ADI) of  
0–0.03 mg/kg bw based on a NOAEL of 0.25 mg/kg bw per day in a 28-day and a 58‑day study in human volunteers, and a safety factor of 10. The only biochemical effect consistently noted in acute, short-term and long-term, or chronic toxicity tests was inhibition of cholinesterase. The JMPR concluded that pirimiphos-methyl is not genotoxic. The 2003 JMPR noted that an acute reference dose (acute RfD) may be required for pirimiphos-methyl but has not yet been established. JMPR (2006) reports an ARfD of 0.2 mg/kg bw based on inhibition of acetylcholinesterase activity in rats from a single-dose study of neurotoxicity in which a NOAEL of 15 mg/kg bw was identified.

USEPA (2006) derived a chronic RfD of 0.002 mg/kg/d for pirimiphos-methyl based on a LOAEL of 0.2 mg/kg/d found in a subchronic toxicity study on the rat. The oral RfD had earlier been 0.01 mg/kg/d (USEPA 1992) based on transient plasma ChE depression in a 56-day human study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0002 mg/kg/d, and an ARfD of 0.015 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pirimiphos-methyl is 0.15 mg/L.

EC (2007) established an ADI of 0.004 mg/kg/d and an ARfD of 0.15 mg/kg/d. EFSA (2011 and 2015 – see <http://www.efsa.europa.eu/en/efsajournal/doc/3974.pdf>) reaffirmed these values.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand for pirimiphos-methyl is 0.02 mg/kg body weight, with a NOEL of 0.25 mg/kg bw from short-term studies on human volunteers. The NOEL is based on the absence of adverse effects at the highest dose tested. The ADI incorporates a safety factor of 10. The Acceptable Daily Intake (ADI) adopted in Australia for pirimiphos-ethyl is 0.0002 mg/kg body weight, with a NOEL of 5 mg/kg bw.

At the maximum recommended dosage for drinking-water of 1 mg/L, a 60 kg adult drinking two litres of water would have an intake of 0.033 mg/kg body weight, compared with the upper limit of the ADI of 0.03 mg/kg body weight. The intake for a 10 kg child drinking one litre of water would be 0.1 mg/kg body weight; for a 5 kg bottle-fed infant drinking 0.75 litre, it would be 0.15 mg/kg body weight. There is uncertainty regarding the level that would cause effects in humans, as the NOAEL on which the ADI is based was the highest dose tested, and so the ADI may be more conservative than is at first apparent. These intake figures are all below the acute reference dose of 0.2 mg/kg body weight and would not result in an acute exposure risk from the initial application of pirimiphos-methyl to drinking-water containers at the recommended dose. In addition, the low solubility and the high log octanol–water partition coefficient of pirimiphos-methyl indicate that the larvicide is very unlikely to remain in solution at the maximum recommended applied dose, so the actual levels of exposure are expected to be lower than those calculated. Exposure from food is generally considered to be low, but occasional high exposures can be experienced. Based on the above calculations, pirimiphos-methyl is not recommended for direct application to drinking-water unless no other effective and safe treatments are available. If pirimiphos-methyl is applied directly to drinking-water, consideration should be given to using alternative sources of water for bottle-fed infants and small children for a period after its application, where this is practical. However, it is noted that exceeding the ADI will not necessarily result in adverse effects (WHO 2017).

As at September 2008 the USEPA describes the cancer classification of pirimiphos methyl as “cannot be determined”.

### Derivation of Maximum Acceptable Value

The provisional MAV for pirimiphos methyl was calculated by the New Zealand Ministry of Health as follows:

0.03 mg/kg x 70 kg x 0.1 = 0.105 mg/L (rounded to 0.1 mg/L)

2 L

where:

* acceptable daily intake = 0.03 mg/kg body weight
* average weight of adult = 70 kg
* proportion of acceptable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult = 2 L/day.

WHO (2008/2011) states that it is not appropriate to set a formal guideline value for pirimiphos-methyl used as a vector control agent in drinking-water. The ADI determined for pirimiphos-methyl by JMPR in 1992 (FAO/WHO 1993) was  
0–0.03 mg/kg of body weight. Young animals do not appear to be significantly more sensitive than adults. At the recommended dose for drinking-water of 1 mg/L, a 60-kg adult drinking two litres of water would have an intake of 0.033 mg/kg of body weight compared with the ADI of 0–0.03 mg/kg of body weight. The intake for a 10-kg child drinking one litre of water would be 0.1 mg/kg of body weight and for a 5-kg bottle-fed infant drinking 0.75 litre it would be 0.15 mg/kg of body weight. There is uncertainty regarding the level that would cause effects in humans, since the NOAEL on which the ADI is based was the highest dose tested, and so the ADI may be more conservative than is at first apparent. These figures are all below the acute reference dose of 0.2 mg/kg of body weight (FAO/WHO 2006). In addition, the low solubility and the high log Kow of pirimiphos-methyl indicate that it is unlikely to remain in solution at the maximum recommended applied dose, so that the actual levels of exposure are likely to be lower than those calculated. Exposure from food is generally considered to be low, but occasional high exposures can be experienced.

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# Pirimisulfuron methyl

CAS No. 86209-51-0. The IUPAC name for pirimisulfuron methyl is methyl 2‑[4,6‑bis(difluoromethoxy)pyrimidin-2-ylcarbamoylsulfamoyl]benzoate. Also called primisulfuron-methyl.

The base compound is primisulfuron: CAS No. 113036-87-6, for which the IUPAC name is 2-[4,6-bis(difluoromethoxy)pyrimidin-2-ylcarbamoylsulfamoyl]benzoic acid. The CAS No. is 2-[[[[[4,6-bis(difluoromethoxy)-2-pyrimidinyl]amino]carbonyl]amino]sulfonyl]benzoic acid.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of pirimisulfuron methyl in drinking-water should not exceed 0.1 mg/L.

Pirimisulfuron is not mentioned in the WHO Guidelines.

### Sources to water

Pirimisulfuron-methyl is a substituted urea herbicide. It appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). There is one formulation (Beacon), which is sold as water dispersible granules. The compound is a selective post-emergence systemic herbicide that is absorbed rapidly by plants and transported throughout the plant roots and foliage. It is often mixed with other herbicides, such as 4-D, dicamba, cyanazine, bromoxynil, and atrazine.

No information is available on the annual usage of specific active ingredients in New Zealand, although pirimisulfuron methyl is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

### Forms and fate in the environment

Pirimisulfuron methyl is moderately soluble in water: 70 mg/L at 20°C (PMEP 2001).

Laboratory tests on well-aerated soils indicated a half-life of less than two months. In soils without oxygen, breakdown of the compounds took nearly three months (RSocC 1991, cited in PMEP 2001). Sunlight has little effect on the breakdown of the compound in soil or in water. Dissipation of the compound under field conditions was much quicker, with a half-life of 3 to 12 days (RSocC 1991, cited in PMEP 2001).

Pirimisulfuron methyl is very mobile in soil in field and laboratory studies. The mobility of the compound in soils indicates that it has the potential to leach to surface water and to groundwater that lies close to the surface in highly vulnerable soils. The breakdown of the compound is much quicker in acidic soils and water rather than in neutral or alkaline soils and water (Walker and Keith 1991).

Primisulfuron is resistant to hydrolysis in alkaline and neutral water. Anaerobic conditions will increase persistence. A half-life of 22 days at a pH of 5 has been reported.

NPIC (1994) quotes for primisulfuron-methyl a soil half-life of 30 days, water solubility of 70 mg/L and a sorption coefficient (soil Koc) of 50. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included pirimisulfuron methyl, so typical concentrations in New Zealand drinking-waters are unknown.

Pirimisulfuron has been found in Waikato groundwater at 0.0027 mg/L (MAF 2006).

Information on typical concentrations in international drinking-waters was unavailable.

### Removal methods

No information is available on the removal of pirimisulfuron methyl from water.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of pirimisulfuron methyl, although a guide to the efficiency of the process cannot be provided.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Recommended analytical techniques

#### Referee method

None listed for pirimisulfuron methyl in the DWSNZ.

#### Some alternative methods

None listed for pirimisulfuron methyl in the DWSNZ.

### Health considerations

There is no information available regarding the greatest source of exposure to pirimisulfuron methyl for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

#### Acute exposure

Pirimisulfuron methyl is a slightly toxic compound with an acute oral LD50 greater than 5,050 mg/kg in the rat, which suggests a low acute oral toxicity when compared with other pesticides. Slight skin irritation was observed in rabbits after dermal application of primisulfuron methyl, but it did not cause skin sensitisation in male guinea pigs (EXTOXNET 1996).

#### Chronic exposure

Rats and mice fed very large amounts of pirimisulfuron methyl for up to 90 days showed no ill effects (RSocC 1991, cited in PMEP 2001). This indicates that even at relatively high levels of exposure (500 mg/kg) there is little toxic effect from the compound over relatively short exposure periods. Male rats fed higher doses of primisulfuron-methyl (up to 1,000 mg/kg) for three months showed a decrease in body weight and a decrease in spleen weight. The lowest dose at which adverse effects were noted was about 150 mg/kg (RSocC 1991, cited in PMEP 2001). When dogs were fed moderate doses of pirimisulfuron methyl for a year, a number of effects were noted at the highest doses tested (125 mg/kg) which included changes in the blood such as increased platelets and anaemia. Other changes included decreased cholesterol, pale livers, and thyroid gland changes.

This evidence suggests that the chronic risks of human exposure to moderate levels of the herbicide for extended periods of time are slight (PMEP 2001).

In a two-generation study, rats were fed moderate doses (250 mg/kg) of pirimisulfuron methyl. Rats had decreased testicular function and the offspring had decreased body weights. No compound related reproductive effects were noted at doses below 50 mg/kg/day (Walker and Keith 1991, cited in PMEP 2001).

Pregnant rabbits fed high doses of pirimisulfuron methyl produced normal offspring. Only at doses of 300 mg/kg and above were there changes in maternal body weight, spontaneous abortion and changes in the maternal stool. In another study, pregnant rats were fed moderate doses of pirimisulfuron methyl. They showed increases in the number of litters having incomplete bone formations, though this study was inconclusive.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.25 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pirimisulfuron-methyl is 1.75 mg/L (no acute one-day value available).

The USEPA has indicated that it is unlikely, given the results of the three studies noted above, that pirimisulfuron methyl is teratogenic to humans (Walker and Keith 1991, cited in PMEP 2001).

No studies have found mutagenic effects.

The International Agency for Research on Cancer has not classified pirimisulfuron methyl for its ability to cause cancer. As at September 2008 the USEPA has classified pirimisulfuron methyl in Group D: not classifiable as to human carcinogenicity. Primisulfuron-methyl is a practically nontoxic compound in USEPA toxicity class IV. A summary of toxicological studies appears in Appendix 1 of Health Canada (2001).

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for pirimisulfuron methyl in drinking-water, as follows:

0.25 mg/kg body weight per day x 70 kg x 0.1 = 0.9 mg/L

2 L

where:

* no observable adverse effect level = 0.25 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent.

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# Polyoxin D

CAS No. 22976-86-9. The IUPAC name for polyoxin D is 4,5-(2-amino-5-O-carbamoyl-2-deoxy-L-xylonamido)-1-(5-carboxy-1,2,3,4-tetrahydro-2,4-dioxopyrimidin-1-yl)-1,5-dideoxy-β-D-allofuranuronic acid. The CAS name is 5-[[2-amino-5-O-(aminocarbonyl)-2-deoxy-L-xylonoyl]amino]-1-(5-carboxy-3,4-dihydro-2,4-dioxo-1(2H)-pyrimidinyl)-1,5-dideoxy-β-D-allofuranuronic acid.

Also called polyoxorim. Polyoxin D zinc salt has CAS No. 146659-78-1.

### Maximum Acceptable Value

Polyoxin D zinc salt does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Polyoxins are nucleoside antibiotic fungicides composed of [heterocyclic](https://en.wikipedia.org/wiki/Heterocyclic) moieties containing [nitrogen](https://en.wikipedia.org/wiki/Nitrogen), usually used on lawns, vegetables and fruits. Polyoxins are produced by a specific bacterium (a Streptomyces sp) naturally found in soil; they work by inhibiting the [biosynthesis](https://en.wikipedia.org/wiki/Biosynthesis) of [chitin](https://en.wikipedia.org/wiki/Chitin), with no residual effects.

Polyoxin D zinc salt appeared on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines in 2017 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

There was no toxicity to land mammals, insects, or birds in various tests. The product label reflects the concern for possible harm to freshwater invertebrates and fish by prohibiting the use or disposal of Polyoxin D Zinc Salt in bodies of water.

Stability: stable at 0 and 12°C (96 hours); complete degradation (95.8 percent) at 54°C for 14 days; no change to metals zinc and iron foil; unstable in sunlight 39.3 percent degradation in 24 hrs. The half life in water at pH 7 is 2.3 days, and 15.9 days in aerobic soil.

It is very soluble in water.

### Typical concentrations in drinking-water

Although the potential exists for a minimal amount of polyoxin D zinc salt to enter groundwater or other drinking water sources if, after application, weather patterns are such that significant rainfall and surface water run-off occur, the health risk to humans is considered negligible based on the evaluations of the submitted toxicity studies, and the low application rate of the active ingredient.

### Analytical methods

#### Some alternative methods

See USEPA (2003).

### Health considerations

No toxicological endpoints were identified. Acute and chronic toxicological studies indicate polyoxin D zinc salt induces minimal toxic affects to humans through oral, dermal, ocular or inhalation exposure. Given the lack of toxicity and limited use sites, this active ingredient is not expected to harm people, pets, wildlife, or the environment when used according to label directions.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EPA. 2015. *Esteem: Polyoxin D zinc salt*. APP202334 – Category C Reduced Risk. Hearing [18 pp] 9 December. <http://www.epa.govt.nz/search-databases/HSNO%20Application%20Register%20Documents/APP202334_APP202334_Hearing_presentation_-_applicant.pdf>

USEPA. 2003. Consideration of eligibility for registration of the new pesticide active ingredient: polyoxin d zinc salt. *Biopesticide Registration Decision Memorandum* [25 pp]. <https://www3.epa.gov/pesticides/chem_search/reg_actions/registration/related_PC-230000_1-Jul-03.pdf>

# Posaconazole

CAS No. 171228-49-2. The IUPAC name for posaconazole is 4-(4-(4-(4-(((3R,5R)-5-(2,4-difluorophenyl)-5-(1,2,4-triazol-1-ylmethyl)oxolan-3-yl)methoxy)phenyl)piperazin-1-yl)phenyl)-2-((2S,3S)-2-hydroxypentan-3-yl)-1,2,4-triazol-3-one. The CAS name is 2,5-anhydro-1,3,4-trideoxy-2-(2,4-difluorophenyl)-4-({4-[4-(4-{1-[(2S,3S)-2-hydroxy-3-pentanyl]-5-oxo-1,5-dihydro-4H-1,2,4-triazol-4-yl}phenyl)-1-piperazinyl]phenoxy}methyl)-1-(1H-1,2,4-triazol-1-yl)- D-threo-pentitol.

Also called Noxafil.

This abbreviated datasheet has only been prepared because so many of the conazoles are pesticides.

### Maximum Acceptable Value

Posaconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Posaconazole is a triazole antifungal drug, active against Candida, Aspergillus and Zygomycetes spp. It can be taken orally or by injection, particularly by immunocompromised people. It receives Pharmac subsidy in certain circumstances.

Posaconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Health considerations

Nil.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Medsafe. 2015. *Noxafil (Posaconazole) Modified Release Tablets and Oral Suspension*. New Zealand Data Sheet. <http://www.medsafe.govt.nz/profs/datasheet/n/Noxafilsusp.pdf>

# Prochloraz

CAS No. 67747-09-5. The IUPAC name for prochloraz is N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]imidazole-1-carboxamide. The CAS name is N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]-1H-imidazole-1-carboxamide. Sometimes sold as the prochloraz-manganese chloride complex (CAS 75747-77-2). Copper and zinc complexes are sold too.

### Maximum Acceptable Value

Prochloraz does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

Prochloraz should not contain more than 0.01 mg/kg of 2,3,7,8-tetrachlorodibenzo-p-dioxin, 100 mg/kg of hexachlorobenzene, and 4 mg/kg of hexachlorodibenzo-p-dioxin.

### Sources to water

Prochloraz is a non-systemic amide or conazole or imidazole broad spectrum fungicide acting as a sterol inhibitor and affecting the vegetative structures of certain fungal pathogens which infect various fruit post-harvest. Prochloraz is chemically related to compounds such as imazalil (qv). There are some reports of it being used to protect timber against fungal attack too.

Prochloraz appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Prochloraz was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in mushrooms; <http://www.nzfsa.govt.nz/>.

### Forms and fate in the environment

The amount of prochloraz that sorbs to soils increases with the organic content; the half-life in soil is about 16–25 days, and prochloraz is broken down by UV light and by bacteria, so probably doesn’t leach to groundwater. It is hydrolysed slowly at pH 9 and very slowly at pH 5 and 7, and is subject to slow photolysis. Prochloraz forms two metabolites in soil: the formylurea (N-formyl-N’-propyl-N’-2(2,4,6-trichlorophenoxy)ethylurea) and urea complexes. See EFSA (2011) for further metabolites.

Prochloraz forms stable complexes with certain metal ions, such as zinc.

Water solubility is about 25–30 mg/L.

NPIC (1994) quotes for prochloraz a soil half-life of 120 days, water solubility of 34 mg/L and a sorption coefficient (soil Koc) of 500. This resulted in a pesticide movement to groundwater rating of moderate.

### Removal methods

No information is available on processes that can be used to remove prochloraz from water.

### Health considerations

The toxicology of prochloraz was first evaluated by JMPR in 1983 when an ADI of  
0–0.01 mg/kg bw was established on the basis of a NOAEL of 0.9 mg/kg bw per day in a two-year study in dogs and a NOAEL of 1.3 mg/kg bw per day in a two-year study in rats. This was reaffirmed in 2001. As well, an acute reference dose (ARfD) of 0.1 mg/kg bw, on the basis of a NOAEL of 10 mg/kg bw per day for effects on the liver at day 3 (increased serum alkaline phosphatase activity) in a 14-day study in dogs, and a safety factor of 100 was established by JMPR in 2001. JMPR concluded that prochloraz was not carcinogenic in rats, but increased incidence of liver adenomas and carcinomas in mice had been observed.

The USEPA derived a RfD of 0.009 mg/kg/d in 1989), where RfD means an estimate of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

EFSA (2011) report an ADI of 0.01 mg/kg body weight based on the NOAEL of 0.9 mg/kg bw/d found in the two-year dog study and applying a safety factor of 100. The agreed acute reference dose (ARfD) of prochloraz technical is 0.025 mg/kg bw based on a NOAEL of 2.5 mg/kg bw/d considering the effects observed in the 90-day dog, multigeneration rat and 14-day dog studies, and applying a safety factor of 100.

Prochloraz is a suspected endocrine disruptor. As at September 2008 the USEPA has classified prochloraz in Group C: a possible human carcinogen, based on a statistically significantly increased incidence and dose-related trend in liver adenomas and carcinomas (combined) in both sexes of one strain of mouse. They state that a concentration of 0.002 mg/L presents a 1 in 100,000 increased risk of cancer.

### Derivation of Maximum Acceptable Value

No MAV.

The Dutch MTR (maximum tolerable risk concentration) in surface water is 0.0013 mg/L (Kuhlau 2008).

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# Procymidone

CAS No. 32809-16-8. The IUPAC name for procymidone is N-(3,5-dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide. The CAS name is 3-(3,5-dichlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,4-dione.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of procymidone in drinking-water should not exceed 0.7 mg/L.

Procymidone is not mentioned in the WHO Guidelines.

### Sources to water

Procymidone is a systemic fungicide used on lupins, grapes, stone fruit, strawberries and some vegetables. It is widely used in horticulture, either as a seed dressing, pre-harvest spray, or (in Australia) post-harvest dip. Procymidone residues were often found in celery, sometimes at greater than the maximum residue limit (MRL) during the December 2009 Food Residue Surveillance Programme: refer NZFSA: <http://www.nzfsa.govt.nz/>.

Procymidone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Procymidone is easily hydrolysed in water at pH 6.3 and above at 45°C, at pH 7.1 and above at 30°C and at pH 8 and above at 15°C. Half-life periods ranging from 30 minutes to 8.1 days were found under these conditions. A major breakdown product of health concern is 3,5-dichloroaniline (qv); the 3,5-DCA metabolite was not detected in grapes, but occurs during fermentation.

Small amounts of cyclopropane-derivatives and chlorophenol-derivatives may be formed in aerobic soil. See EFSA (2011) for a list of metabolites.

Water solubility is about 3–4 mg/L at 20/25°C.

NPIC (1994) quotes for procymidone a soil half-life of seven days, water solubility of 4.5 mg/L and a sorption coefficient (soil Koc) of 1500. This resulted in a pesticide movement to groundwater rating of very low. Its GUS score is 1.89, indicating intermediate leaching potential to groundwater.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 346 zones, did not find any detectable concentrations of procymidone (limit of detection = 0.0002 mg/L) (ESR 2001).

In the three national surveys on pesticides in groundwater done up until 1999, procymidone was found in a concentration range of 0.0001 to 0.0017 mg/L. It is not widely found, with market gardening in Pukekohe being one of the areas in which it was found on a number of occasions. Procymidone has been found nine times, in groundwaters in Pukekohe, Waikato and Marlborough, ranging from 0.00001 to 0.003 mg/L (MAF 2006).

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Procymidone occurred at 0.17 µg/L, ie, 0.00017 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Procymidone occurred at 0.12 µg/L, ie, 0.00012 mg/L.

Procymidone was found in two bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.000076 to 0.00019 mg/L. The bores were in the Waikato and Marlborough regions.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Procymidone was detected in one well at a concentration of 0.056 µg/L, ie, 0.000056 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Procymidone was found in one sample, at 0.08 µg/L, ie, 0.00008 mg/L.

### Removal methods

No information is available on processes that can be used to remove procymidone from water.

### Health considerations

Level causing no toxicological effect:

* mouse: 100 ppm in the diet, equal to 15 mg/kg bw/day
* rat: 250 ppm in the diet, equivalent to 12.5 mg/kg bw/day
* dog: 100 mg/kg bw/day.

Estimates of acceptable daily intake (ADI) of procymidone for humans are 0–0.2 mg/kg bw (IPCS).

In 1989 JMPR established an ADI of 0–0.1 mg/kg bw based on the NOAEL of 12.5 mg/kg bw per day identified in studies of reproductive toxicity in rats. The 2007 meeting established an ADI of 0–0.1 mg/kg bw based on a NOAEL of 12.5 mg/kg bw per day in a two-generation study of reproductive toxicity and a study of developmental toxicity in rats, on the basis of hypospadias and alterations in testes, prostate and epididymis weights, and a safety factor of 100. The ADI was supported by NOAELs of 14 mg/kg bw per day in the two-year study in rats and 15 mg/kg bw per day in the two-year study in mice. The meeting established an ARfD of 0.1 mg/kg bw based on a NOAEL of 12.5 mg/kg bw on the basis of hypospadias (FAO/WHO 2007).

USEPA (1994) established a RfD of 0.035 mg/kg/day, based on a NOEL of 3.5 mg/kg/day based on the results of the rat developmental study. An uncertainty factor of 100 was recommended to account for the inter-species extrapolation and intra-species variability. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.035 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for procymidone is 1.15 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 2.5 mg/kg bw, and the ARfD is 0.03 mg/kg bw. In May 2017 APVMA adjusted this ARfD to 0.1 mg/kg. The ARfD for procymidone only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EC (2007) established an ADI of 0.025 mg/kg/d and an ARfD of 0.035 mg/kg/d. France proposed to set lower ADI and ARfD values (ADI 0.0028 mg/kg bw/d, ARfD 0.012 mg/kg bw) compared with the values derived in the first peer review. Member states and the European Commission confirmed that these toxicological reference values should be used for the risk assessment of MRLs although there was no formal adoption of these values by the Standing Committee on Food Chain and Animal Health (EFSA 2011).

The recommendation (APVMA 2004) for a schedule 7 reclassification in the [Standard for the Uniform Scheduling of Drugs and Poisons](http://www.tga.gov.au/ndpsc/susdp.htm) (SUSDP) was on the grounds that the chemical is a reproductive and developmental toxin in laboratory animals, in the absence of maternal toxicity, and that this mechanism of toxicity is likely to be relevant to human beings.

Procymidone was negative in various mutagenicity assays, there was no evidence of genotoxicity, and its carcinogenicity has not been classified by IARC. As at September 2008 the USEPA has classified procymidone in Group B: a probable human carcinogen. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

The provisional MAV for procymidone in drinking-water was recalculated for non-carcinogenic effects, based on an ADI of 0.1 mg/kg, as follows:

0.1 mg/kg body weight per day x 70 kg x 0.1 = 0.35 mg/L

2 L

However, because procymidone is unlikely to be found in New Zealand drinking-waters, it was decided to retain the 0.7 mg/L MAV from DWSNZ 1995 and 2000. The 0.7 mg/L MAV had been derived by using the proportion of allowable daily intake allocated to drinking-water = 0.2. The 1989 Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues had decided to adopt a fraction of 0.1 instead (*FAO Plant Production and Protection Paper* 99, 1989, and Part II – Toxicology. *FAO Plant Production and Protection Paper* 100/2, 1990, as cited in IPCS INCHEM).

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# Prohexadione-calcium

CAS No. 127277-53-6. The IUPAC and CAS name for prohexadione-calcium is calcium 3-oxido-5-oxo-4-propionylcyclohex-3-enecarboxylate. Sometimes spelt prohexadione calcium. This substance is a derivative of [prohexadione](http://www.alanwood.net/pesticides/prohexadione.html), CAS No. 88805-35-0.

### Maximum Acceptable Value

Prohexadione-calcium is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Prohexadione-calcium is a plant growth regulator, used in Europe on winter wheat and barley, and in the US on apples and pears. It reduces vegetative growth by inhibiting the synthesis of gibberellin, a naturally occurring plant hormone.

Prohexadione-calcium appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

EC (2000) stated that under the proposed and supported conditions of use there are no unacceptable effects on the environment. EFSA (2013) expects DT90 values of prohexadione are expected to be lower than 39 days. One metabolite, tricarballylic acid is a naturally occurring compound detected in a wide range of plants (EFSA 2015).

Prohexadione calcium is not expected to persist in the environment based on laboratory studies submitted. Its low octanol/water partition coefficient and low persistence suggest little or no potential to bioaccumulate. The major route of dissipation is oxidative mineralisation to carbon dioxide in the soil. Prohexadione calcium is likely to be mobile in some soils but its rapid degradation suggests little potential to contaminate most groundwater. Estimated drinking water concentrations from surface water sources are not likely to exceed 0.035 mg/L. The water solubility of prohexadione-calcium is about 170 mg/L (USEPA 2000).

Prohexadione calcium hydrolysis is strongly pH dependant with half-lifes of 4.4 days at pH 5, 65 days at pH 7, and is stable to hydrolysis at pH 9.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See USEPA (2001).

### Health considerations

The ADI for prohexadione-calcium is 0.2 mg/kg/d, and there is no need for an ARfD (EC 2000), reaffirmed by EFSA (2013, 2015, 2017).

The US established a chronic reference dose (cRfD) of 0.80 mg/kg/day, the selection based on both the subchronic and chronic toxicity studies in dogs. Since a similar endpoint of equal severity (minimal and moderate dilation of basophilic tubules) was observed in both studies, the results of the two studies can be evaluated using a single dose-response curve. The no-observed-adverse-effect level (NOAEL) from the subchronic study was used to establish the RfD due to the wider dose spread in the one-year study. The NOAEL of 80 mg/kg/day was based on histopathological changes (dilated basophilic tubules) in the kidneys and clinical chemistry changes seen at the lowest-observed-adverse-effect level (LOAEL) of 200 mg/kg/day. No additional uncertainty factor is needed because there is no increase in the severity of the lesions over time in the chronic study as compared to the subchronic study. The FQPA Safety Factor Committee determined that the FQPA safety factor of 1x is applicable for chronic dietary risk assessment. Thus, the chronic population adjusted dose (cPAD) is equivalent to the chronic RfD of 0.80 mg/kg/day (USEPA 2000).

USEPA (2001) reports the RfD to be 0.2 mg/kg/d, based on a one-year feeding study in dogs with a threshold No Adverse Effect Level (NOAEL) of 20 mg/kg/day, using an uncertainty factor of 100. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.20 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for prohexadione calcium is 1.40 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for prohexadione-calcium is 0.2 mg/kg body weight, with a NOEL of 20 mg/kg bw, and the ARfD is 1.5 mg/kg bw. In January 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

USEPA (2000) stated in two-year chronic toxicity/carcinogenicity studies in rats and mice, prohexadione calcium was negative for carcinogenicity when administered at dose levels adequate for the testing of carcinogenic potential. In accordance with the USEPA Draft Guidelines for Carcinogen Risk Assessment (July 1999), the HIARC classified prohexadione calcium as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

No MAV.

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# Prometryn

CAS No. 7287-19-6. The IUPAC name for prometryn is N2,N4-diisopropyl-6-methylthio-1,3,5-triazine-2,4-diamine. The CAS name is N,N′-bis(1-methylethyl)-6-(methylthio)-1,3,5-triazine-2,4-diamine. Also called prometryne.

### Maximum Acceptable Value

Prometryn is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

### Sources to water

Prometryn is a pre- or post-emergence methylthiotriazine herbicide (triazine), sometimes used with simazine and trifluralin.

Prometryn appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Prometryn is moderately persistent in the soil, with a field half-life of one to three months; it will persist longer under dry or cold conditions, which are not conducive to chemical or biological activity. Volatilisation is not significant under most field conditions.

No significant hydrolysis or breakdown in water, was found when prometryn was tested over a period of 28 days in water ranging from slightly acidic to slightly alkaline and over a variety of test temperatures.

Laboratory mobility data for prometryn indicate that it has the potential to leach into groundwater and will be most mobile in sandy, alkaline soils which contain little organic matter or clay.

The water solubility of prometryn is about 35–40 mg/L.

NPIC (1994) quotes for prometryn a soil half-life of 60 days, water solubility of 33 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of moderate.

If released to soil, prometryne is expected to have very high to slight mobility based upon a range of Kocs from 39.4 to 3,473. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 1.2 x 10-8 atm-cu m/mole. However, estimated half-lifes for volatilisation of prometryne from soil range from 41 to 60 days for shallow to deep placement and varying water evaporation rates. Half-lifes for the biodegradation of prometryne in aerobic and anaerobic soil have been reported as 150 and 360 days, respectively. If released into water, prometryne is expected to adsorb to suspended solids and sediment based upon Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 48 suggests the potential for bioconcentration in aquatic organisms is moderate. Hydrolysis half-lives for prometryne are reported as 52, 78 and 80 days at pHs of 4, 6 and 8, respectively (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

One water utility in the US reported detecting prometryn in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0023 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The manufacturer satisfied the USEPA (1996) that concerns related to hexachlorobenzene and pentachlorobenzene impurities have been addressed.

The triazines are generally well-absorbed by the mammalian gut. While the breakdown of prometryn is not adequately understood, available data indicate that, in rats, most of the herbicide is excreted in urine and faeces within 48 hours of administration.

NOEL: 150 ppm in a two-year feeding study with dogs, equivalent to 3.75 mg/kg body weight (critical effect liver and kidney degeneration and bone marrow atrophy). The USEPA established an oral reference dose (RfD) of 0.04 mg/kg/d (USEPA 1992/1996). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.04 mg/kg/d, and an ARfD of 0.12 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for prometryn is 3.96 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for prometryn is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw.

Prometryn was classified by the USEPA’s Office of Pesticide Program’s Carcinogenecity Peer Review Committee as a Group E Carcinogen (no evidence of human carcinogenic potential).

### Derivation of Maximum Acceptable Value

No MAV.

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# Propachlor

CAS No. 1918-16-7. The IUPAC name for propachlor is 2-chloro-N-isopropylacetanilide, or α-chloro-N-isopropylacetanilide. The CAS name is 2-chloro-N-(1-methylethyl)-N-phenylacetamide. Sometimes called acylide or alpha-propachlor.

### Maximum Acceptable Value

Propachlor is not mentioned in the WHO Guidelines, and does not have a MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L; minor excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

Propachlor should not contain more than 20 g/kg of N,N-diisopropylaniline, or 18 g/kg of 2-chloroacetanilide.

### Sources to water

Propachlor is a pre-emergence and early post-emergence chloracetamide herbicide used against annual grasses and certain broad-leaved weeds, widely used to protect corn, onion, cabbage, rose bushes, and ornamental plants. It was first used in 1965.

Propachlor appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 26.7 tonnes of propachlor were used in New Zealand in 2004, at an application rate of 6,480 grams of active ingredient per hectare.

The EU (2008) requires that Member States shall ensure that:

(a) authorisations for plant protection products containing propachlor are withdrawn by 18 March 2009

(b) no authorisations for plant protection products containing propachlor are granted or renewed from the date of publication of this Decision.

This was based on human health issues, and because it has harmful effects on groundwater and in particular the leaching to groundwater is above 0.0001 mg/L in all modelled scenarios for three relevant metabolites.

### Forms and fate in the environment

The adsorption of the compound to soil particles and organic matter is only moderate. This leads to the potential for leaching through the soil profile and into groundwater. However, all studies show that this potential is unlikely to be realised in practice. Very high rainfall is required to move residues 30 cm down the soil profile. Most authors report that the great majority of residues remain within the upper 4 cm of soil. The characteristics of the soil greatly influence movement of the compound. Most leaching occurs in sandy soil with little organic matter. Concentrations in surface and groundwater in the USA were consistently low, the maxima being at 0.01 mg/L in surface and 0.00012 mg/L in groundwater.

Soil persistence can range from 28 to 42 days post-spraying, and is resistant to photo-decomposition. By far the most significant factor in reducing propachlor levels in soil and water is degradation by micro-organisms. Both bacteria and fungi have been shown to be involved in breakdown of the compound.

Propachlor has three major degradates – propachlor oxanilic acid, propachlor sulfinylacetic acid, and propachlor sulfonic acid that appear to be persistent and very mobile. These three degradates have carboxylic or sulfonic acid functional groups, which render a negative (anionic) character to the molecules under normal environmental conditions. These degradates have a high mobility in soils and, based on laboratory aerobic soil metabolism and terrestrial field dissipation studies, appear to persist much longer than the parent compound. All three degradates were detected through the lowest soil depth interval sampled in the field dissipation studies (USEPA 1998).

Propachlor has a reported half-life in soil of up to three weeks. Almost complete degradation within less than six months has been reported in most studies. Environmental conditions affect the rate of degradation which is favoured by high temperature and soil moisture content. Studies in which longer persistence of propachlor in the soil was reported were conducted under conditions of low temperature or dry soil. Adequate nutrient levels in the soil are also necessary for degradation. The conjugated N-isopropylaniline metabolite is much more persistent than the parent compound. Residues of this metabolite have been found up to two years after the application of propachlor experimentally at higher rates than would normally be used in agriculture.

The major route of loss of propachlor from water is biotic degradation. The rate of loss of propachlor from water is, therefore, dependent on the microbial population. A study on water with few bacteria present showed a half-life of about five months. In another study, cleavage of the ring did not occur within six weeks. Laboratory model ecosystem studies showed almost complete degradation of propachlor within 33 days (IPCS 1992).

The water solubility of propachlor is about 600–700 mg/L; IPCS (1992) reports this as 70 mg/L, almost certainly in error.

NPIC (1994) quotes for propachlor a soil half-life of 6.3 days, water solubility of 613 mg/L and a sorption coefficient (soil Koc) of 80. This resulted in a pesticide movement to groundwater rating of low.

If released to soil, propachlor is expected to have high mobility based upon Koc values in the range of 73 to 125. Volatilisation from moist soil surfaces is expected to occur slowly based upon an estimated Henry’s Law constant of 3.6 x 10-7 atm-cu m/mole. Volatilisation from dry soil surfaces is not expected based upon the vapour pressure of propachlor. Propachlor is not persistent following its application as a herbicide. The biodegradation half-life of propachlor in a sandy loam soil incubated in the dark at 24 to 26°C was 2.7 days and field dissipation half-lifes ranged from 1 to 5.8 days following application of propachlor at a rate of 6 lbs/acre to fields located in Iowa, Nebraska, and Texas. If released into water, propachlor is not expected to adsorb to suspended solids and sediment based upon the range of Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. Propachlor degraded slowly in a lake water/sediment system maintained under anaerobic conditions with a half-life of 146 days. BCF values of 1 to 74 suggest bioconcentration in aquatic organisms is low to moderate. Propachlor did not undergo hydrolysis in aqueous solutions at pH 5, 7, and 9 over the course of a 30-day incubation period (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Six water utilities in the US reported detecting propachlor in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.05 mg/L.

### Removal methods

Some propachlor is adsorbed to some types of soil so treatment processes that remove particulate matter may be reasonably effective at reducing the concentration of propachlor in water; however, the concentration of three major degradates is unlikely to change greatly. Some newer advanced oxidation processes may be more effective.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Propachlor has been tested in short-term and long-term exposure studies on rats, mice and dogs. The liver and kidneys are the target organs. In dogs, the no-observed-adverse-effect level (NOAEL) was 45 mg/kg body weight in a three-month dietary exposure study. In a one-year study on dogs, the NOAEL was 9 mg/kg body weight (250 ppm in diet). The no-observed-effect level (NOEL) in a 24-month dietary exposure study on rats was 50 mg/kg diet (2.6 mg/kg body weight). In an eight-month dietary study in mice, the NOEL was 1.6 mg/kg body weight (10 ppm).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw established in two long-term studies (an 18-month study in mice and a two-year study in rats). The NOELs were based on increased relative liver weights in mice and increased absolute and relative weights of the thyroid and parathyroid glands in rats. The ADI incorporates a safety factor of 100.

EFSA (2011) quote an ADI of 0.016 mg/kg bw/d and an ARfD of 0.58 mg/kg bw.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.05 mg/kg/d; this was based on the rat chronic toxicity study (NOEL = 5.4 mg/kg/day) and a standard uncertainty factor of 100. The oral RfD had earlier been 0.013 mg/kg/d (USEPA 1992) based on decreased weight gain, food consumption, increased relative liver weights in a 90 day feeding study in rats. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 2 mg/L.

As at September 2008 the USEPA has classified propachlor as likely to be carcinogenic to humans. The USEPA (2009/2011) quotes a health advisory of 0.1 mg/L for propachlor, representing a 10-4 cancer risk.

Propachlor is on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at 19 December 2008. ERMA classifies propachlor as being a suspected human mutagen and carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for propachlor is 0.09 mg/L.

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# Propamocarb

CAS No. 24579-73-5. The IUPAC and CAS name for propamocarb is propyl 3‑(dimethylamino)propylcarbamate. It is commonly available as the hydrochloride salt, CAS No. 25606-41-1.

### Maximum Acceptable Value

Propamocarb does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Propamocarb and propamocarb hydrochloride are systemic carbamate soil and foliar fungicides for control of Oomycete diseases. Note that it is not a methyl carbamate so does not inhibit cholinesterase.

Propamocarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Propamocarb hydrochloride does not persist in the soil. Following an adaption phase, it is rapidly decomposed by micro-organisms. The average half-life is less than 30 days; 90 percent of the original material is decomposed within less than 70 days. The DT90 value of propamocarb hydrochloride is expected to be in the range of 57 to 78 days. The material does not leach and with the mineralisation being so rapid, the compound does not contaminate groundwater, even under favourable conditions. Under anaerobic conditions, propamocarb degradation was very slow in bare or flooded soil (DT50 >300 days). The compound is rapidly transferred from the water to the soil in a flooded system. EFSA (2013) states that the DT90 value of propamocarb hydrochloride is expected to range between 57–78 days.

Propamocarb hydrochloride is very stable to hydrolysis and photolysis in sterile aqueous media. However, aquatic micro-organisms rapidly decompose propamocarb hydrochloride (up to 97 percent within 35 days), with CO2 being the major degradate. The material is also readily bound to the sediment.

Propamocarb hydrochloride is highly soluble in water, about 100 percent.

NPIC (1994) quotes for propamocarb hydrochloride a soil half-life of 30 days, water solubility of 100 percent and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

ICPS (1986) derived an ADI for man of 0–0.1 mg/kg b.w. on the basis of minimal nonspecific toxicity (ie, reductions in body weight and food consumption) observed in a two-year feeding study in rats. JMPR adjusted the ADI to 0 to 0.4 mg/kg body weight in 2005, based on a NOEAL of 39 mg/kg/d on the basis of vacuolisation observed in a range of organs in a 52-week study on dogs, using a safety factor of 100.

In a two-year feeding chronic toxicity/carcinogenicity study using rats there was no evidence of carcinogenicity or other treatment-related effect except for a possible reduction in food intake in female rats at the highest level tested. Thus 41 mg/kg/day was considered to be the NOEL (EXTOXNET 1997).

The USEPA (1995) quoted a chronic RfD for propamocarb hydrochloride of 0.11 mg/kg/d based on a two-year feeding study in dogs. This decision is based on the threshold LOEL of 33.3 mg/kg/day in males and females), the lowest dose tested in that study. Body weight gain depression, decreased food efficiency and gastritis were observed in males of this dose group. The Agency applied an uncertainty factor (UF) of 100 to account for both interspecies extrapolation and intraspecies variability. An additional UF of 3 was used to account for the lack of a NOEL. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.12 mg/kg/d, and an ARfD of 2.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for propamocarb hydrochloride is 20 mg/L.

Propamocarb hydrochloride was evaluated by the JMPR in 1984, 1986, 1987 and 2005, when an ADI of 0–0.4 mg/kg bw and an ARfD of 2 mg/kg bw were established. These values were reaffirmed in JMPR (2014).

The EC (2007) derived an ADI of 0.29 mg/kg body weight for propamocarb hydrochloride, and an ARfD of 1 mg/kg/d; these values were reaffirmed by EFSA (2014 and 2015). In order to perform the risk assessment compliant with the risk assessment residue definition, the ADI and ARfD for propamocarb hydrochloride were recalculated to propamocarb equivalents by applying the molecular weight conversion factor. The recalculated ADI and ARfD values for propamocarb are 0.244 mg/kg bw/d and 0.84 mg/kg bw, respectively EFSA (2012, 2013, 2014, 2015).

The Acceptable Daily Intake (ADI) adopted in Australia for propamocarb is 0.4 mg/kg body weight, based on a one-year dietary dog study; a NOAEL of 39 mg/kg bw/d was based on vacuolization in epididymes, lacrimal glands, lymph nodes, oesophageal glands, salivary glands and uterine cervix at the next higher dose (<https://apvma.gov.au/>). The ARfD is 2 mg/kg.

### Derivation of Maximum Acceptable Value

No MAV.

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# Propanil

CAS No. 709-98-8. The IUPAC name for propanil is 3’,4’-dichloropropionanilide. The CAS name is N-(3,4-dichlorophenyl)propanamide. Propanil has occasionally been called DCPA (but so is chlorthal dimethyl).

### Maximum Acceptable Value

WHO (2004/2011/2017) states that although a health-based value for propanil can be derived, this has not been done, because propanil is transformed readily into metabolites that are more toxic. Therefore, a guideline value for the parent compound is considered inappropriate, and there are inadequate data on the metabolites to allow the derivation of a guideline value for them.

In DWSNZ 1995, 2000 and 2005, the provisional MAV for propanil in drinking-water had been 0.02 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.7 mg/L; minor excursions above this level would need to occur over a significant period to be of health concern, as the health-based guideline is based on long-term effects.

Propanil should not contain more than 10 mg/kg of 3,3′,4,4′-tetrachloroazobenzene (TCAB), 2 mg/kg of tetrachloroazoxybenzene or 10 g/kg of 3,4-dichloroaniline (EFSA 2011). The use of propanil is no longer authorised within the EU.

### Sources to water

Propanil may enter source waters as the result of its application as a selective contact acetanilide (or anilide) herbicide. It is used post-emergence (mainly in rice) to control broadleaved and grass weeds. Residues of less than 0.03 mg/L were detected in 162 water samples collected from 16 rice fields treated with 0.4–2.8 kg of propanil per ha, 1–120 days after application. It is also used in a mixture with MCPA for wheat.

It is not registered currently (2005/2008/2017) in New Zealand, although it has been in the past. Propanil does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals).

### Forms and fate in the environment

Propanil is degraded rapidly in water by sunlight to phenolic compounds. In soil propanil is biodegraded to various metabolites with half-lifes ranging from one to 15 days. The recommended average soil half-life is one day.

Propanil has medium mobility in sand, sandy loam and clay loam soils, and has low mobility in silty clay loam and silt loam soils, according to available mobility studies. Based on its mobility characteristics (highly soluble, medium Kd and Koc values), propanil has the potential to reach groundwater, but it is not likely to persist as propanil for a sufficient time to leach in amounts that would be a concern (USEPA 2006).

The available data indicated that hydrolysis or aqueous photolysis may not contribute significantly to the degradation of propanil in shallow aquatic environments. The potential for groundwater exposure by propanil or the metabolite 3,4-DCA above the parametric drinking water limit of 0.1 μg/L is low (EFSA 2011).

The water solubility of propanil ranges from 100 to 200 mg/L and the sorption coefficient is 149 mL/g.

NPIC (1994) quotes for propanil a soil half-life of one day, water solubility of 200 mg/L and a sorption coefficient (soil Koc) of 149. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any detectable concentrations of propanil (limit of detection = 0.0001 mg/L) (ESR 2001).

Although used in a number of countries, propanil has only occasionally been detected in groundwater (WHO 2004).

### Removal methods

No specific information on methods of removing propanil from water is available. However, chlorine has been reported to be effective in the break down of this family of pesticides. Activated carbon treatment is likely to be effective too. Slow sand filtration has no effect on the concentrations of these pesticides.

### Recommended analytical techniques

#### Referee method

Solid phase extraction, HPLC with UV detection (EPA 532).

#### Some alternative methods

1. Liquid–liquid extraction, HPLC with UV detection (EPA 632.1).

2. The following information may be useful:

Propanil can be determined in water samples by extraction with methylene chloride and analysis by gas chromatography with a nitrogen phosphorus detector (eg, Method EPA 507). Confirmation by a second capillary column with different polarity is strongly recommended. No information is available for the limit of quantitation. EFSA (2011) suggests LC-MS for propanil and 3,4-DCA.

### Health considerations

Based on the submitted data, the USEPA (2006) does not expect any potential for the formation of halogenated dibenzo-p-dioxin and dibenzofuran contaminants in measurable quantities during the manufacture of propanil.

Propanil and its metabolites do not appear to accumulate in tissues. Six metabolites have been detected in urine.

Propanil has moderate acute toxicity. Two of its environmental metabolites, 3,4‑dichloroaniline (see datasheet) and 3,3’,4,4’-tetrachlorobenzene are more toxic than the parent compound; these two chemicals, along with tetrachloroazoxybenzene (TCAOB) may also be impurities in the commercial product. Animal studies show that under conditions of long-term exposure, propanil is toxic to red blood cells.

The probable oral lethal dose for humans is 0.5–5 g/kg body weight. Exposure produces local irritation and central nervous system depression. Ingestion causes irritation with a burning sensation in the mouth, oesophagus, and stomach, with gagging, coughing, nausea and vomiting, followed by headache, dizziness, drowsiness and confusion.

Workers from a pesticide plant who were exposed to the propanil metabolite 3,4‑dichloroaniline showed signs of methaemoglobinaemia. Of the 28 workers exposed to 3,4-dichloroaniline and propanil, 17 showed signs of chloracne, which was attributed to the presence of contaminants.

USEPA (2006) quotes a chronic RfD of 0.009 mg/kg/d based on a LOAEL of 9 mg/kg/d from a chronic toxicity/carcinogenicity study in rats; effects noted were increased methaemoglobin; increased spleen weight in females; and enlarged seminal vesicles/ prostates in males. The oral RfD had earlier been 0.005 mg/kg/d (USEPA 1992) based on increased relative spleen weight in females in a two-year feeding study in rats. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.009 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for propanil is 0.063 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.2 mg/kg body weight, with a NOEL of 20 mg/kg bw from a two-year oral study in rats. The NOEL is based on decreased bodyweight gain, mild anaemia and organ weight changes. The ADI incorporates a safety factor of 100.

EFSA (2011) states that the Acceptable Daily Intake (ADI) is 0.02 mg/kg bw/day, based on the LOAEL in the one-year dog study and using an increased safety factor of 300 because of the use of a LOAEL. The Acute Reference Dose (ARfD) is 0.07 mg/kg bw based on the 30-day dog study and applying a safety factor of 100. Reaffirmed by EFSA (2013). It was also concluded that major metabolite 3,4-dichloroaniline (3,4-DCA) had a higher acute toxicity than propanil; nevertheless, no toxicological reference values could be derived for this metabolite.

Propanil is not considered to be genotoxic. However, at least one of propanil’s environmental metabolites (TCAB or 3,3’,4,4’-tetrachloroazoxybenzene) is genotoxic. Data from a limited study in rats do not provide evidence of carcinogenicity. As at September 2008 the USEPA considered there was suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential.

### Derivation of Maximum Acceptable Value

WHO (2004/2011) states that although a health-based value for propanil can be derived, this has not been done, because it is readily transformed into metabolites that are more toxic; therefore, a guideline value for the parent compound is considered inappropriate, and there are inadequate data on the metabolites to derive a guideline value for them. Authorities should consider the possible presence in water of more toxic environmental metabolites.

In the 1995, 2000 and 2005 DWSNZ, the provisional MAV had been derived from the following:

As the limited data available do not provide evidence of carcinogenicity, a tolerable daily intake approach has been used for the derivation of the MAV for propanil in drinking-water. The no-observable-adverse-effect level used in the derivation is from a three-month rat feeding study.

5 mg/kg body weight/day x 70 kg x 0.1 = 0.02 mg/L

2 L/day x 1,000

where:

* no observable adverse effect level = 5 mg/kg body weight per day from a three-month rat feeding study
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and an additional 10 for the short duration of the study and limitations of the database).

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# Propargite

CAS No. 2312-35-8. The IUPAC name for propargite is 2-(4-tert-butylphenoxy)cyclohexyl prop-2-ynyl sulfite. The CAS name is 2-[4-(1,1-dimethylethyl)phenoxy]cyclohexyl 2-propynyl sulfite. The typical ratio of (1RS,2RS)- and (1RS,2SR)-isomers (trans:cis) of the commercial material is 95:5.

### Maximum Acceptable Value

Propargite does not have a MAV in the DWSNZ, propargite is not mentioned in WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L, minor excursions above this level would need to occur over a significant period to be a health concern, because the health-based guideline is based on long-term effects.

### Sources to water

Propargite is a non-systemic sulphite ester acaricide to control mites on a variety of field, fruit, and vegetable crops, as well as ornamentals. Propargite appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Propargite is no longer authorised within the EU (EFSA 2013).

### Forms and fate in the environment

In water or in moist conditions, propargite degrades rapidly under alkaline conditions and is rated as “moderately persistent” to “persistent” under neutral and acid conditions. Soil and aquatic photolysis and aerobic and anaerobic metabolism occur at moderate rates. Because of its high affinity for soil and sediment, propargite has the potential to move off the site of application during rainfall, irrigation, erosion, run-off on soil particles and by drift. Given the moderate to slow degradation rates for metabolism and photolysis, and the high Koc values, propargite will probably be adsorbed to sediments and organic material if transported to surface waters.

Water solubility about 0.2 to 0.5 mg/L. Propargite has been found at 0.001 mg/L in stream water in NSW Australia.

NPIC (1994) quotes for propargite a soil half-life of 56 days, water solubility of 0.5 mg/L and a sorption coefficient (soil Koc) of 4000. This resulted in a pesticide movement to groundwater rating of very low.

### Typical concentrations in drinking-water

In California, 405 wells were sampled to test for propargite residues from 1984 through 1991 and no residues were detected.

### Removal methods

Because of its high affinity for soil and sediment, propargite is likely to be removed from water by treatment processes designed to remove particulate matter.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Propargite generally has been shown to have low acute toxicity via the oral and dermal routes of exposure.

Propargite was first evaluated by the JMPR for residues in 1977 and toxicology in 1978, with subsequent evaluations in 1978, 1979, 1980 and 1982. A periodic review (toxicology) was conducted by JMPR in 1999 when an ADI of 0–0.01 mg/kg bw was estimated and it was concluded that an acute reference dose was not necessary.

The oral Reference Dose (RfD) is based on the assumption that thresholds exist for certain toxic effects. It is expressed in units of mg/kg/day. In general, the RfD is an estimate of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime; the oral RfD for propargite is 0.02 mg/kg/d (USEPA 1990) based on no adverse effects observed at the HDT in a two-year feeding study in dogs. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.04 mg/kg/d, and an ARfD of 0.08 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for propargite is 2.64 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 2 mg/kg bw from a long-term dietary study in rats. The NOEL is based on proliferation of cells in the small intestine (increased jejunal smooth muscle cells). The ADI was established in 1999 and incorporates a safety factor of 1,000. The additional 10-fold safety factor was applied to address the uncertainty due to the narrow margin between the NOEL and the dose level at which jejunal tumours were observed (3 mg/kg bw/day). In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EFSA (2011 and 2013) states that no ADI or ARfD has been set for propargite due to major drawbacks in the genotoxicity data package.

The USEPA has assessed exposure via drinking-water and has determined that there is not a risk of concern. Estimated groundwater and surface water concentrations of propargite are below the USEPA’s concern levels for acute and chronic effects. Although the cancer risk from drinking-water appears to be of concern for surface water sources, the USEPA believes that the monitoring and modelling analyses for propargite have over-estimated exposures in the present case. Moreover, establishing spray buffers around surface waters, as set forth in the RED, is expected to further reduce drinking water exposures.

As at September 2008 propargite is classified in Group B by the USEPA as a probable human carcinogen based on the appearance of intestinal tumours in test animals. The cancer concern was based on a two-year cancer bioassay conducted on Sprague Dawley rats. In that study, propargite caused fatal tumours of the intestine in both male and female rats. Propargite appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

USEPA (2015) stated that overall, there is a lack of convincing evidence for potential interaction with the estrogen or androgen pathways for mammals or wildlife. In the EDSP Tier 1 assays, there was evidence for potential interaction with the thyroid pathway in studies conducted with adult animals, but no such data exists for its effects in the young animals. However, mammalian EDSP Tier 2 testing is not recommended for propargite since additional testing is not expected to impact EPA’s current regulatory point of departures and endpoints for human health risk assessments.

### Derivation of Maximum Acceptable Value

No MAV.

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# Propazine

CAS No. 139-40-2. IUPAC name 6-chloro-N2,N4-diisopropyl-1,3,5-triazine-2,4-diamine. The CAS name is 6-chloro-N,N′-bis(1-methylethyl)-1,3,5-triazine-2,4-diamine.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of propazine in drinking-water should not exceed 0.07 mg/L (70 μg/L). Propazine is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.05 mg/L; minor excursions above this level would need to occur over a relatively long period to be a health concern, as the health-based guideline is based on medium-term effects.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.1 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

### Sources to water

Propazine is used as a pre-emergence selective systemic triazine herbicide that is usually applied to the soil, absorbed through leaves and roots, and acts by inhibiting photosynthesis within the targeted plant. Propazine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), Propazine is available as a suspension concentrate (trade name Agpro Propazine 500) or wettable powder (trade name Gesamil 50WP).

No information is available on the annual usage of specific active ingredients in New Zealand, although propazine is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Propazine has low solubility in water (20°C): 8.6 mg/L (Merck & Co 1996).

If applied to an outdoor environment, propazine has a high potential to leach into groundwater or reach surface waters by run-off. Propazine is resistant to breakdown by hydrolysis. After 28 days, at pH 5, 60 percent of applied propazine remained unhydrolysed; at pH 7, 92 percent remained; and at pH 9, 100 percent remained. However, published literature on propazine and related chloro-s-triazines indicate that the chemical may be more susceptible to hydrolysis after adsorption on to the surface of soil colloids (a surface catalysis effect). Propazine is moderately persistent to degradation under aerobic soil conditions, degrading with half-lifes of 12 to 24 weeks (calculated 15 weeks) in a non-sterile loamy sand and 8 to 12 weeks in a sterile loamy sand soil. Batch equilibrium studies suggest that propazine is mobile.

NPIC (1994) quotes for propazine a soil half-life of 135 days, water solubility of 8.6 mg/L and a sorption coefficient (soil Koc) of 154. This resulted in a pesticide movement to groundwater rating of high. Its GUS score is 3.75, indicating that it will leach to groundwater.

If released to soil, propazine is expected to have moderate mobility based upon Koc values of 84 to 500. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 4.6 x 10-9 atm-cu m/mole. Biodegradation is expected to occur slowly in soil and water surfaces. If released into water, propazine is expected to adsorb to suspended solids and sediment based upon the Koc values. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 17 suggests the potential for bioconcentration in aquatic organisms is low. Chemical hydrolysis is expected to occur slowly in moist soil surfaces with half-lifes of 62 and 127 days measured in two soils (EAWAG accessed February 2015).

Propazine’s two chlorinated degradates, des-ethyl atrazine (DEA) and diaminochlorotriazine (DACT, CAS No. 3397-62.4), are considered to have toxicity equal to the parent compound in respect to their common neuroendocrine mechanism of toxicity (USEPA 2006a).

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included propazine, so typical concentrations in New Zealand drinking-waters are unknown.

Propazine has been detected in drinking-water in the United States. It has been found in 33 out of 1,097 surface water samples and in 15 out of 906 groundwater samples. Contaminated groundwater samples have been collected from eight states. The maximum concentration found in any sample was 0.013 mg/L for surface water and 0.30 mg/L for groundwater.

Propazine has been found 42 times in groundwaters, in Waikato, Nelson, Otago and Southland, ranging from 0.00001 to 0.0025 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Propazine occurred at 0.2 µg/L, ie, at 0.0002 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Propazine occurred at 0.01 to 2.5 µg/L, ie, up to 0.0025 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Propazine occurred at 0.13 to 1.2 µg/L, ie, up to 0.0012 mg/L.

Propazine was found in two bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration in each was 0.0002 mg/L. The bores were in the Southland region.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Propazine was detected in one well at a concentration of 0.24 µg/L, ie, 0.00024 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Propazine was found in two samples, at 0.17 and 3.1 µg/L, ie, up to 0.0031 mg/L.

No information on typical concentrations in international drinking-waters was available.

### Removal methods

Oxidation of triazines by ozone is reported to be effective (Chiron et al 2000). The water chemistry, in particular the alkalinity and pH, will affect the oxidation rate. Use of activated carbon following ozonisation should be considered in order to adsorb oxidation products.

Nanofiltration (membrane technology) in water with a low natural organic matter concentration is reported to remove approximately 50 percent of atrazine and simazine (Agbekodo et al 1996). The percentage is increased to 90 to 100 percent when 3.6 mg/L of natural organic matter is present. Similar results may be expected for propazine because it is from the same chemical family and of comparable molecular size.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of propazine, although a guide to the efficiency of the process cannot be provided.

### Recommended analytical techniques

#### Referee method

Liquid solid extraction, gas chromatography-mass spectrometry (EPA 527).

#### Some alternative methods

Liquid/liquid extraction/gas chromatography-nitrogen/phosphorus detector (EPA 507).

### Health considerations

Absorption of propazine from the gastrointestinal tract has been found to be rapid and similar for all study groups. Within 48 hours of treatment, 82–95 percent of the administered dose was recovered from excreta, predominantly the urine. No specific target organs were identified (USEPA 1998).

The structural similarity of propazine to other triazine herbicides suggests that propazine may cause endocrine effects similar to those caused by atrazine in female rats (USEPA 1998). There is evidence that propazine is associated with neuroendocrine disruption (USEPA 2006a).

There is no information available regarding the greatest source of exposure to propazine for New Zealanders (ie, dermal contact, inhalation, diet: food, water).

#### Acute exposure

The LD50 for acute oral toxicity in rats is greater than 5,050 mg/kg/day (USEPA 1998), which suggests a low toxicity when compared with other pesticides.

Administration of lethal or near lethal doses to rats has caused symptoms of lethargy, muscular weakness, runny nose, emaciation, diarrhoea, and laboured breathing. It is mildly irritating to the skin, eyes, and upper respiratory tract. Contact dermatitis has been reported among workers manufacturing propazine. No cases of poisoning from human ingestion of this herbicide have been recorded (EXTOXNET 2001).

#### Chronic exposure

USEPA has based their NOAEL and LOAEL chronic toxicity concentrations upon decreased body weight (USEPA 1998). Reproductive toxicity is based on decreased ossification and decreased body weight.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 1.5 mg/kg bw from a medium-term (90-day) dog study. The NOEL is based on reduced bodyweight gain. The ADI incorporates a safety factor of 100.

The aRfD and cRfD are derived from toxicity studies on animals and are equal to the NOAEL identified in the studies after an uncertainty factor of 100X is applied to account for both intraspecies variability (ie, differences among humans) at 10X and interspecies extrapolation (ie, uncertainty in extrapolating from animal data to humans) at 10X. The aRfD for propazine is 0.1 mg/kg/day and the resulting aPAD is 0.1 mg/kg/day. The cRfD for propazine is 0.018 mg/kg/day and the resulting cPAD is 0.006 mg/kg/day (USEPA 2006a). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.018 mg/kg/d, and an ARfD of 0.10 mg/kg/d for the metabolite DACT. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for DACT is 3.30 mg/L.

The reference dose or RfD (USEPA 1990/2006/2009/2011) is 0.02 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.7 mg/L.

The International Agency for Research on Cancer has not classified propazine for its ability to cause cancer, but the USEPA has classified it as a Group “C” (a possible human carcinogen) chemical based on significant increases in mammary gland adenomas and adenomas/carcinomas in female Sprague-Dawley rats (USEPA 1998); then in 2005 it was reclassified as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for propazine in drinking-water, as follows:

0.02 mg/kg body weight per day x 70 kg x 0.1 = 0.07 mg/L

2 L

where:

* acceptable daily intake = 0.02 mg /kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent.

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# Propetamphos

CAS No. 31218-83-4. The IUPAC name for propetamphos is (RS)-[(E)-O-2-isopropoxycarbonyl-1-methylvinyl O-methyl ethylphosphoramidothioate]. The CAS name is 1-methylethyl (2E)-3-[[(ethylamino)methoxyphosphinothioyl]oxy]-2-butenoate. Also called 1-methylethyl (E3)-[[ethylamino)methoxyphosphinothioyl]oxy]-2-butenoate.

The technical grade consists of four isomers, two geometric (cis and trans) isomers, and two optical (S- and R-) isomers. The cis form predominates as the active ingredient, usually exceeding 90 percent of the technical product.

### Maximum Acceptable Value

Propetamphos is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Propetamphos is a phosphoramidothioate (organophosphorus) acaricide and insecticide commonly used to control cockroaches, flies, ants, ticks, moths, fleas and mosquitoes on contact; it is an active ingredient in some aerosols. Its veterinary use is for skin parasites such as cattle ticks and skin lice, and in sheep dips to control lice and fly strike. It is not used on crops.

Propetamphos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

In water, half of the initial amount of propetamphos disappeared within 11 days at 24°C under strongly acidic conditions (pH 3). In a weakly acidic solution (pH 6.0), half of the initial amount remained after a year. In neutral water, the half-life was 47 days while in a basic solution (pH 9.0) the half-life was 37 to 41 days. At cooler temperatures, the half-life of the compound is expected to increase significantly (greater than five years at 20°C). Desisopropyl-propetamphos is a major residue.

Water solubility is about 110 mg/L.

### Typical concentrations in drinking-water

No information is available.

### Analytical methods

#### Referee method

A referee method cannot be selected for propetamphos because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

Propetamphos can cause cholinesterase inhibition in humans; that is, it can overstimulate the nervous system causing nausea, dizziness, confusion, and at very high exposures (eg, accidents or major spills), respiratory paralysis and death.

A NOAEL of 0.05 mg/kg/d has been established based on rat studies; the RfD is 0.005 mg/kg. Over a 77-week study the rats exhibited no adverse effects at or below the very low dose of 0.05 mg/kg/day. Dogs fed the compound for six months showed no adverse effects at the dose of 0.05 mg/kg/day. Based on this NOAEL, and using a safety factor of 100, an ADI of 0.0005 mg/kg (ie, 0.03 mg/person) was established (EU 2000).

USEPA (2006) established a PAD of 0.0005 mg/kg/d for both acute and chronic dietary risk. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.0005 mg/kg/d, and an ARfD of 0.0005 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for propetamphos is 0.005 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for propetamphos is 0.001 mg/kg body weight, with a NOEL of 0.1 mg/kg bw.

A two-year carcinogenicity test on rats and a lifetime carcinogenesis study on mice were both negative. The highest dose administered to the rats was 6 mg/kg/day, and the maximum dose administered to the mice was 21 mg/kg/day. This evidence suggests that propetamphos does not cause cancer.

### Derivation of Maximum Acceptable Value

No MAV.

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# Propham

CAS No. 122-42-9. The IUPAC name for propham is isopropyl carbanilate or isopropyl phenylcarbamate. The CAS name is 1-methylethyl phenylcarbamate. Has also been called carbanilic acid, isopropyl ester.

### Maximum Acceptable Value

Propham is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.1 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

Propham should not contain more than 0.1 percent of aniline.

### Sources to water

Propham is used as a herbicide and plant growth regulator, often used as a “potato dust”.

Propham appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Propham was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in capsicums. It is also found in potatoes.

### Forms and fate in the environment

Propham is broken down by soil micro-organisms to mostly aniline and carbon dioxide, with a half-life of about 15 days.

Water solubility is about 30–250 mg/L depending on the pH. There is a high potential to leach to groundwater.

NPIC (1994) quotes for propham (IPC) a soil half-life of 10 days, water solubility of 250 mg/L and a sorption coefficient (soil Koc) of 200. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

No information is available.

### Analytical methods

#### Referee method

A referee method cannot be selected for propham because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

JMPR (1992) stated that the available toxicological data on propham were not adequate to allocate an ADI. On the basis of the effects on the haematological effects in a two-year long-term/carcinogenicity study in rats, a NOAEL of 5.7 and 7.6 mg/kg bw/day in males and females respectively, was determined. There was no evidence of carcinogenicity.

The reference dose or RfD (USEPA 1987/2006/2009/2011) is 0.02 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.6 mg/L. This was based on a 90-day rat feeding study noting the increase in male spleen weight and ChE depression in females from which was derived a NOEL of 50 mg/kg/d; the RfD was calculated using an uncertainty factor of 3000 (USEPA 1987).

Propham is not classifiable as to human carcinogenicity (Group C, IARC) and thus is assigned to weight-of-evidence Group D under the USEPA Guidelines for Carcinogen Risk Assessment.

### Derivation of Maximum Acceptable Value

No MAV.

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# Propiconazole

CAS No. 60207-90-1. The IUPAC name for propiconazole is (2RS,4RS;2RS,4SR)-1-[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole. The CAS name is 1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole.

Propiconazole is a racemic mixture of four stereo-isomers, which are separated in cis- and trans-diastereomers. All four stereo-isomers of propiconazole provide biological activity. The intrinsic activity of each isomer is different from pathogen to pathogen. The broad spectrum and high level of activity of propiconazole is the result of the combined activity of all isomers.

### Maximum Acceptable Value

Propiconazole is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, because the health-based guideline is based on long-term effects.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for propiconazole in water (set by an approval under Part 5 of the HSNO Act) of 0.0001 mg/L (0.1 µg/L).

### Sources to water

Propiconazole is a systemic foliar conazole or triazole fungicide with a broad range of activity. It is used on grasses grown for seed, mushrooms, corn, wild rice, peanuts, almonds, sorghum, oats, pecans, apricots, peaches, nectarines and plums, usually to control fungal pathogens which cause a wide range of problems such as powdery mildew, rusts and leaf spot disease. It can also be used on timber, and as a film preservative in paints and adhesives (eg, for tiles).

Propiconazole slows or stops the growth of the fungus, effectively preventing further infection and/or invasion of host tissues. Propiconazole is considered to be fungistatic or growth inhibiting rather than fungicidal. An EU review (2003) concluded that under the proposed and supported conditions of use there are no unacceptable effects on the environment provided that certain conditions are taken into account, and that none of the manufacturing impurities considered are, on the basis of information currently available, of toxicological or environmental concern.

The USEPA has approved propiconazole as an alternative to CCA for preserving wood used in millwork, shingles and shakes, siding, plywood, structural lumber and timbers and composites that are used in above ground applications only.

Propiconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), under several trade names.

Propiconazole has been found above the maximum residue limit in olive oil (NZFSA).

### Forms and fate in the environment

The soil movement and leaching potential of propiconazole is limited. Leaching in soils that are acidic, and high in clay and organic matter will be restricted to the top  
2–3 inches. In alkaline, low organic matter soils, propiconazole may leach to a maximum depth of 8–10 inches. Therefore leaching into underground water supplies is unlikely. The half-life in aerobic soil is 20–140 days, anaerobic soil 211 days. Based on its vapour pressure (Henry’s Law constant 9.2 x 10-5 Pa.m3/mole) propiconazole is not expected to volatilise from dry soil surfaces, and is stable to hydrolysis.

A high potential for groundwater exposure (80th percentile annual average recharge concentration moving below 1 m) above the parametric drinking water limit of 0.1 μg/L was indicated for relevant groundwater metabolites at all nine pertinent FOCUS groundwater scenarios for the representative uses assessed (EFSA 2017).

Water solubility is about 100–150 mg/L at pH 5.2. No significant hydrolysis, volatilisation or biodegradability has been noted in water.

NPIC (1994) quotes for propiconazole a soil half-life of 110 days, water solubility of 110 mg/L and a sorption coefficient (soil Koc) of 650. This resulted in a pesticide movement to groundwater rating of moderate.

Propiconazole shares common metabolites with other triazole-derivative chemicals, including free triazole (1,2,4-triazole) and triazole-conjugated plant metabolites (such as triazole alanine and triazole acetic acid). 1,2,4-Triazole (CAS No. 288-88-0) appears to be relatively stable in the environment, and may be found in rotational crops and drinking water (USEPA 2006). However, because the risks associated with the free triazoles are all below the USEPA’s level of concern, they are not addressed in as much detail as the risks from propiconazole.

See EFSA (2011) for a list of metabolites. 2,4-Dichlorobenzoic acid is one, and is a possible taste and odour causing compound.

The use of propiconazole in paints and adhesives gives rise to no environmental concerns in relation to groundwater or aquatic and terrestrial biota (ECHA 2014).

### Typical concentrations in drinking-water

No information is available.

### Removal methods

No information is available on processes that can be used to remove propiconazole from water. However, despite its water solubility, it is fairly strongly held in several soil types, so treatment processes that remove particulate matter should be fairly effective at reducing the concentration of propiconazole in water. Some newer advanced oxidation processes are expected to be effective too.

### Analytical methods

#### Referee method

A referee method cannot be selected for propiconazole because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

### Health considerations

IPCS (1987) stated the estimate of acceptable daily intake (ADI) for man is  
0–0.04 mg/kg bw. The NZFSA Dietary Risk Assessment ADI is 0.04 mg/kg bw.

Based on the available chronic toxicity data, the USEPA has established the RfD for propiconazole at 0.01 mg/kg/day. This was based on a 24-month oncogenicity study on mice. Liver toxicity: increased liver weight in males, and increase in liver lesions (masses/raised areas/swellings/nodular areas). LOAEL was 50 mg/kg/day and an uncertainty factor of 100. The uncertainty factor of 100 was applied to account for inter-species extrapolation and intra-species variability (USEPA 2006). The oral RfD had earlier been 0.013 mg/kg/d (USEPA 1992) based on gastric mucosal irritation in a one-year dog feeding study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.10 mg/kg/d, and an ARfD of 0.30 mg/kg/d.

EC (2003) established an ADI of 0.04 mg/kg/d and an ARfD of 0.3 mg/kg. EFSA (2011 and 2012) reaffirmed these values. EFSA (2017) changed the ARfD to 0.1 mg/kg bw.

The chronic RfD for 1,2,4-triazole is 0.05 mg/kg/d, based on reproductive studies in rats (USEPA 2006). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for 1,2,4-triazole. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for propiconazole is 3.0 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.04 mg/kg body weight, with a NOEL of 4 mg/kg bw from a two-year dietary study in rats. The NOEL is based on decreased food consumption and decreased bodyweight gain. The ADI incorporates a safety factor of 100.

JMPR (2007) reports an ADI of 0.07 mg/kg bw for propiconazole, and an ARfD of 0.3 mg/kg bw, and reaffirmed in JMPR (2013, 2014 and 2017). These values cover propiconazole plus all metabolites convertible to 2,4-dichlorobenzoic acid, expressed as propiconazole for the estimation of the dietary intakes.

EFSA (2011) reports that metabolism studies in both mammalians and plants have shown that active substances belonging to the chemical class of triazoles are degraded/metabolised to common metabolites known as triazole derivative metabolites (TDMs), the major ones being the metabolites 1,2,4-triazole, triazole alanine, triazole lactic acid and 1,2,4-triazole acetic acid. These TDMs were initially considered of no toxicological concerns, but further evaluations indicated their toxicological relevance. The toxicological profile for metabolites: 1,2,4-triazole and 1,2,4-triazole acetic acid are ADI: 0.02 mg/kg bw/d; ARfD: 0.06 mg/kg bw. The toxicological profile for metabolite: 1,2,4-triazole alanine is ADI: 0.1 mg/kg bw/d; ARfD: 0.1 mg/kg bw. See datasheet for triazole metabolites for latest ADI and ARfD.

Propiconazole has been reported to cause liver tumours in mice. As at September 2008 the USEPA has classified propiconazole in Group C for carcinogenicity (a possible human carcinogen). The Cancer Peer Review Committee recommended the RfD approach for quantitation of human risk. Therefore, the RfD is deemed protective of all chronic human health effects, including cancer (EXTOXNET 1997).

USEPA (2015) summarised: in vitro assays indicate that propiconazole has the potential to inhibit aromatase and steroidogenesis. However, there was no convincing evidence of estrogen-related effects in the mammalian studies suggesting that the in vitro effects on estradiol production are not relevant to mammals. In the FSTRA, however, there were effects on estrogen-related endpoints that could potentially be attributed to altered steroidogenesis. For the androgen pathway, in vitro assays showed a weak interaction with the androgen receptor, possibly as an AR antagonist. However, the available in vivo studies in mammals do not provide strong evidence for a direct androgenic or anti-androgenic effect from propiconazole. In wildlife, while there was less complementarity for effects in male fish compared to females, the effects of propiconazole on the androgen pathway observed in the FSTRA could also potentially be attributed to altered steroidogenesis. There was no interaction with the thyroid pathway either in mammals or wildlife. Based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for propiconazole since additional testing is not expected to impact EPA’s current regulatory point of departures and endpoints for human health or ecological risk assessments.

### Derivation of Maximum Acceptable Value

No MAV.

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# Propineb

CAS No. 12071-83-9. The IUPAC name for propineb is polymeric zinc propylenebis(dithiocarbamate). The CAS name is [[2-[(dithiocarboxy)amino]-1-methylethyl]carbamodithioato(2−)-κS,κS′]zinc.

### Maximum Acceptable Value

There is no MAV for propineb in the DWSNZ, and propineb is not mentioned in the WHO Guidelines.

### Sources to water

Propineb, a propylene analogue of zineb, is a broad spectrum polymeric dithiocarbamate foliar fungicide often used on grapes, ornamentals, potatoes, tomatoes, tropical fruits and vegetables to control blight, downy mildew and black spot, etc. The zinc content is about 20 percent; arsenic must be <0.02 percent; propylene thiourea must be <0.5 percent of the propineb content (FAO 1980).

Propineb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007). Dithiocarbamates can act as a fumigant by rapidly breaking down into methylisothiocyanate (MITC).

### Forms and fate in the environment

The rapid degradation of the active substance in laboratory experiments (half-life <1 hour) and its absorption properties in the sunlight emission spectrum indicate that direct photodegradation plays a role in degradation of the active substance under environmental conditions.

The major photolysis product detected was propylene thiourea (PTU) – CAS 2122-19-2. PTU is quickly degraded by secondary photodegradation (influence of humic acid), largely to propyleneurea, and to a lesser extent 4-imethylimidazoline and propylenediamine. Water solubility of PTU is 9–10 percent.

Propyleneurea (PU) is another important metabolite; water solubility is >20 percent. See JMPR (2004) for further discussion on metabolites.

The dithiocarbamates may also be metabolised to sulfoxides, isothiocyanate, and COS (USEPA 2001).

The half-life of propineb in soil is two to eight days, the major metabolite being propylene urea (PU). It does not leach. PU has low to moderate persistence (DT50:  
1.9–45.9 days). In soil laboratory incubations under aerobic conditions in the dark, propineb exhibited very low to low persistence, forming the major (>10 percent AR) metabolites PU (maximum 42 percent AR), PTU (maximum 31 percent AR), propineb-DIDT (maximum 26 percent AR) and 4-methyl-imidazoline (maximum 12 percent AR), which exhibited low to moderate, very low to low, very low and low persistence, respectively. Propineb is immobile in soil. PU and PTU exhibited very high soil mobility, propineb-DIDT exhibited medium mobility, and 4-methyl-imidazoline exhibited high to low soil mobility. It was concluded that the adsorption of all these compounds was not pH dependent (EFSA 2016).

In laboratory incubations in dark aerobic natural sediment water systems, propineb exhibited very low persistence, forming the major metabolites PU, propineb-DIDT and PTU (maximum 50, 36 and 27 percent AR in water, respectively, all exhibiting low persistence) and 4-methyl-imidazoline (maximum 17 percent AR in water) (EFSA 2016).

The potential for groundwater exposure by propineb and its soil metabolites PU, PTU, propineb-DIDT and 4-methyl-imidazoline above the parametric drinking water limit of 0.1 μg/L, was assessed as low in the geoclimatic conditions represented by all nine FOCUS groundwater scenarios, consequent to the representative uses that have been assessed (EFSA 2016).

Solubility in water <10 mg/L at 20°C; an exact determination of the water solubility is not possible in consequence of decomposition of propineb by hydrolysis. The compound decomposes in alkaline or acid media forming propylene diamine, carbon disulfide and propylene thiourea.

### Typical concentrations in drinking-water

No information is available.

### Removal methods

No information is available.

### Analytical methods

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2016).

### Health considerations

Propineb shows no genotoxic effects in vitro and in vivo and no carcinogenic potential.

PTU: no signs of carcinogenic potential in rats. Dose related increase in the rate of liver tumours (epigenetic) in mice. PU: elevated incidence of liver tumours (epigenetic) in mice.

The most sensitive parameter indicating treatment related effects in the long-term studies have been the thyroids of rats. Enlarged thyroids and decreased levels of protein-bound iodine were seen at 5 mg/kg bw/d.

IPCS (1977) refers to an ADI of 0.005 mg/kg bw; this was adjusted to 0.007 mg/kg in 1993, based on the NOAEL from the short-term thyroid function study in rats (10 ppm, equal to 0.74 mg/kg bw/day) using a safety factor of 100. ARfD (acute reference dose) is 0.1 mg/kg/d bw.

The lowest relevant NOAEL for propineb: 2.5 mg/kg bw/d (chronic rat); lowest relevant NOAEL for PTU: 0.14 mg/kg bw/d (chronic mouse); lowest relevant NOAEL for PU: 7.1 mg/kg bw/d (chronic mouse).

The 1993 JMPR established an ADI for propineb of 0–0.007 mg/kg bw. The 1999 JMPR reviewed the toxicology of the metabolite PTU and established an ADI and acute RfD for PTU of 0–0.0003 mg/kg bw and 0.003 mg/kg bw respectively.

EC (2003) derived an ADI for propineb of 0.007 mg/kg bw/d, and 0.0003 mg/kg bw/d for PTU; the respective ARfDs were 0.1 and 0.003 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia for propineb is 0.0005 mg/kg body weight, with a NOEL of 0.05 mg/kg bw, and the ARfD is 2 mg/kg bw. In February 2017 APVMA adjusted this ARfD to 0.003 mg/kg based on a developmental rat study; a NOAEL of 0.32 mg/kg bw/d was based on skeletal variations at the next higher dose. This group ARfD value which includes propineb and propylene thiourea (PTU) only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

The Acceptable Daily Intake (ADI) adopted in Australia for propylene thiourea (PTU) is 0.0005 mg/kg body weight, with a NOEL of 0.05 mg/kg bw, and the ARfD is 0.003 mg/kg bw.

EFSA (2016) reports: for propylene thiourea (PTU) an acceptable daily intake (ADI) is 0.002 mg/kg bw per day based on the rat multigeneration study (uncertainty factor (UF) 100) supported by the chronic mouse study; and the acute reference dose (ARfD) is 0.012 mg/kg bw based on rat developmental toxicity studies (UF 100). For the amino-acid conjugates of PTU and for PTU-S-trioxide, the reference values of PTU can be applied. For the metabolite propyleneurea (PU), both the ADI and ARfD are 0.008 mg/kg bw per day based on the carcinogenicity study in mice, and applying an UF of 1,000 because of the lack of reproductive toxicity data. For the metabolite propineb-DIDT, the ADI and the ARfD are 0.0005 mg/kg bw per day based on the 28‑day rat study, and applying an UF of 1,000 because of the limited database. For the metabolites PDA, 4-methyl-imidazoline and 2-methylthio-4-methylimidazoline no reference values could be determined on the basis of the available data (data gap for PDA). For propineb, the ADI is 0.025 mg/kg bw per day based on the chronic rat study (UF 100); the ARfD is 0.09 mg/kg bw based on the rat subchronic neurotoxicity study (UF 100).

### Derivation of Maximum Acceptable Value

There are limited and insufficient data on propineb on which to propose a MAV for drinking-water.

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# Propoxur

CAS No. 114-26-1. The IUPAC name for propoxur is 2-isopropoxyphenyl methylcarbamate. The CAS name is 2-(1-methylethoxy)phenyl methylcarbamate. Has occasionally been called PHC. It is listed by some authorities as its trade name, Baygon.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for propoxur in drinking-water.

WHO (2004 and 2011) states that propoxur is unlikely to occur in drinking-water, so have not developed a guideline value for drinking-water.

The USEPA (2006/2009/2011) established a lifetime health advisory for Baygon of 0.003 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

Propoxur should not contain more than 3 percent of o-isopropoxyphenol.

### Sources to water

Propoxur is a non-systemic carbamate insecticide and acaricide which was introduced in 1959. Propoxur is not used on food crops. It is used against mosquitoes in outdoor areas, for flies in agricultural settings, for fleas and ticks on pets, as an acaricide, on lawns and turf for ants, on flowering plants, and in private dwellings and public buildings. It is also used as a molluscicide, a chemical that kills snails. It is effective against cockroaches, aphids and leafhoppers. Propoxur is one of the chemicals that have, to a large extent, replaced DDT in the control of black flies and mosquitoes. WHO (1976) states that it has been used in hospitals, factories and stables at a concentration of 0.5 percent active ingredient against ants, flies, fleas, cockroaches, woodlice, mosquitos, bedbugs and ticks.

Propoxur appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). One trade name is Baygon. This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Because it is both highly soluble in water (1,700–2,000 mg/L or 0.2 percent) and has a lengthy soil half-life (28 days), and does not adsorb strongly to soil particles, propoxur has a high potential for groundwater penetration. In one study, there was practically no loss of propoxur from a silt-loam soil to which it was applied during a six-month period, but 25 percent of applied Baygon was lost from sand in 100 days. It is hydrolytically stable at acid or neutral pH (3–7) but degrades rapidly in alkaline conditions. In another study, propoxur was very mobile in sandy loam, silt loam and silty clay soils. The rate of biodegradation increases in soils that have been exposed previously to propoxur or other methylcarbamate pesticides.

NPIC (1994) quotes for propoxur a soil half-life of 30 days, water solubility of 1,800 mg/L and a sorption coefficient (soil Koc) of 30. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

No information is available.

### Removal methods

No information is available.

### Analytical methods

#### Referee method

A referee method cannot be selected for propoxur because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for propoxur for the above reason. However, the following method is recommended:

Reverse phase HPLC using a fluorescence detector  
(EPA 531.2; APHA 6610B which is in the supplement, S–1 to S–9).

### Health considerations

Carbamates generally are excreted rapidly in urine and do not accumulate in mammalian tissue. If exposure does not continue, cholinesterase inhibition reverses rapidly.

In rats, propoxur poisoning resulted in brain pattern and learning ability changes at lower concentrations than those which caused cholinesterase-inhibition and/or organ weight changes. The oral LD50 in mice is 23.5 mg/kg, 40 mg/kg in guinea pigs. Twelve-month old male goats have an oral LD50 greater than 800 mg/kg. The oral LD50 for technical propoxur in rats was 50 mg/kg for males and 104 mg/kg for females.

The JMPR (1989) concluded that propoxur showed moderate acute toxicity in the animal species examined. After reviewing all available data from in vitro and in vivo short-term tests, the JMPR concluded that there was no evidence of genotoxicity. The JMPR recommended an ADI of 0.02 mg/kg bw/day for propoxur.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.004 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.1 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 0.2 mg/kg bw.

Propoxur did not cause mutations in six different types of bacteria. A derivative of propoxur (N-nitroso) is mutagenic. Propoxur appeared in the USEPA September 2008 list in Group B: a probable human carcinogen, based on male rat bladder tumours. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

There are limited and insufficient data on propoxur on which to propose a MAV for drinking-water.

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# Propyzamide

CAS No. 23950-58-5. The IUPAC name for propyzamide is 3,5-dichloro-N-(1,1-dimethylprop-2-ynyl)benzamide. The CAS name is 3,5-dichloro-N-(1,1-dimethyl-2-propynyl)benzamide. Has sometimes been called proponamide, and been called pronamide in the US.

### Maximum Acceptable Value

Propyzamide is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.07 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, because the health-based guideline is based on long-term effects.

In Japan there is a surveillance level of 0.008 mg/L for propyzamide in drinking-water.

### Sources to water

Propyzamide is an amide herbicide commonly used pre- and/or post-emergence for control of certain grasses, broadleaf weeds, blackberry and nightshade, in lettuce, playing fields, lawns, legume seed crops and pasture.

EC (2003) stated that the overall conclusion from their evaluation is that it may be expected that plant protection products containing propyzamide will fulfil the safety requirements laid down in Article 5(1)(a) and (b) of Directive 91/414/EEC, and that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health.

As a result of risk concerns for children identified in the 8 March 2002 risk assessment, Dow AgroSciences agreed to voluntarily cancel all product labelled for residential use (USEPA 2002).

Propyzamide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The persistence of propyzamide in the soil is variable (half-life 2–13 months), depending on soil type and climatic conditions. Decomposition of the herbicide is slow at temperatures below 15ºC but accelerates at temperatures above this level. Persistence is greatest in sandy soils with low organic matter. The main metabolites are 3,5-dichlorobenzoic acid, 2-(3,5-dichlorophenyl)-4,4-dimethyl-5-methylene-oxazoline and N-(1,1-dimethylacetonyl)-3,5-dichlorobenzamide.

EFSA (2013) reports that in studies on the degradation of propyzamide in soil, the highest DT90 value for propyzamide was 140 days; for the soil metabolite RH-24644 a DT90 of 126 days was reported. Similar data were obtained in the field degradation studies, where DT90 value for propyzamide was reported to be 184 days.

Water solubility is about 8–11 mg/L. Its soil half-life suggests little propyzamide will leach to water. The half-life in water is 18–24 days, and it is resistant to hydrolysis and photolysis.

NPIC (1994) quotes for pronamide a soil half-life of 60 days, water solubility of 15 mg/L and a sorption coefficient (soil Koc) of 800. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

No information is available.

### Removal methods

Propyzamide binds fairly strongly to some soil types so treatment processes that remove particulate matter may reduce the concentration of propyzamide effectively.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

In the UK (DEFRA 1996) an ADI was set at 0.03 mg/kg bw/day, derived from a NOEL of 2.7 mg/kg bw/day in the two-year chronic feeding study in the mouse using a 100-fold safety margin. On the evidence of the data submitted, they considered propyzamide to be of no immediate toxicological concern. In subchronic toxicity studies using rats, the liver, thyroid and pituitary appear to be the target organs.

The Acceptable Daily Intake (ADI) adopted in Australia for propyzamide is 0.02 mg/kg body weight, with a NOEL of 1.9 mg/kg bw from a long-term (two-year) dietary study in mice. The NOEL is based on evidence of significant liver damage and an increased incidence of hepatocellular tumours. The ADI incorporates a safety factor of 100, and was first established in 1994. The safety factor does not include the evidence that the compound is a carcinogen for several organs.

EC (2007) and EFSA (2012 and 2013) established an ADI of 0.02 mg/kg/d and considered that an ARfD was unnecessary.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.08 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 3 mg/L.

The USEPA (2009/2011) quotes a health advisory of 0.1 mg/L for pronamide, representing a 10-4 cancer risk. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

In chronic feeding studies, pronamide causes an increased incidence of liver cancer in male mice, and benign testicular and thyroid tumours in rats. As at September 2008 the USEPA has classified pronamide in Group B (a probable human) carcinogen. People may be exposed to residues of pronamide in a number of food crops, meat and milk. However, chronic exposure to pronamide in the diet is at a very low level (only a small fraction of the RfD), and is not a cause for concern at this time. Pronamide is not mutagenic, but may be a potential endocrine disruptor. Propyzamide is classified as a category 3 carcinogen in the EC.

For pronamide, there is no convincing evidence for a potential interaction with the estrogen pathway. The available data indicate that androgen-related effects observed in mammals are likely due to the alterations in the liver enzyme levels resulting in enhanced testosterone metabolism and clearance. However, while there are some uncertainties regarding the potential causes of the observed effects on male parameters in the first FSTRA, these effects in concert with those observed in the other Tier 1 and OSRI studies suggest that there may be potential for interaction with the androgen pathway in fish. For the thyroid pathway, there is evidence for potential interaction of pronamide in mammals but not in amphibians. Based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for pronamide since additional testing is not expected to impact EPA’s current regulatory point of departures and endpoints for human health risk assessments (USEPA 2015).

### Derivation of Maximum Acceptable Value

No MAV.

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# Proquinazid

CAS No. 189278-12-4. The IUPAC name for proquinazid is 6-iodo-2-propoxy-3-propylquinazolin-4(3H)-one. The CAS name is 6-iodo-2-propoxy-3-propyl-4(3H)-quinazolinone.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for proquinazid, and the WHO Guidelines do not mention it.

### Sources to water

Proquinazid belongs to the new group of fungicides, the quinazolinones or azanaphthalenes, and is used to protect against powdery mildew on cereals and grapes.

Proquinazid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

The parent compound was by far the most significant component of the residue in tests on grapes and wheat grain. Proquinazid has potential to bioaccumulate and is expected to have low soil mobility. Proquinazid can be classified as “slightly degradable” (DT50 in whole aquatic systems 60–180 days) to “fairly degradable” (DT50 20–60 days) in water/sediment systems. The soil half-life (with 12 hours sunshine per day) is 38 days (APVMA 2012).

The soil degradation studies demonstrated that both parent and the major soil metabolite IN-MM671 are highly persistent in soil (proquinazid: DT90 of 231 days; IN‑MM671: a DT90 of 1,310 days) (EFSA 2009).

Water solubility is about 1 mg/L.

### Removal methods

In water/sediment systems, proquinazid partitions rapidly into the sediment so treatment processes that remove particulate matter should reduce the concentration of proquinazid in water.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See APVMA (2012).

### Health considerations

Proquinazid has low acute oral toxicity in rats.

The toxicological profile of proquinazid was investigated and sufficient data were available to conclude on an ADI value of 0.01 mg/kg bw/day and an ARfD of 0.2 mg/kg bw/day (EFSA 2009, 2012 and 2015).

The ADI in Australia for proquinazid was established at 0.01 mg/kg bw/day based on a NOAEL of 1.2 mg/kg bw/day in a two-year study in rats and applying a default safety factor of 100. The ARfD for proquinazid was established at 0.2 mg/kg bw/d based on a LOAEL of 19 mg/kg bw/d in 90-day dietary study in dogs and using a default 100-fold safety factor to account for potential inter- and intra-species differences, which is considered sufficient for the minor and largely transient effects seen (APVMA 2012). The ARfD was adjusted in February 2017 to 1 mg/kg based on an acute neurotoxicity rat study; a NOAEL of 100 mg/kg bw was based on reduced motor activity at the next higher dose (<https://apvma.gov.au/>).

COM (2005) concluded that the mutagenicity data submitted provided evidence that proquinazid is not an in-vitro or in-vivo mutagen.

USEPA (2014) established an acute RfD (= aPAD) of 0.05 mg/kg/d, and a chronic RfD (= cPAD) of 0.004 mg/kg/d. The cPAD for proquinazid will protect for carcinogenic effects because it is below the level that caused changes in liver enzyme regulation and liver toxicity.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2012. *Public Release Summary on the Evaluation of the New Active Proquinazid in the Product Dupont Talendo® Fungicide*. APVMA Product Number 64165 [53 pp]. <http://www.apvma.gov.au/consultation/public/2012/prs_proquinazid.php>

COM. 2005. *Statement on Mutagenicity and Carcinogenicity of Proquinazid (Cholangiocarcinoma in the rat)*. COM/05/S4 and COC/05/S1. Committee on Mutagenicity and Carcinogenicity of Proquinazid (Cholangicarcinoma in the Rat). [http://www.iacoc.org.uk/statements/Proquinazid.htm#](http://www.iacoc.org.uk/statements/Proquinazid.htm)

EFSA. 2009. Conclusion on the peer review of the pesticide risk assessment of the active substance proquinazid. *EFSA Journal* 7(10): 1350 [132 pp]. [http://www.efsa.europa.eu/fr/scdocs/doc/1350.pdf and for 2015](http://www.efsa.europa.eu/fr/scdocs/doc/1350.pdf%20and%20for%202015): <http://www.efsa.europa.eu/en/efsajournal/pub/4280>

EFSA. 2012. Reasoned opinion on the modification of the existing MRLs for proquinazid in tomatoes, aubergines and cucurbits with edible peel. *EFSA Journal* 10(9): 2896 [27 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/2896.pdf>

USEPA. 2014. Proquinazid: pesticide tolerances. *Federal Register* 79 FR 18810–15 [6 pp]. EPA-HQ-OPP-2012-0164. FRL-9903-11. 2014-07563. <https://www.federalregister.gov/articles/2014/04/04/2014-07563/proquinazid-pesticide-tolerances>

# Prothioconazole

CAS No. 178928-70-6. The IUPAC name for prothioconazole is (RS)-2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-2,4-dihydro-1,2,4-triazole-3-thione. The CAS name 2-[2-(1-chlorocyclopropyl)-3-(2-chlorophenyl)-2-hydroxypropyl]-1,2-dihydro-3H-1,2,4-triazole-3-thione.

The active substance used in the pesticide formulations is a racemic mixture of the two stereoisomers (R –and S – enantiomer).

### Maximum Acceptable Value

The DWSNZ do not have a MAV for prothioconazole, and the WHO Guidelines do not mention it.

### Sources to water

Prothioconazole is a broad-spectrum systemic conazole, triazole or triazolinthione fungicide.

Prothioconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](https://eatsafe.nzfsa.govt.nz/web/public/acvm-register%20and%20select%20entire%20register)).

### Forms and fate in the environment

Prothioconazole and the metabolite prothioconazole-desthio are stable to hydrolysis at environmentally relevant pHs and temperatures. Prothioconazole is rapidly photodegraded to prothioconazole-desthio in water under favourable light conditions; however, prothioconazole-desthio is persistent under further irradiation. Prothioconazole together with prothioconazole-desthio are considered stable to photodegradation on loamy sand soil. Prothioconazole photodegradation on soil is insignificant compared to metabolism. The major transformation product detected in both dark and irradiated samples is prothioconazole-desthio. Median DT90 field soil degradation values of prothioconazole and prothioconazole-desthio are 5.5 days and 140 days, respectively.

The aerobic aquatic metabolism of prothioconazole cannot be calculated adequately because prothioconazole quickly degrades to prothioconazole-desthio. Furthermore, both chemicals are of similar toxicity and there is considerable unextracted material in the studies. In addition to prothioconazole-desthio, prothioconazole degrades to prothioconazole-S-methyl, 1,2,4-triazole, prothioconazole-triazolinone, prothioconazole-triazolylketone, and CO2. Prothioconazole-desthio appears to degrade more quickly in aerobic water/sediment systems than in aerobic soil alone; half-lifes in various water/sediment systems range from 17.4 to 75.3 days. Half-lifes are longer in anaerobic conditions.

Water solubility is about 5,000 mg/L at pH 4 and 300 mg/L at pH 8.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The endpoint for prothioconazole from the developmental toxicity study in rabbits was selected for the acute dietary exposure scenario to females 13–49 years old, with a NOAEL of 2 mg/kg/day, and a developmental toxicity LOAEL of 10 mg/kg/day, based on multiple malformations including malformed vertebral body and ribs, and arthrogryposis. An uncertainty factor (UF) of 1000X (10X for interspecies extrapolation, 10X for intraspecies variations, 10X for database uncertainty) was applied, resulting in an aRfD/aPAD of 0.002 mg/kg/day (USEPA 2007). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes an ARfD of 0.02 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for prothioconazole is 0.66 mg/L.

The endpoint from the chronic/oncogenicity study in rats was selected for the chronic dietary exposure scenario, with a NOAEL of 1.1 mg/kg/day, and a LOAEL of 8 mg/kg/day, based on liver histopathology in males and females [hepatocellular vacuolation and fatty change (single cell, centrilobular, and periportal)]. An uncertainty factor (UF) of 1000X (10X for interspecies extrapolation, 10X for intraspecies variations, 10X for database uncertainty) was applied, resulting in an cRfD/cPAD of 0.001 mg/kg/day (USEPA 2007). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a chronic RfD of 0.01 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a chronic RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

The Acceptable Daily Intake (ADI) for prothioconazole adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1.1 mg/kg bw, and the ARfD is 0.03 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

The EU (2007) had established an ADI and ARfD of 0.01 mg/kg/d. EFSA (2014, 2015) states that the toxicological profile of prothioconazole was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.05 mg/kg bw per day and 0.2 mg/kg bw, respectively. The toxicological profile of prothioconazole-desthio was also evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI and an ARfD being established at 0.01 mg/kg bw per day and 0.01 mg/kg bw, respectively. Prothioconazole-desthio is more toxic than parent prothioconazole, therefore, the ADI and ARfD were established for the metabolite.

JMPR (2009) considered that the definition of the residue (for the estimation of dietary intake) for animal commodities should be the sum of prothioconazole-desthio, prothioconazole-desthio-3-hydroxy, prothioconazole-desthio-4-hydroxy and their conjugates expressed as prothioconazole-desthio. An ADI of 0–0.05 mg/kg bw was established for prothioconazole based on the NOAEL of 5 mg/kg bw per day, identified on the basis of gross and microscopic changes in the liver and kidneys in a two-year study of toxicity and carcinogenicity in rats treated by gavage, and a safety factor of 100. An ARfD of 0.8 mg/kg bw was established for women of childbearing age based on a NOAEL of 80 mg/kg bw per day, identified on the basis of a marginally increased incidence of supernumerary rudimentary ribs that might be attributable to a single exposure at 750 mg/kg bw per day in a study of developmental toxicity in rats, and with a safety factor of 100. The meeting concluded that the establishment of an ARfD for the general population was not necessary on the basis of its low acute toxicity, the lack of evidence for any acute neurotoxicity and absence of any other toxicologically relevant effect that might be attributable to a single dose (FAO/WHO 2008). An ADI of 0–0.01 mg/kg bw was established for prothioconazole-desthio based on the NOAEL of 1.1 mg/kg bw per day, identified on the basis of microscopic changes in the liver and ovaries in a two-year dietary study of toxicity and carcinogenicity in rats, and with a safety factor of 100. An ARfD of 0.01 mg/kg bw was established for women of childbearing age based on a NOAEL of 1 mg/kg bw per day, identified on the basis of increased incidence of supernumerary rudimentary ribs that might be attributable to a single exposure at 3 mg/kg bw per day in a study of developmental toxicity in rats, and with a safety factor of 100. Although the increased incidence at 3 mg/kg bw per day was only significant on the basis of the number of fetuses, this was the lower limit of a clear dose-related response curve. The meeting also established an ARfD of 1 mg/kg bw for the general population based on a NOAEL of 100 mg/kg bw, identified on the basis of clinical signs in studies of toxicity in mice and rats given single doses, and a safety factor of 100. These values were reaffirmed in JMPR (2014 and 2017).

EFSA (2014, 2015) also reports data for the metabolites:

* 1,2,4-triazole, triazole acetic acid and triazole lactic acid; ADI 0.02 mg/kg/d; ARfD 0.06 mg/kg
* triazole alanine: ADI 0.1 mg/kg/d; ARfD 0.1 mg/kg. See datasheet for triazole metabolites for latest ADI and ARfD.

The USEPA has concluded prothioconazole and its metabolites are not carcinogenic, and are classified “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EU. 2007. *Review Report for the Active Substance Prothioconazole*. *SANCO*/3923 /07 – final [10 pp]. <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2012. Reasoned opinion on the modification of the existing MRLs for prothioconazole in rape seed, linseed, poppy seed and mustard seed. *EFSA Journal* 10(11): 2952 [35 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm>

EFSA. 2014. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for prothioconazole according to Article 12 of Regulation (EC) No 396/2005. *EFSA Journal* 12(5): 3689 [72 pp]. <http://www.efsa.europa.eu/en/efsajournal/doc/3689.pdf>

FAO/WHO. 2008. *Evaluations: Part II – Toxicological* 197–326. Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues. <http://www.inchem.org/> or <http://www.inchem.org/documents/jmpr/jmpmono/v2008pr01.pdf>

JMPR. 2009. *Prothioconazole* (232) [42 pp]. <http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/lpe/en/>

JMPR. 2014. Pesticide residues in food. *Evaluations 2014.* Joint FAO/WHO Meeting on Pesticide Residues*.* <http://www.fao.org/agriculture/crops/thematic-sitemap/theme/pests/jmpr/en/>

USEPA. 2007. *Pesticide Factsheet: Prothioconazole* [55 pp]. <http://www.epa.gov/opprd001/factsheets/>

USEPA. 2007. *Prothioconazole: Human Health Risk Assessment* [220 pp]. <http://www.epa.gov/opprd001/factsheets/>

# Prothiofos

CAS No. 34643-46-4. The IUPAC name for prothiofos is (RS)-(O-2,4-dichlorophenyl O-ethyl S-propyl phosphorodithioate). The CAS name is O-(2,4-dichlorophenyl) O-ethyl S-propyl phosphorodithioate. A trade name in New Zealand is Tokuthion. Sometimes called prothiophos or dichloropropaphos.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for prothiofos, and the WHO Guidelines do not mention it.

### Sources to water

Prothiofos is a broad spectrum phenyl organothiophosphate (organophosphate) insecticide. It is used in New Zealand to control mealy bug on grapes. Applied at 500 g of active ingredient per hectare, usually once per season on dormant vines (<http://www.epa.govt.nz/search-databases/HSNO%20Application%20Register%20Documents/APP201045_Summary%20and%20Analysis%20-%20Grapes.pdf>). After 1 July 2023 prothiofos will no longer able to be manufactured in or imported into New Zealand.

Prothiofos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). It has been used in recent years as an alternative to dieldrin and heptachlor. Prothiofos appears on the list of active ingredients to be removed in July 2003 under Directive 91/414/EEC.

### Forms and fate in the environment

Prothiofos is moderately persistent in soil (aerobic soil half life about 45 days) and water, with the main removal process being volatilisation and photolysis. It binds fairly strongly to particles so is not expected to leach to groundwater.

Hydrolysis DT50 in buffer (22ºC) 120 days (pH 4), 280 days (pH 7), 12 days (pH 9). Photodegradation DT50 13 hours (<http://www.capl.sci.eg/ActiveIngredient/Prothiofos.html>).

Reported metabolites include O-2,4-dichlorophenyl O-ethyl phosphate and 2,4‑dichlorophenol.

Water solubility is about 0.07 mg/L.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of prothiofos.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Residues have been found overseas in apples, avocado and peppers. NZFSA often find prothiofos in grapes.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand is 0.0001 mg/kg body weight, with a NOEL of 0.01 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

IPCS. 1986. Organophosphorus insecticides: a general introduction. *Environmental Health Criteria* 63. INCHEM. International Programme on Chemical Safety. <http://www.inchem.org/documents/ehc/ehc/ehc63.htm>

PAN. 2002. *EU Pesticides Clear Out*. <http://www.pan-uk.org/pestnews/Issue/pn57/pn57p8.htm>

# Pymetrozine

CAS No. 123312-89-0. The IUPAC name for pymetrozine is (E)-4,5-dihydro-6-methyl-4-(3-pyridylmethyleneamino)-1,2,4-triazin-3(2H)-one. The CAS name is 4,5-dihydro-6-methyl-4-[(E)-(3-pyridinylmethylene)amino]-1,2,4-triazin-3(2H)-one.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for pymetrozine, and the WHO Guidelines do not mention it.

### Sources to water

Pymetrozine is a systemic pyridine azomethine antifeedant insecticide (it appears to act by preventing insects from inserting their stylus into the plant tissue). Pymetrozine, a new pesticide, is a replacement for organophosphate pesticides with the same use patterns. The insecticide is approved by the EC (2002) for use on fruits, vegetables, potatoes, oilseeds, hops, ornamentals and tobacco.

Pymetrozine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The aerobic soil half-life of pymetrozine and its metabolites has been measured in months, and in anaerobic conditions, >1 year. The half-life in water can be as low as a week. The environmental fate profile for pymetrozine indicates no major issues in the areas of soil persistence, mobility, and fish bioaccumulation. Minimal environmental residues of this chemical in drinking-water resources are expected. Water solubility is about 300 mg/L, from pH 5 to 9.

Pymetrozine dissipates from water mainly by partition to the sediment. Single first order DT50 of pymetrozine in the whole systems ranges between 289 and 495 days. See EFSA (2014) for an extended discussion on environmental fate and degradation products.

JMPR (2014) reports: Henry’s Law constant = <3.0 × 10–6 Pa m3 mol–1. The partition coefficient (n-octanol/water) = -0.2 at 25°C and pH 7. The hydrolysis half-life at pH 5 is 5 to 10 days; it is stable at pH 7. The photolytic half-life in water, pH 7, 25°C is 4.3 to 6.8 days.

### Typical concentrations in drinking-water

Pymetrozine is not expected to pose a risk of contaminating groundwater (due to its low mobility).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

USEPA (2004) stated that, based on chronic toxicity studies in the dog and rat, a reference dose (RfD) of 0.0057 mg/kg/day is proposed for pymetrozine. Metabolites of pymetrozine are considered to be of equal or lesser toxicity than the parent. The aRfD for pymetrozine for all populations except females (13+ years old) is 0.42 mg/kg-bw/day and is based on a lowest observable adverse effect level (LOAEL) of 125 mg/kg/day from an acute neurotoxicity study in rats and a 300X uncertainty factor. The acute population adjusted-dose (aPAD) for females (13+ years old) is 0.10 mg/kg-bw/day and is based on a NOAEL of 10 mg/kg-bwt/day from a rabbit developmental toxicity study and a 100X uncertainty factor. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.008 mg/kg/d, and an ARfD of 0.008 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pymetrozine is 0.05 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for pymetrozine is 0.006 mg/kg body weight, with a NOEL of 0.57 mg/kg bw.

The EC (2002) derived an acceptable daily intake (ADI) for humans of 0.03 mg/kg bw based on 90-day and one-year dog studies, and adopting a safety factor of 100. The ARfD was 0.1 mg/kg bw based on a rabbit developmental toxicity study, and a 28-day rat gavage study with a safety factor of 100 (restated in EFSA 2012 and 2013).

This was revised by EFSA (2014): The acceptable daily intake (ADI) and the acceptable operator exposure level (AOEL) for pymetrozine are both 0.03 mg/kg bw per day on the basis of the 90-day and one-year dog studies, applying an uncertainty factor of 100. The acute reference dose (ARfD) is 0.1 mg/kg bw on the basis of the rabbit developmental toxicity study, supported by the 28-day rat study and applying an uncertainty factor of 100. These values were reaffirmed in EFSA (2017).

EFSA (2017) states that the potential for groundwater exposure above the parametric drinking water limit of 0.1 μg/L has been identified as a critical area of concern for the relevant metabolite CGA371075 (4,6-dimethyl-1,2,4-triazine-3,5(2H,4H)-dione) in all the pertinent groundwater scenarios for all four representative uses assessed.

As at September 2008 the USEPA has classified pymetrozine as likely to be carcinogenic to humans because tumours occurred in two species (rat and mouse), in two sexes (mouse), and in two types (liver benign hepatoma and/or carcinoma). Mechanistic arguments have been advanced to explain the carcinogenicity. However, these have not been sufficient to eliminate the need for quantitative risk assessment. Because of the limited sites, low use rates, and low exposure, the risks to humans is below the level of concern. Pymetrozine is not mutagenic. It produced some neurotoxic effects, but the frequency and magnitude were low. It produced developmental effects in pups, but only at levels toxic to parents.

The triazine containing metabolites (CGA-294849 and GS-23199) are likely to be of toxicological concern. It was noted that these compounds are azapyrimidines and analogues of thymine and uracil. The uracil analogue of GS-23199 is a mutagen. The metabolite GS-23199 can serve as a marker for CGA-215525, CGA-249257, and CGA‑294849 for risk assessment purposes. These compounds are all “azauracils” that may lend to the carcinogenic nature of pymetrozine.

The pyridine-containing metabolites such as nicotinyl alcohol and trigonelline are not of toxicological concern at the levels observed in tomatoes (ca 0.01–0.1 ppm). This is in part based on the recommended daily dietary allowance for nicotinic acid being  
6–19 mg. Concentrations of nicotinamide and nicotinic acid compounds in ruminants are similar to those observed in tomatoes and, therefore, are also not of toxicological concern.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

EC. 2002. *Review Report for the Active Substance Pymetrozine*. European Commission, Health & Consumer Protection Directorate-General. 7455/VI/98-FINAL [34 pp]. See: <http://ec.europa.eu/sanco_pesticides/public/index.cfm>

EFSA. 2012. Reasoned opinion on the modification of the existing MRLs for pymetrozine in lamb`s lettuce and beans (with pods). *EFSA Journal* 10(10): 2939 [20 pp], and *EFSA Journal* 10(10): 2919 [67 pp]. <http://www.efsa.europa.eu/en/publications/efsajournal.htm> and <http://www.efsa.europa.eu/en/efsajournal/pub/3348.htm> (2013). See 2014 [102 pp] for Conclusion: <http://www.efsa.europa.eu/en/efsajournal/doc/3817.pdf>

EFSA. 2017. Pesticide risk assessment for the active substance pymetrozine in light of negligible exposure data submitted. *European Food Safety Authority (EFSA)* 15(1). <http://onlinelibrary.wiley.com/doi/10.2903/j.efsa.2017.4678/full>

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USEPA. 2000. *Pymetrozine: Factsheet, New Chemical*. Office of Prevention, Pesticides and Toxic Substances [22 pp]. <http://www.epa.gov/opprd001/factsheets/>

USEPA. 2004. Pymetrozine: notice of filing a pesticide petition to establish a tolerance for a certain pesticide chemical in or on food. *Federal Register* 69(111): 32346–51. Notices, 9 June. <https://www.gpo.gov/fdsys/pkg/FR-2004-06-09/pdf/FR-2004-06-09.pdf>

# Pyraclostrobin

CAS No. 175013-18-0. The IUPAC name for pyraclostrobin is methyl 2-[1-(4-chlorophenyl)pyrazol-3-yloxymethyl]-N-methoxycarbanilate. The CAS name is methyl [2-[[[1-(4-chlorophenyl)-1H-pyrazol-3-yl]oxy]methyl]phenyl]methoxycarbamate.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for pyraclostrobin, and it is not mentioned in the WHO Guidelines.

The specifications for the active ingredient, pyraclostrobin, permit a maximum content of 0.0003 percent (3 mg/kg of feed) of the impurity dimethyl sulfate. Dimethyl sulfate is both mutagenic and carcinogenic (ICPS 2003).

### Sources to water

Pyraclostrobin is a systemic carbanilate or pyrazole or strobilurin or strobin fungicide, most commonly used on fruit, grains and some vegetables. The strobilurin fungicides act through inhibition of mitochondrial respiration by blocking electron transfer within the respiratory chain, which in turn causes important cellular biochemical processes to be severely disrupted, and results in cessation of fungal growth.

Pyraclostrobin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). NZFSA has often found pyraclostrobin in grapes.

### Forms and fate in the environment

The aerobic soil half-life has been estimated at about one to four months, and three days in anaerobic soils. See IUPAC for metabolites. Pyraclostrobin is not mobile in soils so is not expected to reach groundwater. EFSA (2013) concluded that the residues of pyraclostrobin resulting from the soil uptake are not expected to exceed 0.01 mg/kg. EFSA (2014) states soil degradation studies found the highest DT90 value of pyraclostrobin, based on the field and laboratory studies, is 230 and 163 days, respectively. The soil desmethoxy metabolite (500M07) shows higher persistency in the soil with a DT90 value amounting to 529 days.

Pyraclostrobin breaks down rapidly in water by photolysis but is stable in the dark. Water solubility is about 2 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The JMPR meeting (IPCS 2003; JMPR 2006) concluded pyraclostrobin has no mutagenic or genotoxic properties either in vitro or in vivo, and is unlikely to pose a carcinogenic risk to humans. The meeting established an acceptable daily intake (ADI) of 0.03 mg/kg bw based on a NOAEL of 3.4 mg/kg bw per day identified in two two-year studies in rats, on the basis of reduced body-weight gain and altered liver and stomach histology at 200 mg/kg and using a 100-fold safety factor. The meeting established an acute RfD of 0.05 mg/kg bw, based on the NOAEL of 5 mg/kg bw per day for foetal toxicity at 10 mg/kg bw per day in the study of developmental toxicity in rabbits and using a 100‑fold safety factor. These values were reaffirmed in JMPR (2014).

However, the EC (2004) ARfD is 0.03 mg/kg/d; the ARfD was also 0.03 mg/kg/d. This was reaffirmed by EFSA (2011/2014).

The Acceptable Daily Intake (ADI) adopted for pyraclostrobin in Australia is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw, and the ARfD is 0.05 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.034 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyraclostrobin is 1.65 mg/L.

The USEPA (2009) classified pyraclostrobin as “not likely to be carcinogenic to humans” based on no treatment-related increase in tumours in both sexes of rats and mice, which were tested at doses that were adequate to assess carcinogenicity, and the lack of evidence of mutagenicity.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Pyrazophos

CAS No. 13457-18-6. The IUPAC name for pyrazophos is ethyl 2‑diethoxyphosphinothioyloxy-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylate or O‑6-ethoxycarbonyl-5-methylpyrazolo[1,5-a]pyrimidin-2-yl O,O-diethyl phosphorothioate. The CAS name is ethyl 2-[(diethoxyphosphinothioyl)oxy]-5-methylpyrazolo[1,5-a]pyrimidine-6-carboxylate.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for pyrazophos, and it is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; excursions above this level even for a short period are of concern, as the health-based guideline is based on short-term effects.

Pyrazophos should not contain more than 2 g/kg of sulfotep.

### Sources to water

Pyrazophos is described as a systemic organophosphorus or phosphorothiolate fungicide, and as a [pyrazolopyrimidine organothiophosphate insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#pyrazolopyrimidine_organothiophosphate_insecticides). It is especially active against powdery mildews and is generally used both for preventive and curative treatments. Major uses are on cereals, cucurbits and some fruits (eg, grapes), with lesser use on vegetables.

Pyrazophos does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals (or pesticides)). Since 2014 pyrazophos is no longer able to be manufactured in or imported into New Zealand.

### Forms and fate in the environment

The soil half-life has been estimated at about 40 days, and in water, about 10 days. Water solubility is about 4.2 mg/L. The [Adsorption Coefficient](http://www.pesticideinfo.org/Docs/ref_waterair1.html#Koc) (Koc), a measure of how strongly a chemical adheres to soil in preference to remaining dissolved in water, is 646. The California Department of Pesticide Regulation has determined that pesticides with a Koc less than 1,900 have potential to contaminate groundwater.

### Removal methods

The fairly long soil half-life suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of pyrazophos in water; activated carbon treatment should enhance the removal.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The JMPR meeting (IPCS 1992) concluded, after consideration of the long-term studies and the genotoxicity data that pyrazophos was unlikely to pose a carcinogenic hazard for humans. An ADI of 0.004 mg/kg bw was allocated on the basis of NOAELs in the two-year study in dogs and the three-generation study in rats, using a 100-fold safety factor. There was no ARfD.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.007 mg/kg body weight, with a NOEL of 0.07 mg/kg bw from a 10-day oral study in humans. The NOEL is based on headaches and decreased plasma cholinesterase activity at 0.15 mg/kg bw/day. The ADI incorporates a safety factor of 10.

### Derivation of Maximum Acceptable Value

No MAV.

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# Pyrethrin and Pyrethroids

CAS No. for pyrethrin I is 121-21-1. The IUPAC name is (Z)-(S)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (1R,3R)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate, or (Z)-(S)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (1R)-trans-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate, or (Z)-(S)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (+)-trans-chrysanthemate. The CAS name is (1S)-2-methyl-4-oxo-3-(2Z)-2,4-pentadienylcyclopenten-1-yl (1R,3R)-2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylate.

CAS No. for pyrethrin II is 121-29-9. The IUPAC name is (Z)-(S)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (E)-(1R,3R)-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate, or (Z)-(S)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl (E)-(1R)-trans-3-(2-methoxycarbonylprop-1-enyl)-2,2-dimethylcyclopropanecarboxylate, or (Z)-(S)-2-methyl-4-oxo-3-(penta-2,4-dienyl)cyclopent-2-enyl pyrethrate. The CAS name is (1S)-2-methyl-4-oxo-3-(2Z)-2,4-pentadienyl-2-cyclopenten-1-yl (1R,3R)-3-[(1E)-3-methoxy-2-methyl-3-oxo-1-propenyl]-2,2-dimethylcyclopropanecarboxylate.

CAS No. for all six pyrethrins is 8003-34-7. The individual components include [cinerin I](http://www.alanwood.net/pesticides/cinerin%20i.html) (CAS No. 25402-06-6), [cinerin II](http://www.alanwood.net/pesticides/cinerin%20ii.html) (CAS No. 121-20-0), [jasmolin I](http://www.alanwood.net/pesticides/jasmolin%20i.html) (CAS No. 4466-14-2), [jasmolin II](http://www.alanwood.net/pesticides/jasmolin%20ii.html) (CAS No. 1172-63-0), [pyrethrin I](http://www.alanwood.net/pesticides/pyrethrin%20i.html) and [pyrethrin II](http://www.alanwood.net/pesticides/pyrethrin%20ii.html).

See also UKPIS (1998 update) and ATSDR (2003) for further details.

Individual datasheets have been prepared for allethrin, bifenthrin, cyfluthrin, cyhalothrin, cypermethrin, deltamethrin, esfenvalerate, flumethrin, phenothrin, permethrin, resmethrin and tau-fluvalinate (fluvalinate is included in that datasheet).

A small amount of information on flucythrinate and tefluthrin has been included here rather than prepare separate datasheets.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for the six pyrethrins in water, CAS No. 8003-34-7 (set by an approval under Part 5 of the HSNO Act) of 0.00001 mg/L (0.01 µg/L).

### Sources to water

Pyrethrum is a naturally occurring mixture of chemicals found in certain chrysanthemum flowers. Pyrethrum was first recognised as having insecticidal properties around 1,800 in Asia and was used to kill ticks and various insects such as fleas and mosquitos. Six individual chemicals have active insecticidal properties in the pyrethrum extract, and these compounds are called pyrethrins. Pyrethrins are often used in household insecticides and products to control insects on pets or livestock. The naturally-occurring pyrethrins are esters of chrysanthemic acid (pyrethrin I, cinerin I, and jasmolin I) and esters of pyrethric acid (pyrethrin II, cinerin II, and jasmolin II).

Pyrethroids are manufactured chemicals that are very similar in structure to the pyrethrins, but are often more toxic to insects, as well as to mammals, and last longer in the environment than pyrethrins. More than 1,000 synthetic pyrethroids have been developed, but less than a dozen of them are currently used in the United States.

Commercially available pyrethroids include: allethrin\*, bifenthrin, bioallethrin\*, bioresmethrin\* cyfluthrin, cyhalothrin, cypermethrin, cyphenothrin\*, deltamethrin, esbiothrin\*, esfenvalerate (fenvalerate), fenpropathrin\*, flucythrinate\*, flumethrin, permethrin, phenothrin\*, resmethrin\*, tau-fluvalinate, tefluthrin\*, tetramethrin\*, tralomethrin\* and transfluthrin\*.

With the exception of deltamethrin, pyrethroids are a complex mixture of isomers. Those marked with an \* do not appear to be registered separately for use in New Zealand; however, some products that are registered include an ingredient using the general term “pyrethrins”.

Pyrethrins and pyrethroids are often combined commercially with other chemicals called synergists, such as piperonyl butoxide, piperonyl sulfoxide, and sesamex, which enhance the insecticidal activity of the pyrethrins and pyrethroids. The synergists prevent some enzymes from breaking down the pyrethrins and pyrethroids, thus increasing their toxicity.

Many pyrethrins and pyrethroids appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Since all six pyrethrins are structurally very similar, they are expected to have similar environmental fate properties (USEPA 2006). Based on structure analysis, degradates of pyrethrins are expected to lose their toxicological activity. The major routes of dissipation for pyrethrins in the environment are photolysis (both in water and soil, with half-lifes of less than one day in both cases) and to a lesser degree, aerobic soil metabolism. Hydrolysis under alkaline conditions is an important route of dissipation for pyrethrins in water (half-life at pH 9 is 14–17 hours); however, this reaction appears to be relatively slow under neutral or acidic conditions, which are more likely to occur in the environment.

The natural pyrethrins and many pyrethroids are rapidly degraded in the environment via photolysis, hydrolysis (slowly), and biodegradation. The environmental persistence times of many of these compounds are in the range of one to two days. The least persistent pyrethroids are allethrin, phenothrin, resmethrin, and tetramethrin. In general, the degradative processes that occur in the environment lead to less toxic products. Their strong soil binding properties mean they are not likely to leach to groundwater.

NPIC (1994) quotes for pyrethrins a soil half-life of 12 days, water solubility of 0.001 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

EFSA (2017) reports that tefluthrin has a maximum soil DT90 observed in the field dissipation studies ranged between 98 and 424 days.

See EFSA (2013) for detailed discussion.

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Pyrethrins and pyrethroids are used extensively as effective insecticides, but pose relatively little hazard to mammals (including humans); pyrethroids are some 2,250 times more toxic to insects than mammals. Exposure of the general population to pyrethrins and pyrethroids is mainly via the diet, especially vegetables and fruits that have been sprayed with these insecticides. These compounds are contained in many household insecticides, pet sprays, and shampoos. Some pyrethroids are also used as lice treatments that are applied directly to the head. A common treatment for scabies is the application of a pyrethroid to the affected skin surface excluding the scalp. The use of these products can lead to exposure.

There is evidence from animal studies that pyrethrins and pyrethroids might be capable of causing cancer in humans, but the evidence comes from animals that ingested very large amounts for a lifetime. As at May 2002 the USEPA classified pyrethrins as likely to be carcinogenic to humans, but in 2008 pyrethrins were described as “not likely to be carcinogenic to humans at doses that do not cause mitogenic response in the liver cell proliferation”. IARC has classified deltamethrin, fenvalerate and permethrin as Class 3 (not classifiable as to its carcinogenicity to humans).

Pyrethrins and pyrethroids are extremely toxic to fish and environmentally beneficial insects such as bees.

The 2000 JMPR agreed that the residue definition for compliance with the MRL and for estimating dietary intake is total pyrethrins, calculated as the sum of the six biologically active pyrethrin esters: pyrethrin 1, pyrethrin 2, cinerin 1, cinerin 2, jasmolin 1 and jasmolin 2 after calibration with the World Standard Pyrethrum Extract. Pyrethrins were last evaluated toxicologically by the 2003 JMPR. It confirmed the ADI of 0.04 mg/kg bw established by the 1972 JMPR and reaffirmed by the 1999 JMPR, and the ARfD of 0.2 mg/kg bw established by the 1999 JMPR (JMPR 2005).

Acceptable Daily Intakes (ADI) adopted in Australia are as follows:

* pyrethrum extract: 0.04 mg/kg body weight
* tefluthrin: 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw
* the ARfD for pyrethrins is 0.2 mg/kg.

The ADI and ARfD adopted by the EC for pyrethrin are as follows (reaffirmed by EFSA 2013):

|  |  |
| --- | --- |
| **ADI** | **ARfD (mg/kg/d bw)** |
| 0.04 | 0.2 |

EFSA (2017) reports an ADI of 0.005 mg/kg/d for tefluthrin and an ARfD of 0.005 mg/kg bw; plant metabolites are less toxic than the parent compound.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.044 mg/kg/d, and an ARfD of 0.07 mg/kg/d for pyrethrins. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyrethrins is 0.70 mg/L.

EXTOXNET (1996) quotes an ADI of 0.02 mg/kg/d for flucythrinate.

There is evidence that pyrethrins are associated with endocrine disruption (USEPA 2006).

### Derivation of Maximum Acceptable Value

No MAV.

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# Pyridate

CAS No. 55512-33-9. The IUPAC name for pyridate is O-6-chloro-3-phenylpyridazin-4-yl S-octyl thiocarbonate. The CAS name is O-(6-chloro-3-phenyl-4-pyridazinyl) S-octyl carbonothioate.

### Maximum Acceptable Value

WHO (2004 and 2011) did not derive a guideline value because pyridate is not persistent and is only rarely found in water. Their 0.1 mg/L GV had previously appeared in their 1998 publication.

In DWSNZ 1995, 2000 and 2005, the provisional MAV for pyridate in drinking-water had been 0.1 mg/L.

### Sources to water

Pyridate, a phenylpyridazine herbicide, may enter source waters as a result of its use as a foliar-acting contact herbicide for dicotyledonous plants and some grassy weeds.

Pyridate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)), as the emulsifiable concentrate Tough 450 EC.

### Forms and fate in the environment

Pyridate has a low water solubility (1.5 mg/L at pH 7) and relatively low mobility (rapidly adsorbed by sediments) so is not expected to be found in groundwater. It is not persistent and is hydrolysed, photodegraded and biodegraded rapidly. Under favourable conditions its environmental half-life in soils and water is of the order of a few days. The major metabolite is pydridafol, 6-chloro-3-phenyl-pyridazin-4-ol, has a half-life in soil of one to two months.

In aerobic and anaerobic soils pyridate rapidly hydrolyses to pyridafol and was then remains essentially stable. Pyridafol (CL 9673) exhibits very high to medium mobility and pyridafol-O-methyl high to low mobility in soil. Pyridate is rapidly hydrolysed in buffer aqueous solutions (22°C, pH 5, 7 and 9) to pyridafol, which is stable under these conditions. Pyridafol is rapidly photolysed in water forming two major metabolites. The degradation of pyridate was investigated in two dark aerobic water/sediment systems in a new study submitted in the updated dossier. In both systems pyridate is rapidly transformed into pyridafol, that becomes a major component in water and sediment phases. Fate and behaviour of pyridafol was investigated separately in two additional water sediment studies. Pyridafol is relatively stable in all these systems (DT50 whole system = 150 days to 491 days) (EFSA 2014).

### Typical concentrations in drinking-water

No New Zealand data, and very few data from overseas, are available for pyridate in drinking-water supplies.

### Removal methods

No information on methods of removing pyridate is available. However, because it is adsorbed to particulate matter, treatment processes using coagulation and/or filtration should reduce its concentration.

### Recommended analytical techniques

#### Referee method

No referee method has been given for pyridate because no method meets the required criteria.

#### Some alternative methods

No alternative methods have been recommended for pyridate because no methods meet the required criteria. However, the following information may be useful:

The main pyridate metabolite may be determined by high performance liquid chromatography followed by ultraviolet absorption at 254 or 280 nm (Chemie Linz). Pyridate-D and 2,4-dichlorophenoxypropionic acid isooctyl ester may be determined using a method in which the sample is dissolved in chloroform and extracted with sodium hydroxide, followed by addition of morpholine and measurement of the compounds by UV absorption at 298 nm. No quantitative limits are cited. And EFSA (2014) states that the residue definition for monitoring in water (and soil) was set as metabolite CL 9673, compound that can be monitored in drinking water and surface water by HPLC-MS/MS with a LOQ of 0.05 μg/L (equivalent to 0.09 μg/L pyridate).

### Health considerations

Following oral administration, pyridate is absorbed rapidly by the gut and distributed to the organs. It is hydrolysed in the blood and in artificial intestinal juices of rats. Pyridate is excreted rapidly, mainly in urine.

Pyridate has been tested in long-term feeding studies in rats and mice and symptoms reported included increased liver weight, decreased body growth. The oral LD50 in rats is >2,000 mg/kg bw.

USEPA (2000) quotes the chronic RfD (and cPAD) for pyridate at 0.11 mg/kg/day. This RfD is based on a NOAEL of 10.8 mg/kg/day from the chronic/carcinogenicity study in rats where decreased body weight gain was reported at the LOAEL of 67.5 mg/kg/day. This dose was supported by the results of the three-generation reproduction toxicity study. The NOAEL was 10.8 mg/kg/day based on the reported decrease in pup weights at 67.5 mg/kg/day on postnatal day 14 and 21 in both generations. An uncertainty factor of 100 (10X for interspecies extrapolation and 10X for intraspecies variation) was used. The acute Reference Dose (RfD) is 0.2 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.11 mg/kg/d, and an ARfD of 0.20 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyridate is 2.0 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.2 mg/kg body weight, with a NOEL of 18 mg/kg bw.

EC (2001) established an ADI of 0.036 mg/kg/d but did not allocate an ARfD. EFSA (2014) derived an acceptable daily intake (ADI) of 0.036 mg/kg bw per day, on the basis of the relevant parental NOAEL of 3.6 mg/kg bw per day in the multigeneration study in rats based on increased relative kidney weights in both sexes (F1 and F2 generation) at 18.8 mg/kg bw per day. An uncertainty factor of 100 was applied. Their agreed acute reference dose (ARfD) is 0.4 mg/kg bw based on the relevant maternal NOAEL of 165 mg/kg bw per day for mortalities observed at 400 mg/kg bw per day in the developmental toxicity study in rats. A standard uncertainty factor of 100 plus an additional uncertainty factor of 4 was applied because of the severity of the effect.

The International Agency for Research on Cancer has not evaluated pyridate. No evidence of carcinogenicity was found in long-term feeding studies in rats and mice. The available evidence indicated that pyridate is not genotoxic. USEPA (2000) states that pyridate is not carcinogenic in either the rat or the mouse, therefore, no carcinogenic endpoint was selected. EFSA (2014) states that based on available genotoxicity studies the substance is unlikely to be genotoxic.

### Derivation of Maximum Acceptable Value

WHO (2004 and 2011) did not develop a guideline value because pyridate is not persistent and is only rarely found in water.

In the 1995, 2000 and 2005 DWSNZ, the provisional MAV had been derived from the following:

A tolerable daily intake approach (WHO 1998) has been used for the derivation of the provisional MAV of pyridate in drinking-water. The no-observable-adverse-effect level used in the derivation is based on increased kidney weight in a two-year rat feeding study.

3.5 mg/kg body weight/day x 70 kg x 0.1 = 0.1 mg/L

2 L/day x 100

where:

* no observable adverse effect level = 3.5 mg/kg body weight per day for increased kidney weight in a two-year rat feeding study
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter and intra-species variation).

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# Pyrimethanil

CAS No. 53112-28-0. The IUPAC chemical name of pyrimethanil is N‑(4,6‑dimethylpyrimidin-2-yl)aniline. The CAS name is 4,6-dimethyl-N-phenyl-2-pyrimidinamine.

### Maximum Acceptable Value

Pyrimethanil does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for pyrimethanil in water (set by an approval under Part 5 of the HSNO Act) of 0.00001 mg/L (0.01 µg/L).

Pyrimethanil should not contain more than 1 g/kg of aniline. The commercial product usually contains up to 0.5 g/kg cyanamide (see hydrogen cyanamide datasheet); EC (2010) states that due to toxicological concerns, this level must not be exceeded.

### Sources to water

Pyrimethanil is an anilinopyrimidine fungicide commonly used pre-harvest and post-harvest on fruit trees and some vegetables. NZFSA has often found pyrimethanil in grapes.

Pyrimethanil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Pyrimethanil has been found above the maximum residue limit for lemons in 2011/12 (NZFSA).

### Forms and fate in the environment

The half-life of pyrimethanil in aerobic soil is about 30 days and 80 days in anaerobic soil (FAO 2007). Pyrimethanil is stable to hydrolysis and photolysis at pHs 5, 7 and 9 (PMEP). Water solubility is about 120 mg/L.

The major metabolite is 2-amino-4,6-dimethylpyrimidine which is expected to be moderately mobile and more persistent in the environment than the parent. Lesser metabolites, but still important, are 4-[(4,6-dimethyl-2-pyrimidinyl)amino]phenol and 4,6-dimethyl-2-(phenylamino)-5-pyrimidinol and 4,6-dimethylpyrimidine-2-amine. See EFSA (2011) for a list of metabolites.

### Typical concentrations in drinking-water

There is potential for chronic dietary exposure to pyrimethanil and 2-amino-4,6-dimethylpyrimidine in drinking-water. However the USEPA (2004) does not expect the aggregate exposure to exceed 100 percent of the chronic Population Adjusted Dose (cPAD).

### Analytical methods

#### Referee method

No MAV.

### Health considerations

An ADI of 0.17 mg/kg (rat study, safety factor 100) has been derived, and from the evaluation of the available toxicological data base of pyrimethanil, EC (2010) also concluded that there is no need to establish an acute reference dose (ARfD). These values were reaffirmed by EFSA (2011, 2018).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.2 mg/kg body weight, with a NOEL of 17 mg/kg bw, and the ARfD is 0.85 mg/kg bw. In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The 2007 JMPR meeting established an acceptable daily intake (ADI) of 0–0.2 mg/kg bw based on a NOAEL of 17.0 mg/kg bw per day on the basis of increased cholesterol and GGT levels, and histopathological changes in the liver and thyroid at 221 mg/kg bw per day in a two-year study in rats, and using a safety factor of 100. This ADI is supported a by two-generation study of reproduction in rats in which the NOAEL for parental systemic toxicity was 23.1 mg/kg bw per day, on the basis of decreased body weights and body-weight gains at 293.3 mg/kg bw per day. This ADI is also supported by the NOAEL of 20.0 mg/kg bw per day, in males in a two-year study of toxicity in mice; this NOAEL was identified on the basis of increased incidences of urinary tract lesions including bladder distension and thickening seen at 210.9 mg/kg bw per day. The meeting concluded that it was not necessary to establish an ARfD for pyrimethanil because no toxicity could be attributable to a single exposure in the available database, including a study of developmental toxicity in rats and rabbits. Observations in the study of acute toxicity in rats and clinical signs of toxicity in the pyrimethanil database appeared at doses of 640 mg/kg bw per day and greater were not considered to be relevant for establishing an ARfD since they were transient, non-specific and occurred at high doses. The meeting also considered clinical signs (vomiting) in several studies of toxicity in dogs; these were considered to be local effects and therefore not relevant in establishing an ARfD (FAO/WHO 2007). These values were reaffirmed in JMPR (2013 and 2015).

The USEPA (2004) established an oral reference dose (RfD) of 0.17 mg/kg/d bw for pyrimethanil based on a no-observed-effect level (NOEL) of 17 mg/kg/d in a rat chronic feeding toxicity study and an uncertainty factor of 100. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.17 mg/kg/d, and an ARfD of 1.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyrimethanil is 10 mg/L.

Pyrimethanil is a suspected endocrine disruptor.

As at September 2008 the USEPA classified pyrimethanil in Group C: a possible human carcinogen, based on thyroid follicular cell tumours in both sexes of the two-year rat study (NOAEL = 17 mg/kg/day). The Agency’s Cancer Peer Review Committee recommended a threshold or Margin of Exposure (MOE) approach because the thyroid tumours associated with administration of pyrimethanil in Sprague-Dawley rats may be due to a disruption in the thyroid-pituitary status.

### Derivation of Maximum Acceptable Value

No MAV.

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# Pyriproxyfen

CAS No. 95737-68-1. The IUPAC chemical name of pyriproxyfen is 4-phenoxyphenyl (RS)-2-(2-pyridyloxy)propyl ether. The CAS name is 2-[1-methyl-2-(4-phenoxyphenoxy)ethoxy]pyridine. Also spelt pyriproxifen.

### Maximum Acceptable Value

The DWSNZ (2008) state that based on health considerations, the concentration of pyriproxifen in drinking-water should not exceed 0.4 mg/L.

The WHO Guidelines 2008, 2011 and 2017 state that a guideline value is not considered appropriate for pesticides used for vector control in drinking-water. WHO (2011/2017) states that the recommended dosage of pyriproxyfen in potable water in containers should not exceed 0.01 mg/L.

### Sources to water

Pyriproxyfen belongs to the class of juvenile hormone mimics and is a broad-spectrum insect growth regulator with insecticidal activity against public health insect pests such as houseflies, cockroaches and mosquitoes. It is a WHOPES-recommended insecticide for the control of mosquito larvae, particularly to control dengue fever, including direct application to water. In agriculture and horticulture, pyriproxyfen has registered uses for the control of scale, whitefly, bollworm, jassids, aphids and cutworms.

Pyriproxifen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Pyriproxyfen degrades rapidly in soil under aerobic conditions, with a half-life of  
6.4–36 days. It disappeared from aerobic lake water sediment systems with half-lifes of 16 and 21 days. Pyriproxyfen appeared to be degraded much more slowly in anaerobic lake water sediment systems. As pyriproxyfen is a fairly new pesticide, few environmental data have been collected. The high log octanol–water partition coefficient of pyriproxyfen (log P KOW = 5.37) indicates that it is likely to adhere to particulate matter.

EFSA (2013) lists six metabolites.

Water solubility is about 0.35–0.40 mg/L.

### Typical concentrations in drinking-water

No detectable concentrations were found in surface water collected from five sites in Orange County, California (WHO 2007).

### Removal methods

No information is available on removal during water treatment. However, the relatively low aqueous solubility and high octanol–water partition coefficient suggest that pyriproxyfen should be removed by adsorption on to activated carbon and may possibly be removed during coagulation (WHO 2007).

### Analytical methods

#### Referee method

Pyriproxyfen can be analysed by extraction into dichloromethane, followed by column chromatography clean-up. The residue is then determined by gas–liquid chromatography with a nitrogen–phosphorus detector (FAO/WHO 1999).

#### Some alternative methods

Pyriproxyfen in water can be analysed by extraction with an organic solvent followed by high-performance liquid chromatography and an ultraviolet detector. The detection limit is 0.0001 mg/L (Walters 2001). See WHO (2008) for further information.

### Health considerations

The USEPA (2001; 2002) derived a chronic RfD of 0.35 mg/kg/d, based on a NOAEL of 35.1 mg/kg/d and uncertainty factor of 100 from a subchronic toxicity and chronic toxicity feeding study on the rat. There were no effects observed in oral toxicity studies including developmental toxicity studies in rats and rabbits that could be attributable to a single dose (acute) exposure. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.35 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyriproxifen is 2.45 mg/L (no acute one-day value available.)

Pyriproxyfen was evaluated by the FAO/WHO JMPR in 1999 and 2001. The 1999 JMPR established an ADI of 0–0.1 mg/kg bw, on the basis of a NOAEL of 10 mg/kg bw from two one-year studies in dogs and a safety factor of 100, and also concluded that it was not necessary to establish an acute reference dose because of low acute toxicity of pyriproxyfen. The 2001 JMPR assessed the safety of pyriproxyfen as a mosquito larvicide in potable water and concluded that intake at the target concentration for control would not present unacceptable risks (JMPR 2006).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.07 mg/kg body weight, with a NOEL of 7 mg/kg bw. Intake of pyriproxyfen from all sources is generally low and below the ADI.

EC (2010) established an ADI of 0.1 mg/kg/d, and considered that an ARfD was inappropriate. Reaffirmed in EFSA (2013).

The acute oral toxicity of pyriproxyfen is low, with LD50 values above 5,000 mg/kg of body weight in mice, rats and dogs.

The maximum recommended dosage in drinking-water of 0.01 mg/l for vector control would be equivalent to less than 1 percent of the upper limit of the ADI allocated to drinking-water for a 60 kg adult drinking two litres of water per day. For a 10 kg child drinking one litre of water, the exposure would be 0.01 mg, compared with an exposure of 1 mg at the upper limit of the ADI. For a 5 kg bottle-fed infant drinking 0.75 litre per day, the exposure would be 0.0075 mg, compared with an exposure of 0.5 mg at the upper limit of the ADI. The low solubility and the high log octanol–water partition coefficient of pyriproxyfen indicate that it is unlikely to remain in solution at the maximum recommended applied dose, and the actual levels of exposure are likely to be even lower than those calculated (WHO 2011/2017).

Based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for pyriproxyfen since additional testing is not expected to impact EPA’s current regulatory point of departures and endpoints for human health or ecological risk assessments (USEPA 2015).

JMPR concluded that pyriproxyfen was not genotoxic or carcinogenic to humans. In short- and long-term studies of the effects of pyriproxyfen in mice, rats and dogs, the liver (increases in liver weight and changes in plasma lipid concentrations, particularly cholesterol) was the main toxicological target.

As at September 2008 the USEPA has classified pyriproxyfen in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

The MAV in the 2005 and 2008 DWSNZ for pyriproxyfen in drinking-water had been derived as follows:

10 mg/kg body weight/day x 70 kg x 0.1 = 0.35 mg/L (rounded to 0.4 mg/L)

2 L x 100

where:

* no observable adverse effect level = 10 mg/kg body weight per day based on increased relative liver weight and increased total plasma cholesterol concentration in male dogs in two one-year toxicity studies
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult per day = 2 L
* uncertainty factor = 100 for intra- and interspecies variation.

This MAV is not intended to be used when considering the use of pyriproxyfen as a vector control agent in drinking-water.

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# Pyroxasulfone

CAS No. 447399-55-5. The IUPAC chemical name for pyroxasulfone is 5‑(difluoromethoxy)-1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-ylmethyl 4,5-dihydro-5,5-dimethylisoxazol-3-yl sulfone or 3-[5-(difluoromethoxy)-1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-ylmethylsulfonyl]-4,5-dihydro-5,5-dimethylisoxazole The CAS name is 3-[[[5-(difluoromethoxy)-1-methyl-3-(trifluoromethyl)-1H-pyrazol-4-yl]methyl]sulfonyl]-4,5-dihydro-5,5-dimethylisoxazole. Marketed in New Zealand as Sakura 850 WG.

### Maximum Acceptable Value

Pyroxasulfone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Pyroxasulfone, a derivative of 3-sulfonylisoxazoline, is described as an oxazole or [pyrazole](http://www.alanwood.net/pesticides/class_herbicides.html#pyrazole_herbicides) herbicide, used against weeds in wheat.

Pyroxasulfone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at June 2018 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Pyroxasulfone is stable in acidic and neutral conditions and slightly degradable in alkaline conditions (pH 9). Photolysis is only expected to be a minor degradation pathway for pyroxasulfone.

In aerobic aquatic conditions (water/sediment systems) pyroxasulfone dissipates by a combination of partitioning to the sediment from the water phase and also degradation in water and sediment. The half-life for degradation of pyroxasulfone in the complete system (sediment plus water) was similar to that of aerobic soil and ranged from 108 to 127 days. The DT50 for dissipation from the water phase ranged from 50 to 54 days. Under field conditions in summer pyroxasulfone rapidly degraded in both water and sediment, with half-lifes being less than 16 and 77 hours, respectively. Pyroxasulfone is degraded marginally faster in anaerobic conditions than aerobic conditions (APVMA 2011).

Several metabolites of pyroxasulfone have been identified from environmental fate studies; M1 and M3 are formed in the aquatic environment at the highest percentages, and M1 is formed at the highest percentages in soil. The active ingredient and the metabolite M1 are classed as persistent in the environment. The persistence and mobility of pyroxasulfone and its more persistent metabolite M1 may result in contamination of groundwater (EPA 2018).

Pyroxasulfone is mobile in soils, with KOC values of up to 120. M1 is also is also highly mobile in soil.

The normalised half-life (DT50) of pyroxasulfone in a range of soil is of the order of 6 to 80 days. M1 is persistent in soil: DT50 range of 28 to 160 days in a range of aerobic soil conditions (EPA 2018).

Water solubility is 3.5 mg/L.

### Typical concentrations in drinking-water

Based on the Pesticide Root Zone Model/Exposure Analysis Modelling System and Pesticide Root Zone Model Ground Water, the estimated drinking water concentrations of pyroxasulfone for acute exposures are estimated to be 16.7 parts per billion (ppb) for surface water and 210 ppb for groundwater (USEPA 2017).

### Analytical methods

### Health considerations

Applying a safety factor of 10 for potential interspecies difference, 10 for potential intra species differences and 10 to account for the seriousness of the observed health effects to the NOAEL of 2 mg/kg bw/d results in an ADI of 0.002 mg/kg bw/d. Applying a safety factor of 10 for potential interspecies difference, 10 for potential intra species differences and 10 to account for the seriousness of the observed health effects to the NOAEL of 100 mg/kg bw results in an ARfD of 0.1 mg/kg bw (APVMA 2011).

USEPA (2017) derived an acute RfD of 1.0 mg/kg/d and a chronic RfD (and cPAD) of 0.02 mg/kg/d. They concluded it was “not likely to be carcinogenic to humans” at doses that do not cause crystals with subsequent calculi formation resulting in cellular damage of the urinary tract. Risk is quantified using a non-linear (ie, RfD) approach.

Pyroxasulfone was not considered to be genotoxic in vivo, and was not a reproductive toxicant in rats or teratogenic in rats and rabbits, and pyroxasulfone did not produce immunotoxic effects in mice or rats. One-year studies in dogs and rats as well as the two-year carcinogenicity study in rats all yielded a NOEL of approximately 2 mg/kg bw/d. While the toxic endpoints in dogs were muscular and sciatic nerve degeneration, the effects in rats include bladder mucosa hyperplasia and bladder transition cells papilloma in addition to cardiomyopathy and sciatic nerve effects. Other effects produced by pyroxasulfone include cardiac toxicity (increased cardiomyopathy in mice and rats), liver toxicity (centrilobular hepatocellular hypertrophy) and kidney toxicity (increased incidence of chronic progressive nephropathy in dogs) (APVMA 2011).

### Derivation of Maximum Acceptable Value

No MAV.

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# Pyroxsulam

CAS No. 422556-08-9. The IUPAC chemical name for pyroxsulam is N‑(5,7‑dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)pyridine-3-sulfonamide. The CAS name is N-(5,7-dimethoxy[1,2,4]triazolo[1,5-a]pyrimidin-2-yl)-2-methoxy-4-(trifluoromethyl)-3-pyridinesulfonamide. Marketed in New Zealand as Crusader.

### Maximum Acceptable Value

Pyroxsulam does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Pyroxsulam is described as a pyridine, sulfonamide or triazolopyrimidine post-emergence systemic herbicide, commonly used on cereals.

Pyroxsulam appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Cloquintocet-mexyl (CAS No. 99607-70-2), is added to most pyroxsulam formulations as an herbicide “safener.” Safeners selectively protect crops (eg, wheat) from herbicide damage without reducing activity in target weed species. (Dow 2011). Although not listed on the New Zealand Register, a datasheet has been prepared for cloquintocet mexyl.

### Forms and fate in the environment

Pyroxsulam displays very low to moderate persistence in soils, with half-lifes around 0.8 to 15.2 days. See EFSA (2013) for persistence of metabolites. Primary routes of degradation include aqueous photolysis, aerobic soil metabolism, and possibly aerobic aquatic metabolism. The chemical appears to persist under anaerobic conditions. It was stable to the abiotic processes of soil photolysis and hydrolysis (USEPA 2008).

Pyroxsulam and most metabolites have high soil mobility but are not expected to contaminate groundwater (EFSA 2013).

The potential for groundwater contamination by pyroxsulam is low because of its low use rates, short soil half-life, and the limited mobility observed in field studies (DOW 2011).

Water solubility (20°C) is about 16 mg/L at pH 4; 3,200 mg/L at pH 7; 1.4 percent at pH 9. Henry’s Law constant is 6.94 x 10-7 Pa m3 mol-1 at 20°C. The partition coefficient is (pH 7 buffer solution) logPow = -1.01 ± 0.05 (EFSA 2013).

### Analytical methods

### Health considerations

In the metabolism study in rats, pyroxsulam was rapidly absorbed and excreted via the urine and faeces with the majority being eliminated by 12 and 24 hours post-dosing, respectively (USEPA 2008).

The USEPA (2008) derived a chronic RfD of 1.0 mg/kg/d, based on the increased absolute and relative liver weights and increased incidence of hepatocellular clear cell foci of alteration in males noted in the carcinogenicity study in mice. As there is no acute endpoint, an acute dietary risk assessment is not needed. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for pyroxsulam is 7.0 mg/L. (No acute one day value available.) Pyroxsulam is classified as “not likely to be carcinogenic to humans”.

The Acceptable Daily Intake (ADI) adopted in Australia is 1 mg/kg body weight, with a NOEL of 100 mg/kg bw. In June 2013 APVMA stated that an ARfD was considered to be unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EFSA (2013) quotes an ADI of 0.9 mg/kg bw/d based on the NOAEL of 89 mg/kg bw per day found in the one-year dog study and applying a uncertainty factor of 100. No acute reference dose (ARfD) is proposed for pyroxsulam. EC (2013) adopted the same values.

Pyroxsulam is not genotoxic in vitro or in vivo.

### Derivation of Maximum Acceptable Value

No MAV.

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# Quinoxyfen

CAS No. 124495-18-7. The IUPAC name for quinoxyfen is 5,7-dichloro-4-quinolyl 4‑fluorophenyl ether, and the CAS name is 5,7-dichloro-4-(4-fluorophenoxy)quinoline.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for quinoxyfen in drinking-water; quinoxyfen is not referred to in the WHO Guidelines.

The impurity 4,5,7-trichloroquinoline (TCQ) must not exceed 0.2 percent (wet basis, 0.25 percent dry basis) in the technical specification (EU 2003).

### Sources to water

Quinoxyfen is a quinoline fungicide commonly used against powdery mildew on a variety of crops. It is also available in combination with the curative active ingredient fenpropimorph.

Quinoxyfen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Soil dissipation studies found half-lifes from 13 to 190 days (EC 2003), and quinoxyfen appears not to leach; there was no evidence of mobility of the metabolite, 3‑hydroxyquinoxyfen, and this was not expected to be a significant metabolite. Half-lifes in water are reported at three to seven days, and 42 to 211 days in sediment. Refer to JMPR (2006) for further discussion on metabolites.

Quinoxyfen is stable under aqueous hydrolysis at pH 7 and 9, but degrades slowly under acidic hydrolysis conditions. The half-life at pH 4 at 25°C is about 75 days. The hydrolysis product was identified as DCHQ (JMPR 2006). The JMPR meeting concluded that quinoxyfen is relatively stable under aerobic conditions in soil and at neutral and alkaline pH in water, it undergoes rapid photolytic degradation in water systems, and that residues of quinoxyfen in rotational crops are unlikely.

In an anaerobic flooded soil incubation at 20°C, quinoxyfen had a half-life of 289 days. In a laboratory soil photolysis study at 25°C, quinoxyfen had a half-life of 206 days when equated to sunlight conditions in southern England. In satisfactory field dissipation studies carried out at four sites in France, two in Germany, two in the UK and in California (USA) and Ontario (Canada), all spray applications to the soil surface on bare soil plots in late spring, quinoxyfen residues remaining in the top 20 cm had best fit DT50 in the range from 14.7 to 588 days. In an aerobic aquatic mineralisation study at 21°C in fresh water, quinoxyfen had half-lifes of 115 and 129 days. In laboratory incubations at 20°C in dark aerobic natural sediment water systems, quinoxyfen moved to the sediment and had whole system half-lifes of 16–136 days (four different sediment water systems investigated). The rate of decline of quinoxyfen in a laboratory sterile aqueous photolysis experiment at 25°C was estimated to have a half-life of 18 minutes (EFSA 2018).

Based on the rapid degradation of quinoxyfen in water and its high tendency to sorb to soils, no surface water or groundwater contamination is expected (USEPA 2003).

Quinoxyfen exhibits the hazard properties of both a persistent bioaccumulative and toxic (PBT) and very bioaccumulative (vPvB) substance (EFSA 2018).

The solubility of quinoxyfen in water is 0.05–0.1 mg/L.

### Typical concentrations in drinking-water

No information available.

### Removal methods

No information available.

### Analytical methods

#### Some alternative methods

See JMPR (2006). EFSA (2018): in water: LC-MS/MS, LOQ = 0.05 μg/L.

### Health considerations

EC (2003) quotes an ADI of 0.2 mg/kg/d based on a one-year dog, two-year rat and two-generation study; an ARfD (acute reference dose) was not required. Reaffirmed in EFSA (2013).

USEPA (2003)derived a chronic RfD of 0.2 mg/kg/day based on a no observed adverse effect level (NOAEL) of 20 mg/kg/day from chronic rat, chronic dog, and rat reproduction studies and uncertainty factor of 100. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.20 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for quinoxyfen is 1.40 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for quinoxyfen is 0.2 mg/kg body weight, with a NOEL of 20 mg/kg bw; an ARfD is not necessary.

The 2005 JMPR decided that an acute RfD is unnecessary. The meeting established an ADI for quinoxyfen of 0–0.2 mg/kg bw based on NOAELs of 20 mg/kg bw per day identified in three studies: the 24-month study in rats, on the basis of reduced body-weight gain, liver and kidney effects at 80 mg/kg bw per day; the one-year study in dogs, on the basis of reduced food consumption and body-weight gain, haematological effects, and liver effects at 200 mg/kg bw per day; and the two‑generation study of reproductive toxicity in rats, based on a reduction in body‑weight gain in pups at 110 mg/kg bw per day during lactation; and with the application of a 100-fold safety factor.

The USEPA (2003)stated that using the Guidelines for Carcinogen Risk Assessment, it is proposed that quinoxyfen be classified as Group E for carcinogenicity (no evidence of carcinogenicity) based on the results of studies in two species.

JMPR (2006) reports that in a 104-week study, rats received diets containing quinoxyfen at variable concentrations to given mean intakes of 0, 5, 20 or 80 mg/kg bw per day. There were no treatment-related changes in survival or tumour incidences. The only significant findings were at the highest dose: an increase in liver weight at 20 mg/kg bw per day after 24 months was not considered to be adverse as there was no dose-related response and no associated histopathology findings. The meeting concluded that quinoxyfen was unlikely to be genotoxic. On the basis of the absence of carcinogenicity in rodents and the absence of genotoxicity, the meeting concluded that quinoxyfen is unlikely to pose a carcinogenic risk to humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Quintozene

CAS No. 82-68-8. The IUPAC and CAS name is pentachloronitrobenzene. Also known as 1,2,3,4,5-pentachloro-6-nitro-benzene, and sometimes called PCNB.

### Maximum Acceptable Value

There are insufficient data to determine a MAV for quintozene in drinking-water. WHO (2004 and 2011) states that quintozene is unlikely to occur in drinking-water, so did not develop a guideline value for drinking-water.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.03 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, because the health-based guideline is based on long-term effects.

Hexachlorobenzene (HCB) is an impurity, but has been reduced to <0.1 percent since 1988; before that, levels up to 3 percent were not uncommon, and the earliest commercial products could contain up to 30 percent. Currently quintozene should not contain more than 75 mg/kg of hexachlorobenzene. Other impurities may include pentachlorobenzene, and tetrachloronitrobenzene. See organic chemicals section for a datasheet on pentachlorobenzene. There is also a datasheet for hexachlorobenzene in the pesticides section.

### Sources to water

Quintozene is used as an organochlorine (and nitroaniline) soil fungicide on lawns and ornamental crops, as a seed treatment of field crops and vegetables (eg, barley, corn, cotton, oats, rice, and wheat), and as a slime inhibitor in industrial waters. The fungicide is often used in combination with insecticides and other fungicides including carbaryl, imazalil, tridimenol, etridiazole, and fuberidazole.

Quintozene appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

In 2011 the Environmental Risk Management Authority revoked the approvals for the fungicide quintozene, due to dioxin impurities. Quintozene is used commercially on seedlings, bulbs and recreational turf in New Zealand. The decision to review the substance came after dioxin impurities were found in quintozene products in Australia at levels that may have presented health risks to workers who frequently applied them. Dioxins are persistent organic pollutants (POPs), and are on the list of substances covered by the Stockholm Convention. As a party to the Convention, New Zealand is committed to reducing releases of dioxin to the environment.

### Forms and fate in the environment

[14C]Quintozene was incubated in sterile aqueous buffer containing less than 1 percent acetonitrile as co-solvent at 25°C and pH 5, 7 and 9 for 30 days. The half-life could not be determined experimentally as there was too little degradation; it was estimated to be more than 180 days. No hydrolysis products were detected at any pH;  
96–106 percent of the initial radioactivity was recovered.

The photodegradation of [14C]quintozene was determined at 25°C and pH 5 after 32 hours continuous exposure to a xenon arc lamp. The half-life was 13.4 hours (R2 = 0.99). Polar photodegradation products, accounting for 50 percent of the applied radioactivity after 32 hours, were identified as a mixture of 8 to 10 isomeric chlorophenols and/or chloronitrophenols formed by dechlorination of the benzene ring and subsequent hydroxylation at the same position(s). Pentachloroaniline has also been detected. Identification was by derivatisation with chloroacetic anhydride and MS. Volatile photodegradation products accounted for 20 percent of the applied radioactivity after 32 hours, none individually exceeding 10 percent of the original quintozene. The recovered 14C accounted for 88 to 96 percent of the applied radioactivity.

IPCS (1989) reports a soil half-life of four to 10 months.

Over 80 metabolites have been identified for PCNB. The predominant metabolites of PCNB in the environment are pentachloroaniline (PCA), pentachlorothioanisole (PCTA), and pentachlorobenzene. PCNB and its metabolites are very persistent in the environment. PCNB alone has a measured aerobic soil metabolism half-life of over six months (but more like two to three weeks in anaerobic soils); PCNB and its metabolites combined have an aerobic soil metabolism half-life of close to three years. PCNB and its metabolites have persistence properties that exceed national and international thresholds for identifying persistent chemicals. Quintozene is unstable in soil under photolytic conditions. In sandy loam soil exposed to simulated sunlight quintozene had a half-life of 28.5 days. Pentachloroaniline was the only significant degradation product. See USEPA (2006); JMPR (1998).

The solubility of quintozene in water is 0.4–0.5 mg/L.

NPIC (1994) quotes for PCNB a soil half-life of 21 days, water solubility of 0.44 mg/L and a sorption coefficient (soil Koc) of 5,000. This resulted in a pesticide movement to groundwater rating of very low.

### Typical concentrations in drinking-water

No information available.

### Removal methods

No information available. However, the low water solubility and extreme persistence in soil suggest that treatment processes that remove particulate matter should be effective at reducing the concentration of quintozene and many of its degradation products in water.

### Analytical methods

#### Referee method

A referee method cannot be selected for quintozene because a MAV has not been established and therefore the sensitivity required for the referee method is not known.

#### Some alternative methods

No alternative methods can be recommended for quintozene for the above reason.

### Health considerations

Ex USEPA IRIS: A two-year feeding study with dogs (four males and four females/group) given diets containing 0, 30, 180, or 1080 mg/L indicated that PCNB (1.4 percent hexachlorobenzene) caused liver weight increases, increased liver-to-body weight ratios, elevated serum alkaline phosphatase levels, and microscopically observed cholestatic hepatosis with secondary bile nephrosis at 1,080 mg/L (the highest dose tested). An interim sacrifice at one year occurred with one dog/sex/group; the remaining animals were sacrificed at two years. The cholestatic changes were observed in all animals given diets containing 180 and 1,080 mg/L PCNB, and one of three male dogs in the 30 mg/L dose group exhibited the microscopic changes (no female dogs were affected). The authors noted that these histopathologic changes were moderate in the 1,080 mg/L group and minimal in the 180 mg/L group. Based on these results, 30 mg/L was the NOEL and 180 mg/L was the LEL in dogs. An uncertainty factor of 100 was used to account for the inter- and intraspecies differences. An additional UF of 3 was used since the database for chronic toxicity is incomplete. Conversion factor: 1 mg/L = 0.025 mg/kg/day (assumed dog food consumption).

The ADI of 0.01 mg/kg bw was established by the 1995 JMPR for quintozene containing less than 0.1 percent hexachlorobenzene.

USEPA (2006) derived a chronic RfD of 0.01 mg/kg/day (cPAD of 0.001 mg/kg/d) from a NOAEL of 1.0 mg/kg/d based on a chronic/oncogenicity study (rat) LOAEL = 150 mg/kg/day observing hepatocelluar hypertrophy and hyperplasia, and thyroid hypertrophy. The oral RfD had earlier been 0.003 mg/kg/d (USEPA 1992) based on liver toxicity in a two-year dog feeding study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.01 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for PCNB is 0.70 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for quintozene is 0.007 mg/kg body weight, with a NOEL of 0.7 mg/kg bw from a long-term (two-year) dietary study in dogs. The NOEL is based on evidence of mild liver toxicity (increased absolute and relative liver weights, hepatocyte enlargement and granulosis, and increased serum alkaline phosphatase and cholesterol). The ADI incorporates a safety factor of 100.

Chlorothalonil and pentachlorophenol, two pesticides in the same general family as PCNB, do not appear to result in the same health endpoints. The endpoints used to assess human health risks for PCNB are primarily thyroid hypertrophy and hepatocellular hypertrophy and hyperplasia (USEPA 2006).

Quintozene is a slightly toxic compound in USEPA toxicity class III. As at September 2008 the USEPA considers pentachloronitrobenzene to be a possible human carcinogen and ranked it in Group C. IARC consider quintozene not classifiable as to human carcinogenicity, Group 3.

USEPA (2015) found that there was no convincing evidence of potential interaction with the estrogen or androgen pathways. However, PCNB may potentially interact with the estrogen pathway in wildlife based on the complementarity effects observed within the FSTRA along with the results of the Tier 1 steroidogenesis assay. For the thyroid pathway, there is evidence of potential interaction of PCNB in mammals based on alterations on thyroid hormone levels and subsequent changes in thyroid histopathology.

### Derivation of Maximum Acceptable Value

There are limited and insufficient data on quintozene on which to propose a MAV for drinking-water.

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# Quizalofop-p-ethyl

CAS No. 76578-12-6 (quizalofop). The IUPAC name for quizalofop is (RS)-2-[4-(6-chloroquinoxalin-2-yloxy)phenoxy]propionic acid. The CAS name is 2-[4-[(6-chloro-2-quinoxalinyl)oxy]phenoxy]propanoic acid. The ethyl ester is quizalofop-ethyl (CAS No. 76578-14-8).

Quizalofop-p-ethyl (CAS No. 100646-51-3) is the (R)-isomer of the ethyl ester. Quizalofop-p-tefuryl is also available (CAS No. 119738-06-6).

Quizalofop is sometimes called quizalifop.

### Maximum Acceptable Value

Quizalofop-p-ethyl does not have a MAV in the DWSNZ; quizalofop-p-ethyl is not mentioned in the WHO Guidelines.

### Sources to water

Quizalofop-p-ethyl is an aryloxyphenoxypropionic post-emergence herbicide, an acetyl CoA carboxylase inhibitor, commonly used to control annual and perennial grass weeds in vegetable crops, and pampas grass in reserves.

Quizalofop-p-ethyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Quizalofop-p-ethyl degrades fairly quickly (DT90 up to three days) to quizalofop (the acid) which is moderately persistent in soils, with a reported half-life of 60 days (EFSA 2017) states DT90 of 603 days). It may be more rapidly broken down in soil with high microbial activity. It is moderately to strongly sorbed to soils, and studies indicate very low soil mobility. It should not leach significantly into water.

While the laboratory studies indicate that dissipation occurs quickly via aerobic and anaerobic degradation, the field studies suggest that quizalofop-p-ethyl is persistent in the field. Based on acceptable laboratory environmental fate studies, quizalofop-p-ethyl is stable to hydrolysis at pH 5 and 7. Hydrolysis occurs at pH 9 with a half-life of two days. Quizalofop-p-ethyl is stable to photolysis in water and soil, the photolysis study shows half-lifes of 38 and 43 days in soil and 55 days in water.

The solubility of quizalofop-p-ethyl in water is about 0.4 mg/L.

NPIC (1994) quotes for quizalofop-ethyl a soil half-life of 60 days, water solubility of 0.31 mg/L and a sorption coefficient (soil Koc) of 510. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

No information available.

### Removal methods

No information available.

### Analytical methods

#### Referee method

No MAV.

### Health considerations

Being a relatively new product, there is not a lot of data available. One short-term study (90 days) with rats produced no effects at the moderate dose level of 128 mg/kg. This appears to be the highest dose that has been tested for this compound in chronic feeding experiments (EXTOXNET 1993). Available data show that the target organ in test animals has consistently been the liver in rats and dogs. It is possible that testes may be a target organ in some species.

To assess risk associated with chronic dietary (oral) exposures to quizalofop, a chronic reference dose (cRfD) of 0.009 mg/kg/day has been established. The cRfD was selected from a combined chronic/carcinogenicity toxicity study in rats in which no effects were noted at 0.9 mg/kg/day and anemia and liver effects were noted at 4 mg/kg/day (USEPA 2007). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.009 mg/kg/d quizalofop-P-ethyl. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for quizalofop-P-ethyl is 0.063 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for quizalofop-ethyl and quizalofop-p-tefuryl is 0.01 mg/kg body weight, with a NOEL of 1.3 mg/kg bw.

The Acceptable Daily Intake (ADI) established by EC (2010) for quizalofop-P-ethyl is 0.009 mg/kg/d with an ARfD considered unnecessary. The ADI for quizalofop-P-tefuryl is 0.013 mg/kg body weight, with an ARfD of 0.1 mg/kg bw.

A drinking-water assessment produced estimated drinking-water concentrations (EDWC) of 0.005 mg/L for acute exposure, 0.002 mg/L for chronic exposure, and 0.001 mg/L for cancer exposure. For groundwater sources, the predicted EDWC was 0.0002 mg/L for both acute and chronic exposure. EFSA (2012) propose an ADI of 0.009 mg/kg bw per day (0.0083 mg/kg bw per day when expressed as quizalofop-P equivalent). No ARfD was deemed necessary.

Considering that the three ester variants share the same residue definition based on quizalofop, the lowest acceptable daily intake (ADI) set for quizalofop-P-ethyl (0.009 mg/kg bw per day) and the lowest acute reference dose (ARfD) set for quizalofop-P-tefuryl (0.1 mg/kg bw) were corrected by their molecular weights to a value of 0.0083 mg/kg bw day and 0.08 mg/kg bw, respectively, to be expressed as quizalofop equivalent. These values were taken into account to conduct an overall consumer risk assessments considering all quizalofop ester variants (EFSA 2017).

In an 18-month carcinogenicity study on mice, increased liver weights, changes in blood chemistry, and some changes in liver tissue structure were detected, but no carcinogenic or tumour-causing activity was reported. This study suggests that this compound is not carcinogenic. As at September 2008 the USEPA has classified quizalofop-ethyl in Group D: not classifiable as to human carcinogenicity. Quizalofop-ethyl appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

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# Resmethrin

CAS No. for resmethrin is 10453-86-8. The IUPAC name for resmethrin is 5‑benzyl‑3‑furylmethyl (1RS,3RS;1RS,3SR)-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate, or 5-benzyl-3-furylmethyl (1RS)-cis-trans-2,2-dimethyl-3-(2-methylprop-1-enyl)cyclopropanecarboxylate, or 5-benzyl-3-furylmethyl (±)-cis-trans-chrysanthemate. The CAS name is [5-(phenylmethyl)-3-furanyl]methyl 2,2-dimethyl-3-(2-methyl-1-propen-1-yl)cyclopropanecarboxylate.

Resmethrin is a mixture of four optical isomers; the (1R, trans)- and 1R, cis)- isomers have strong insecticidal activity, whilst the (1S, trans)- and (1S, cis)- isomers do not. Relative proportions are approximately 4:1:4:1, respectively. Some subsets of isomers of this substance have their own ISO common names, eg, [bioresmethrin](http://www.alanwood.net/pesticides/bioresmethrin.html) and [cismethrin](http://www.alanwood.net/pesticides/cismethrin.html).

Refer also to the datasheet for pyrethrin and pyrethroids.

### Maximum Acceptable Value

The DWSNZ do not have a MAV for any pyrethrins or pyrethroids; they are not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.1 mg/L for bioresmethrin (CAS No. 28434-01-7). Minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Resmethrin does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Bioresmethrin and resmethrin appear in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Resmethrin is one of the least persistent pyrethroids.

Octanol-Water Partition Coefficient (Kow): 2.63 x 105 or log Kow = 5.43. Henry’s constant: 1.3 x 10-7 atm·m3/mol. Soil Sorption Coefficient (Koc): 1 x 105. Resmethrin is degraded in the environment primarily by photolysis. The typical half-life of resmethrin in the soil is 30 days. Resmethrin has low water solubility and high adsorption potential to organic material and sediment. Therefore resmethrin has low soil mobility and is unlikely to contaminate groundwater. Resmethrin is degraded by photooxidation in the environment resulting in several metabolites, including (+)-trans-chrysanthemic acid, which is more toxic (NPIC). NPIC (1994) quotes for resmethrin a soil half-life of 30 days, water solubility of 0.01 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Removal methods

Because pyrethrins and pyrethroids are strongly attracted to particles, coagulation and many filtration processes should remove them readily.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The USEPA classified resmethrin in 2005 as “likely to be carcinogenic to humans”. Resmethrin appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

The USEPA (1988) developed a chronic RfD of 0.03 mg/kg/d for resmethrin. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.035 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for resmethrin is 0.245 mg/L (no acute one-day value available.)

The Acceptable Daily Intakes (ADI) adopted in Australia are:

* bioresmethrin: 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw
* resmethrin: 0.1 mg/kg body weight, with a NOEL of 10 mg/kg bw.

JMPR did not allocate an ADI or ARfD for bioresmethrin.

### Derivation of Maximum Acceptable Value

No MAV.

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# Rotenone

CAS No. 83-79-4. The IUPAC name for rotenone is (2R,6aS,12aS)-1,2,6,6a,12,12a-hexahydro-2-isopropenyl-8,9-dimethoxychromeno[3,4-b]furo[2,3-h]chromen-6-one. The CAS name is (2R,6aS,12aS)-1,2,12,12a-tetrahydro-8,9-dimethoxy-2-(1-methylethenyl)[1]benzopyrano[3,4-b]furo[2,3-h][1]benzopyran-6(6aH)-one.

### Maximum Acceptable Value

Rotenone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

However, the Environmental Protection Authority of New Zealand ([www.epa.govt.nz](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\AppData\Local\Microsoft\Windows\Temporary%20Internet%20Files\Content.Word\www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has set (by an approval under Part 5 of the HSNO Act) a tolerable exposure limit (TEL) of 0.006 mg/L in drinking water, and an environmental exposure limit (EEL) in water of 0.00025 mg/L (0.25 µg/L).

### Sources to water

Rotenone is used as a broad-spectrum, selective, non-systemic [insecticide](http://en.wikipedia.org/wiki/Insecticide). It is the main piscicide used internationally for eradicating and controlling pest fishes in freshwaters. Rotenoids occur naturally in the roots and stems of several plants, particularly species belonging to genus Lonchocarpus or Derris, rotenone being the major and most important component. It is the active ingredient in Derris Dust (many other trade names exist), commonly used in New Zealand to control white butterfly and aphids; home gardeners probably use more than market gardeners. Rotenone is used alone or in combination with pyrethrins, pyrethrum, and piperonyl butoxide. In human and veterinary medicine rotenone has been applied directly to treat lice, ticks, scabies and other ectoparasites. Rotenone has been used in sheep dips from the 1800s to the present day (Sheep Dip Factsheet No. 1, see <http://www.trc.govt.nz/assets/Publications/guidelines-procedures-and-publications/Land-management-2/sheepdip-factsheet-1.pdf>).

Rotenone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The purity of rotenone preparations varies widely, depending on origin. Identified impurities include dehydrorotenone and rotenonone.

### Forms and fate in the environment

Rotenone is rapidly broken down in soil and water (with a half-life of one to three days for both aerobic aquatic and anaerobic aquatic soils) yielding water soluble non-toxic products. Nearly all its toxicity is lost in five to six days of spring sunlight, or two to three days of summer sunlight. It does not readily leach from soil and it is not expected to be a groundwater pollutant (EXTOXNET 1996).

Rotenone is very toxic to most aquatic organisms and can have serious impact on aquatic ecosystems. Its application can disrupt the trophic structure of the system, not only eliminating fish but their food sources as well (ie, zooplankton). In some circumstances rotenone treatment can cause an increase in blue/green algae, due to the removal of invertebrate predators. From NSW Government (2013).

Water solubility is about 0.2 mg/L at 20°C.

NPIC (1994) quotes for rotenone a soil half-life of three days, water solubility of 0.2 mg/L and a sorption coefficient (soil Koc) of 10,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See DoC (2003).

### Health considerations

Rotenone is a highly specific metabolic poison that inhibits the respiration of cells by blocking the mitochondrial electron transport, and thus ultimately depriving cells of oxygen and reducing the production of cellular energy. From NSW Government (2013).

The RfD is quoted in EXTOXNET (1996) as 0.004 mg/kg/d, based on reduced weight found in a two-generation rat reproduction study with a NOEL of 0.38 mg/kg/d (USEPA 1988). Evidence for teratogenic and carcinogenic activity of rotenone is inconclusive. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0004 mg/kg/d, and an ARfD of 0.015 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for rotenone is 0.495 mg/L.

Rotenone is not included on any existing lists as an endocrine-disrupting pesticide. Studies on dogs at high doses produced adverse changes in blood chemistry. In dogs fed rotenone at 10 mg/kg per day for six months, weight loss and haematological effects were found. A No Observed Adverse Effect Level (NOAEL) of 0.4 mg/kg per day has been determined for rats (two-year study), and dogs (16-month study) (PAN UK).

In 2000 it was reported that injecting rotenone into rats caused symptoms of [Parkinson’s disease](http://en.wikipedia.org/wiki/Parkinson%27s_disease) to develop, although this is unlikely to occur under normal usage. The study does not directly suggest that rotenone exposure is responsible for Parkinson’s disease in humans but is consistent with the belief that chronic exposure to environmental toxins increases the likelihood of the disease.

Rotenone is highly toxic to fish: most values for the 96-hour LC50 (lethal concentration required to kill half the test organisms) for different fish species and for daphnids (water fleas) lie in the range of 0.02 to 0.2 mg/L. Use of rotenone in New Zealand for fisheries management has been very limited although it has been used to eliminate grass carp from small lakes. See DoC (2003 and 2008) for further information.

An ARfD was not considered necessary in Australia.

### Derivation of Maximum Acceptable Value

No MAV.

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# Saflufenacil

CAS No. 372137-35-4. The IUPAC name for saflufenacil is N′-{2-chloro-4-fluoro-5-[1,2,3,6-tetrahydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)pyrimidin-1-yl]benzoyl}-N-isopropyl-N-methylsulfamide. The CAS name is 2-chloro-5-[3,6-dihydro-3-methyl-2,6-dioxo-4-(trifluoromethyl)-1(2H)-pyrimidinyl]-4-fluoro-N-[[methyl(1-methylethyl)amino]sulfonyl]benzamide. Has also been called benzamide.

### Maximum Acceptable Value

Saflufenacil does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Saflufenacil is a selective amide or uracil herbicide developed for the control of broadleaf weeds by pre-plant and pre-emergence applications to cereal small grains, corn, chickpeas, cotton, edible beans, edible peas, lentils, lupine, sorghum, soybeans and sunflowers; post-emergence applications to fruit tree orchards, nut tree orchards, and vineyards; and fallow croplands and non-agricultural areas, including pine plantations, rights-of-way, and bare ground. Additionally, saflufenacil is used as a dessicant and/or defoliant on sunflowers.

Saflufenacil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Saflufenacil may be sold mixed with other pesticides, such as imazethapyr and dimethenamid-P.

### Forms and fate in the environment

Saflufenacil is non-volatile, hydrophilic, and mobile to highly mobile in soil, and may readily move into surface water through run-off and/or to groundwater, depending on the permeability of the soil. The solubility of the compound is pH-dependent; at environmentally relevant pH values, saflufenacil is expected to be ionic. The compound dissipates in the environment through both abiotic and biotic degradation and by leaching. It is not expected to persist in aerobic soils (half-life 1–5 weeks) or alkaline water bodies (half-life <1 week), but may be moderately persistent in acidic to neutral water bodies (half-life 4–10 weeks).

Saflufenacil is moderately photolysed in clear, near-surface water (half-lifes of 56 days in a sterile pH 5 buffer and 22 days in unsterile pH 7.1 pond water. In anaerobic aquatic systems, saflufenacil degraded with a half-life of 29.4 days in one system (pH 5.5–8.5).

JMPR (2011) reports: vapour pressure at 20°C = 4.5 x 10-15 Pa. Henry’s Law constant = 1.07 x 10-20 atm.m3/mol. Water solubility at 25°C and pH 5 = 25 mg/L and pH 7 = 2,100 mg/L. The octanol/water partition coefficient at 25°C = logPow = 2.6. The half-life of saflufenacil was calculated using the non-linear first order model. The average aerobic degradation DT50 values for saflufenacil were approximately 22 days for the Idaho soil, 17 days for the Illinois soil, four days for the New Jersey soil and 17 days for the Wisconsin soil; metabolites are discussed. The half-life in water at pH 7 is >190 days, and at pH 9 about five days.

Saflufenacil has 14 major degradates that were isolated in submitted environmental fate studies. Seven of them are included with the parent as residues of concern. Due to the structural similarity of these degradates to the parent and a lack of toxicity data, they are assumed to have equivalent toxicity to the parent (USEPA 2009).

Trifluoroacetic acid (TFA) is a common metabolite (EFSA 2012). EFSA (2014) states that TFA is very soluble in water and has a low octanol/water partition coefficient (log Pow = -0.2 at pH 7 which indicates that it has a low potential for bioaccumulation. TFA is a strong organic acid. TFA is highly stable and not easily degraded chemically or by photolysis in the natural environment.

Water solubility is about 20 mg/L at pH 4 to 5; 2,100 mg/L at pH 7; it decomposes at pH 9.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See EFSA (2012).

### Health considerations

Saflufenacil has low acute toxicity via the oral, dermal and inhalation routes of exposure.

The acute oral reference dose or RfD (USEPA 2009) is 5.0 mg/kg/d, based on an acute neurotoxicity study. The acute RfD was calculated by dividing the No-Observed-Adverse-Effect-Level (NOAEL) of 500 mg/kg/day from this study by an uncertainty factor (UF) of 100. The chronic dietary RfD is 0.046 mg/kg/d based on a NOAEL of 4.6 mg/kg/d from a chronic carcinogenic mouse study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.046 mg/kg/d, and an ARfD of 5.0 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for saflufenacil is 50 mg/L.

The JMPR 2011 meeting established an acceptable daily intake (ADI) of 0–0.05 mg/kg bw on the basis of a NOAEL of 4.6 mg/kg bw per day in the carcinogenicity study in mice, based on microcytic hypochromic anaemia (MHA) at 13.8 mg/kg bw per day, and using a safety factor of 100. This ADI was supported by the NOAEL of 6.2 mg/kg bw per day observed in the chronic toxicity and carcinogenicity study in rats, on the basis of MHA and anogenital region smeared with urine in female rats seen at 31.4 mg/kg bw per day. It is further supported by the NOAEL of 5 mg/kg bw per day observed in the developmental toxicity study in rats on the basis of increased skeletal anomalies at 20 mg/kg bw per day. The meeting also concluded that it was not necessary to establish an acute reference dose (ARfD) for saflufenacil in view of its low acute toxicity and the absence of developmental toxicity or any other toxicological effects that would be likely to be elicited by a single dose. MHA is not considered to be an appropriate end-point to establish an ARfD because it is not expected to appear after single exposure due to the mechanism of toxicity by which it is produced (FAO 2011, JMPR 2011 reaffirmed in 2017.)

The Acceptable Daily Intake (ADI) adopted in Australia for saflufenacil is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg (<https://apvma.gov.au/>). The ARfD is 0.017 mg/kg. In February 2017 APVMA adjusted this ARfD to 0.05 mg/kg based on a developmental rat study – a NOAEL of 5 mg/kg bw/d was based on an increased incidence of bent scapula and wavy ribs in the absence of maternal toxicity at the next higher dose. The ARfD for salflufenacil only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

EFSA (2012 and 2014) established an Acceptable Daily Intake (ADI) value of 0.046 mg/kg bw/d and the Acute Reference Dose (ARfD) of 0.05 mg/kg bw, both using uncertainty factors of 100. For the metabolite trifluoroacetic acid (TFA) EFSA (2014) concluded that it is possible to derive a tentative ADI of 0.05 mg/kg bw per day and a tentative ARfD at the same level (0.05 mg/kg bw), based on a NOAEL of 10 mg/kg bw per day and an uncertainty factor of 100 for intra- and inter-species variation plus an additional factor of 2 to extrapolate from subchronic to chronic study duration.

Saflufenacil is classified as “not likely carcinogenic to humans”, based on no evidence of increased incidence of tumours at the tested doses in rats and mice. Saflufenacil was neither mutagenic in bacterial cells nor clastogenic in rodents in vivo, and was considered not to pose a mutagenic concern (USEPA 2009). JMPR concluded that saflufenacil was not carcinogenic in mice or rats, and was unlikely to be genotoxic in vivo, and that saflufenacil is unlikely to pose a carcinogenic risk to humans (FAO 2011).

### Derivation of Maximum Acceptable Value

No MAV.

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# Sethoxydim

CAS No. 74051-80-2. The IUPAC name for sethoxydim is (5RS)-2-[(EZ)-1-(ethoxyimino)butyl]-5-[(2RS)-2-(ethylthio)propyl]-3-hydroxycyclohex-2-en-1-one. The CAS name is 2-[1-(ethoxyimino)butyl]-5-[2-(ethylthio)propyl]-3-hydroxy-2-cyclohexen-1-one.

Clethodim (qv) and sethoxydim share a common moiety, which accounts for the major part of their structures. Their structures differ in two parts: the oxime oxygen bears an ethyl group in sethoxydim but a 3-chloroallyl group in clethodim, and the imino carbon bears an n-propyl group in sethoxydim but an ethyl group in clethodim (JMPR 2002).

### Maximum Acceptable Value

Sethoxydim does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Sethoxydim is a [cyclohexene oxime (cyclohexanone) selective postemergence herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#cyclohexene_oxime_herbicides) used to control annual and perennial grass weeds in broad-leaved vegetable, fruit, field and ornamental crops.

Sethoxydim appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Sethoxydim has a weak tendency to adsorb to soil particles. Laboratory soil leaching tests have suggested that sethoxydim could leach through soil. However, in field tests, sethoxydim did not leach below the top four inches of soil and it did not persist. On soil, photodegradation of sethoxydim takes less than four hours. Its half-life on a loamy sand at pH 6.8 was four to five days, and on a loam soil at pH 7.4 was 11 days. Sethoxydim is unlikely to contaminate groundwater or surface waters because it is not persistent under most conditions.

In water, photodegradation of sethoxydim takes less than one hour, but is fairly stable to hydrolysis, with a half-life of about 40 days at pH 7 and 25°C.

Water solubility is about 4,700 mg/L at pH 7; 25 mg/L at pH 4.

NPIC (1994) quotes for sethoxydim a soil half-life of five days, water solubility of 4,390 mg/L and a sorption coefficient (soil Koc) of 100. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The Acceptable Daily Intake (ADI) is 0.09 mg/kg/day based on a NOEL of 8.86 in a one-year dog feeding study and a 100-fold safety margin. Doses above the NOEL produced equivocal evidence for the occurrence of anemia.

The oral reference dose or RfD (USEPA 1989) is 0.09 mg/kg/d, based in mild anaemia in male dogs over a 12-month diet study. A rat developmental study was used to select the dose and endpoint for establishing the acute reference dose (RfD) of 1.8 mg/kg/day. The acute RfD was calculated by dividing the No-Observed-Adverse-Effect-Level (NOAEL) of 180 mg/kg/day from this study by an uncertainty factor (UF) of 100 (10X for interspecies extrapolation and 10X for intraspecies variation) USEPA (2005). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.14 mg/kg/d, and an ARfD of 1.8 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for sethoxydim is 18 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for sethoxydim is 0.18 mg/kg body weight, with a NOEL of 18 mg/kg.

Sethoxydim is not likely to be a carcinogenic in humans based on lack of evidence of carcinogenicity in rats and mice.

### Derivation of Maximum Acceptable Value

No MAV.

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# Simazine

CAS No. 122-34-9. The IUPAC name for simazine is 6-chloro-N2,N4-diethyl-1,3,5-triazine-2,4-diamine. The CAS name is 6-chloro-N,N’-diethyl-1,3,5-triazine-2,4-diamine. Also called 2-chloro-4,6-bis(ethylamino)-s-triazine, 2,4-bis(ethylamino)-6-chloro-s-triazine or 4,6-bis(ethylamino)-2-chlorotriazine.

### Maximum Acceptable Value

Based on health considerations, the concentration of simazine in drinking-water should not exceed 0.002 mg/L (2 g/L).

The maximum contaminant level or MCL (USEPA 2006/2009/2011) is 0.004 mg/L. The maximum acceptable concentration for simazine in Canada is 0.01 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Simazine is a chlorinated triazine systemic herbicide and soil sterilant, a class of herbicide that also includes the pesticides atrazine and propazine. Simazine may enter source waters as a result of its use pre-emergence to control broadleaved and grass weeds in a wide variety of crop, orchard and non-crop areas. It has been formulated in various countries in combination with many other pesticides.

Simazine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The total annual usage of simazine in New Zealand in the late 1980s was 71,700 kg with the majority of use being in the North Island. The highest usage was in the Tauranga county (11,200 kg).

Because available monitoring data were insufficient to demonstrate that, in large areas, concentrations of the active substance and its breakdown products will not exceed 0.0001 mg/L in groundwater, EC (2003) concluded that no plant protection products containing the active substance concerned are expected to satisfy in general the requirements laid down in Article 5(1)(a) and (b) of Council Directive 91/414/EEC – no longer used in the UK.

### Forms and fate in the environment

Simazine can be degraded through hydrolysis and N-dealkylation. Simazine applied to soil will remain primarily in the upper 5 cm. Microbial degradation may contribute significantly to the removal of simazine from soil. Its half-life in soil ranges from 28 to 170 days with a recommended average half-life of 60 days. Health Canada (1986) states that the movement of simazine through the soil layers is pH-dependent; it is more soluble at lower pH, whereas it binds more to the clay or organic matter in soil at higher pH. Simazine is less likely to leach than other triazine herbicides; the extent of leaching decreases with an increase in organic matter and clay content.

In a study with four New Zealand soils, with acid pH (5.4 to 5.5) and organic carbon levels of 4.6 and 9.4 percent, the half-life times were 25 and 32 days, respectively (Rahman and Holland 1985).

Biological processes are also principally responsible for the removal of simazine from water. Its persistence in aquatic environments is dependent upon many factors, including the amount of algae and weeds present. Dissipation studies in pond and lake water with simazine gave variable results, with half-times ranging from 50 to 700 days. The main metabolites are 2-amino-4-chloro-6-ethylamino-s-triazine, 2-chloro-4-ethylamino-6-amino-s-triazine and 2,4-diamino-6-chloro-s-triazine, and are not expected to be any more persistent than the parent compound.

Simazine’s chlorinated degradates des-isopropyl atrazine (DIA) and diaminochlorotriazine (DACT, CAS No. 3397-62-4) are shown in studies to be more mobile than simazine, and therefore more likely to leach to groundwater than the parent compound. Hydroxy-atrazine, on the other hand, is less mobile than simazine, and has less leaching potential than the parent compound (USEPA 2006a).

Even though it has fairly low solubility in water (3.5 to 5 mg/L) it can leach to groundwater. Its sorption coefficient is 130 mL/g. Its vapour pressure is 8.1 × 10-7 Pa at 20°C, the log octanol-water partition coefficient of simazine is reported to be 1.94; it is therefore not likely to bioaccumulate to a significant degree in human or animal tissue (Health Canada 1986).

NPIC (1994) quotes for simazine a soil half-life of 60 days, water solubility of 6.2 mg/L and a sorption coefficient (soil Koc) of 130. This resulted in a pesticide movement to groundwater rating of high. Its GUS score is 3.61, indicating that it will leach to groundwater.

USGS (2006) give the following values: log Kow = 2.18; log Koc (where Koc is in mL/g) = 2.11; water solubility = 5 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -3.46; half-life in aerobic soil = 91 days; half-life in water = >32 days.

If released to soil, simazine is expected to have high to slight mobility based upon Koc values ranging from 78 to 3,559. Sorption was observed to increase with decreasing pH. Volatilisation from moist and dry soil surfaces is not expected to occur based upon an estimated Henry’s Law constant of 9.4 x 10-10 atm-cu m/mole and this compound’s vapour pressure, respectively. Microbial breakdown in soil results in degradation of simazine at highly variable rates, with half-lifes range from 27 to 102 days (median 49 days). Temperature and moisture are the main factors affecting the rates. N‑Desethyl simazine and 2-chloro-4,6-bisamino-s-triazine have been identified as metabolites. If released into water, some adsorption of simazine to suspended solids and sediment in the water column is expected based upon the Koc values. Biodegradation in surface water samples from three ponds in Japan, ranged from 0 to 30 percent and 0 to 24 percent after four and seven days incubation, respectively. Volatilisation of simazine from water surfaces is not expected to occur based upon its estimated Henry’s Law constant. BCFs ranging from <1 to 55 suggest bioconcentration in aquatic organisms is low to moderate. Simazine is stable at pH 7 and 9 but the hydrolysis half-life at pH 5 and 25°C is 70 days. The product of simazine hydrolysis is 2‑hydroxy-4,6-bis(ethylamino)-s-triazine (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Simazine has been detected in tile drainage from an orchard in Canterbury and has also been detected at low concentrations in groundwater in South Canterbury.

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, found simazine in one zone at a concentration of 0.0002 mg/L (10 percent of the MAV), with the median concentration being “nd” (limit of detection = 0.0001 mg/L). The P2 programme in 2001 found simazine in a sample at 5 percent of its MAV (ESR 2001).

Simazine has been found 71 times in groundwaters throughout New Zealand, ranging from 0.00001 to 0.0016 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Simazine occurred at 0.06 to 1.6 µg/L, ie, up to 0.0016 mg/L, about the same as the MAV.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Simazine occurred at 0.01 to 0.32 µg/L, ie, up to 0.00032 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Simazine occurred at 0.012 to 0.42 µg/L, ie, up to 0.00042 mg/L.

Simazine was found in 11 bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.00001 to 0.000089 mg/L. The bores were in the Manawatu, Tasman, Marlborough, Canterbury, Otago and Southland regions.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Simazine was found in 10 wells, from 0.01 to 0.13 µg/L, ie, up to 0.00013 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Simazine was found in five samples, from 0.015 to 0.099 µg/L, ie, up to 0.0001 mg/L.

Simazine was detected in nine of 440 surface water samples (mean detectable concentration 0.0006 mg/L) from three Ontario river basins surveyed from 1981 to 1985 (detection limit 0.0002 mg/L); a total of only 800 kg had been used in these areas in 1983. Simazine was detected in 55 of 1,199 samples of municipal and private drinking water supplies in Nova Scotia (1986), Quebec (1986), Ontario (1979 to 1986), Manitoba (1986) and Alberta (1978 to 1986) (detection limits ranged from 0.000025 to 0.001 mg/L). The maximum concentration reported was 0.023 mg/L, obtained from a private well in Ontario (Health Canada 1986).

Simazine is frequently detected in groundwater and surface water at concentrations of up to a few micrograms per litre (WHO 2004).

194 water utilities in the US reported detecting simazine in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0078 mg/L.

### Removal methods

Simazine can be removed from water by a number of methods: activated carbon adsorption (0.0001 mg/L should be achievable using GAC, WHO 2004/2011/2017); ion exchange; and oxidation by chlorine, chlorine dioxide, ozone, hydrogen peroxide, potassium permanganate and most of the newer advanced oxidation processes. Coagulation, filtration, and softening processes are relatively ineffective in removing simazine from water.

### Recommended analytical techniques

#### Referee method

Liquid/Solid Extraction and Capillary Column Gas Chromatography/Mass Spectrometry (EPA 525).

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector (EPA 507).

### Health considerations

Simazine is absorbed by the gut of rats and mice and distributed to various tissues, with the highest concentrations in the spleen, liver and kidney.

USSR workers manufacturing simazine and propazine reported 124 cases of contact dermatitis. The serious cases lasted 7–10 days and involved erythema (reddening of the skin), oedema and a vesiculopapular reaction that sometimes progresses to the formation of bullae (watery blisters). A study showed an association between ovarian tumours and exposure to triazine herbicides, but the number of subjects included in the study was limited.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw from a long-term (two-year) dietary study in rats. The NOEL is based on decreased survival, decreased bodyweight gain, and evidence of anaemia. The ADI incorporates a safety factor of 100.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.02 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.7 mg/L. This is based on a NOAEL of 1.8 mg/kg/d and UF of 100 (USEPA 2006a). The oral RfD had earlier been 0.005 mg/kg/d (USEPA 1994). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.018 mg/kg/d, and an ARfD of 0.10 mg/kg/d for the metabolite DACT.

Simazine does not appear to be genotoxic in mammalian systems. Recent studies have shown an increase in mammary tumours in the female rat, but no effects in the mouse. Although there is limited evidence in experimental animals for the carcinogenicity of simazine, the International Agency for Research on Cancer has classified simazine in Group 3 (not classifiable as to its carcinogenicity to humans).

As at May 2002 the USEPA had classified simazine in Group C: a possible human carcinogen, but in Apr 2005, they reclassified it as “not likely to be carcinogenic to humans”. USEPA (2015) found that based on weight of evidence considerations, EDSP Tier 2 testing is not recommended for simazine since additional testing will not impact current EPA established regulatory endpoints for human health or ecological risk assessment.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV. The no-observable-adverse-effect level used in the derivation is from a rat study for carcinogenicity and long-term toxicity study based on weight changes, effects on haematological parameters, and an increase in mammary tumours.

The MAV for simazine in drinking-water was derived as follows:

0.52 mg/kg body weight/day x 70 kg x 0.1 = 0.0018 mg/L (rounded to 0.002 mg/L)

2 L/day x 1,000

where:

* no observable adverse effect level = 0.52 mg/kg body weight per day established for long-term toxicity in the rat (based on weight changes, effects on haematological parameters and an increase in mammary tumours)
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for possible non-genotoxic carcinogenicity).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for simazine is 0.004 mg/L.

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# Sodium tetrathiocarbonate

CAS No. 7345-69-9. Sometimes referred to as sodium tetrathiocarb or tetrathio-peroxycarbonic acid disodium salt. The CAS No. for carbon disulphide (CS2) is 75-15-0. Carbon disulphide has been called carbon bisulfide.

Carbon disulphide has a datasheet in the Inorganic Chemicals section.

### Maximum Acceptable Value

Sodium tetrathiocarbonate (and carbon disulphide) do not have a MAV in the DWSNZ, and are not mentioned in the WHO Guidelines.

### Sources to water

Sodium tetrathiocarbonate is classed as a non-systemic, non-persistent inorganic soil fumigant, fungicide and nematicide, commonly used on fruit, eg, for the for the control of Phylloxera in grapes. Because the degradate, carbon disulphide, is the pesticide, sodium tetrathiocarbonate does not appear in some pesticide listings. Carbon disulfide residues have been found in celery and spinach during the Food Residue Surveillance Programme (refer NZFSA <http://www.nzfsa.govt.nz/>).

Sodium tetrathiocarbonate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

The USEPA regulation establishing a tolerance for residues of the nematicide, insecticide, and fungicide carbon disulfide in or on the raw agricultural commodities grapefruit, grapes, lemons, and oranges at 0.1 part per million (ppm) is required because of the application of sodium tetrathiocarbonate (PMEP 1993). Carbon disulfide is a naturally occurring compound found in grapes and citrus at 5 to 20 parts per billion and up to 1 to 73 ppm in Shiitake mushrooms.

Carbon disulfide is an industrial chemical used in the manufacture of rayon fibres (major use), cellophane, pesticides, in the production of cellulose and rubber chemicals, as a solvent for cleaning and extraction; as an extractant for olive oil, and in the production of adhesives. Carbon disulfide is a natural product of anaerobic biodegradation. In nature, minute amounts occur in coal tar and in crude petroleum. Other sources include animal waste, in particular pig urine and faeces, fish processing, plastic and refuse combustion, synthetic fibre and starch manufacture, natural gas and volcanoes.

Because carbon disulphide is volatile it is not expected to be found in natural waters.

### Forms and fate in the environment

Sodium tetrathiocarbonate stoichiometrically converts to carbon disulfide, sodium hydroxide, hydrogen sulfide, and sulfur in the soil after application.

Sodium tetrathiocarbonate water solubility is extremely high, one product being sold as a 402 g/L solution, ie, about 40 percent. Carbon disulphide water solubility is about 300 mg/L.

Carbon disulfide is not expected to be removed significantly from the aquatic phase through adsorption. The low Koc value, calculated from water solubility data, is 54, which indicates high soil mobility, but it probably will be less mobile in soils of high organic content. Carbon disulfide released to soils in spills should rapidly volatilise to the atmosphere, but a portion of the compound remaining on soil surfaces could be available for transport into groundwater since it does not have much affinity for soil particles.

Carbon disulfide is stable to hydrolysis in the pH region of environmental concern (pH 4 to 10). The volatilisation half-life from a saturated water solution has been estimated to be 11 minutes. The compound apparently does not undergo biodegradation at rates that are competitive with its volatilisation from surface waters (ATSDR 1996).

If released to soil, carbon disulfide is expected to have moderate mobility based upon an estimated Koc of 270. Volatilisation from moist soil surfaces is expected to occur based upon a Henry’s Law constant of 1.44 x 10-2 atm-cu m/mole at 24°C. Carbon disulfide may potentially volatilize from dry soil surfaces given its vapour pressure. If released into water, carbon disulfide is not expected to adsorb to suspended solids and sediment in the water column based upon the estimated Koc. Volatilisation from water surfaces is expected to be an important fate process based upon carbon disulfide’s Henry’s Law constant. Estimated volatilisation half-lifes for a model river and model lake are 2.6 hours and 3.5 days, respectively. BCFs of <6.1 and <60 in carp suggest bioconcentration in aquatic organisms is low to moderate. Carbon disulfide hydrolyses slowly to carbon dioxide and hydrogen disulfide in alkaline solutions. The half-life for hydrolysis at pH 9 is approximately 1.1 years (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Studies have demonstrated that carbon disulphide, from sodium tetrathiocarbonate application, is not a residual groundwater contaminant (PMEP 1997).

### Health considerations

Developmental toxicity studies with sodium tetrathiocarbonate were performed in the rat and rabbit. The developmental toxicity no observed effect level (NOEL) for the rabbit study was 150 mg/kg/day (PMEP 1997).

Sodium tetrathiocarbonate was negative in a bacterial gene mutation study with and without S9 activation, unscheduled mammalian DNA synthesis, and in vitro chromosomal aberration without S9 activation, but weakly positive with S9 activation (PMEP 1993). Sodium tetrathiocarbonate is not mutagenic or genotoxic (PMEP 1997).

Inhalation of carbon disulfide is the commonest route of absorption of carbon disulphide in man, and the main health risk (see IPCS 1993). The oral reference dose (RfD) is 0.1 mg/kg/d based on foetal toxicity/malformations (USEPA 1990). No reports are available to indicate any carcinogenic or mutagenic effects of carbon disulfide. In 2013 USEPA removed sodium tetrathiocarbonate from the endocrine disruptor screening program because the pesticide was not in use; see <https://www.federalregister.gov/articles/2013/06/14/2013-14232/endocrine-disruptor-screening-program-final-second-list-of-chemicals-and-substances-for-tier-1>.

A minimal oral risk level (MRL: an estimate of daily human exposure to a dose of a chemical that is likely to be without an appreciable risk of adverse non-cancerous effects over a specified duration of exposure) of 0.01 mg/kg/day was derived for acute exposure to carbon disulfide. This MRL was derived based on the inhibition of enzyme activities, specifically decreases in the activities of several hepatic microsomal cytochrome P-450-dependent drug-metabolising enzymes and cytochrome P-450 content. A LOAEL of 3 mg/kg/day was established for this effect. Also, the effect was minimal since the inhibition of enzyme activities was selective and reversible. This dose was divided by an uncertainty factor of 300 (3 for use of a minimal LOAEL, 10 for extrapolation from animals to humans, and 10 for interhuman variability) to yield the calculated MRL of 0.01 mg/kg/day.

ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of 0.01 mg/kg/day for acute-duration oral exposure (1–14 days) for carbon disulfide.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for carbon disulfide is 0.7 mg/L.

### Derivation of Maximum Acceptable Value

No MAV.

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# Spinetoram

CAS No. 187166-40-1 + 187166-15-0. Spinetoram consists of two closely related active ingredients. The IUPAC name for spinetoram is:

(a) bridged fused ring systems nomenclature:

(i) a mixture of 50 to 90 percent of (XDE-175-J): (2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-2-(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyloxy)-13-[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-14-methyl-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione

(ii) and 50 to 10 percent of (XDE-175-L): (2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-2-(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyloxy)-13-[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione

or

(b) extended von Baeyer nomenclature:

(i) a mixture of 50 to 90 percent of (1S,2R,5R,7R,9R,10S,14R,15S,19S)-7-(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyloxy)-15-[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-19-ethyl-14-methyl-20-oxatetracyclo[10.10.0.02,10.05,9]docos-11-ene-13,21-dione

(ii) and 50 to 10 percent of (1S,2S,5R,7S,9S,10S,14R,15S,19S)-7-(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyloxy)-15-[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methylpyran-2-yloxy]-19-ethyl-4,14-dimethyl-20-oxatetracyclo[10.10.0.02,10.05,9]docosa-3,11-diene-13,21-dione.

The CAS name is (2R,3aR,5aR,5bS,9S,13S,14R,16aS,16bR)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyl)oxy]-13-[[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,4,5,5a,5b,6,9,10,11,12,13,14,16a,16b-hexadecahydro-14-methyl-1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione, mixture with (2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-2-[(6-deoxy-3-O-ethyl-2,4-di-O-methyl-α-L-mannopyranosyl)oxy]-13-[[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione.

### Maximum Acceptable Value

Spinetoram does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Spinetoram is a multi-component tetracyclic macrolide in the class of spinosyn insecticides, developed for the control of lepidopterous larvae, leafminers, and thrips on a variety of crops. Its mode of action is disruption of nicotinic/gamma amino butyric acid-gated chloride channels. NZFS (2010) has established residues for spinetoram in potatoes, tomatoes, apples and pears.

Spinetoram is a fermentation product of Saccharopolyspora spinosa and is an analogue of the insecticide spinosad (qv).

Spinetoram appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Under aerobic conditions, spinetoram applied to soil was degraded relatively rapidly in all soils tested; XDE-175-L was degraded faster than XDE-175-J. After one year of incubation, 1.2 to 2.8 percent and 0.3 to 2.9 percent of applied XDE-175-J and XDE-175-L respectively (dose rate, 0.21 mg/kg soil; 25°C) remained as the parent in US soils tested. In European soils except the loamy sand, after 127 days of incubation, 2.0 to 4.9 percent and 1.4 to 5.0 percent of applied XDE-175-J and XDE-175-L respectively (dose rate, 0.80 mg/kg soil; 20°C) remained as the parent. In the loamy sand, 50 percent and 33 percent of the applied XDE-175-J and XDE-175-L respectively (dose rate, 0.80 mg/kg soil; 20°C) remained as the parent). In the sandy loam maintained at 10°C, 4.9 percent and 2.1 percent of the applied XDE-175-J and XDE-175-L respectively (same dose rate as at 20°C) remained as the parent.

The half-life of spinetoram was calculated to be 21 days and 13 days for XDE-175-J and XDE-175-L respectively at 0.21 mg/kg dose rate (25°C) and 20 days and 14 days for XDE-175-J and XDE-175-L respectively at 0.80 mg/kg dose rate (20°C). When maintained at 10°C the half-life was 21 days and 16 days for XDE-175-J and XDE-175-L respectively at 0.80 mg/kg dose rate. The half-life of XDE-175-J and XDE-175-L under anaerobic condition was much longer than the half-life under aerobic condition.

Spinetoram has a high affinity to adsorb to soil and sediment, so is not expected to leach to groundwater.

See JMPR (2008) for discussion on metabolites.

Spinetoram degrades rapidly by photolysis in water with half-lifes of the major and minor components 0.5 and 0.3 days, respectively (Dow 2006).

|  |  |  |  |
| --- | --- | --- | --- |
| **Water solubility at 20°C, in mg/L** | **XDE-175-J** | **XDE-175-L** | (JMPR 2008) |
| Unbuffered | 10 | 31.9 |  |
| pH 5 | 423 | 1.6 |  |
| pH 7 | 11.3 | 47 |  |
| pH 9 | – | 2.0 |  |
| pH 10 | 6.3 | – |  |

### Recommended analytical techniques

#### Some alternative methods

See JMPR (2008).

### Health considerations

The JMPR 2008 meeting established an acceptable daily intake (ADI) 0–0.05 mg/kg bw based on an overall NOAEL of 5.0 mg/kg bw per day, identified on the basis of arteritis, accompanied by necrosis of the arterial walls in the affected organ(s), in studies of toxicity in dogs, and with a safety factor of 100. Although arteritis was observed only in some dogs, at an incidence that was within the range for historical controls, the incidence of arteritis at the LOAEL was greater in the concurrent controls and clear effects were found at higher doses in another study. Additionally, the structurally related compound spinosad had also been observed to cause arteritis in dogs given spinosad for one year, at doses not dissimilar to the LOAEL for the present study. Hence, the meeting concluded that while there was some uncertainty as to the toxicological significance of the finding of arteritis at the LOAEL for spinetoram, use of the overall NOAEL from studies of toxicity in dogs as a basis for establishing the ADI was scientifically justified. The meeting concluded that it was not necessary to establish an acute reference dose (ARfD) for spinetoram on the basis of its low acute toxicity, the absence of neurotoxic potential and of developmental or any other effects of relevance for acute exposure in studies of longer duration. Effects on gestational survival of pups observed in the multigeneration study in rats were most likely to be secondary to maternal toxicity, which was not a consequence of acute exposure. FAO/WHO (2008). JMPR (2012 and 2017) reaffirmed these ADI and ARfD values.

USEPA (2009) considers spinetoram and spinosad to be toxicologically equivalent. This conclusion was based on the following: (1) spinetoram and spinosad are large molecules with nearly identical structures and (2) the toxicological profiles for each are similar (generalised systemic toxicity) with similar doses and endpoints chosen for human-health risk assessment. This is not a consideration for cumulative assessment where the concepts of mechanism of toxicity and potency are evaluated; rather, spinosad and spinetoram should be considered toxicologically identical in the same manner that metabolites are generally considered toxicologically identical to the parent. Dogs appear to be the most toxicologically sensitive species to spinetoram exposure. The USEPA derived a chronic RfD (and cPAD) of 0.0249 mg/kg/d based on a NOAEL of 2.49 mg/kg/d; an acute RfD was unnecessary. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0249 mg/kg/d for both spinosad and spinetoram. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for spinetoram and spinosad is 0.174 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for spinetoram is 0.06 mg/kg body weight, with a NOEL of 6 mg/kg bw. An ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

The Acceptable Daily Intake (ADI) is 0.025 mg/kg bw per day, based on the one-year dog study. The Acute Reference Dose (ARfD) is 0.1 mg/kg bw based on the rat multigeneration study. All reference values were derived with the use of an uncertainty factor (UF) of 100 (EFSA 2013 and EC 2013).

### Derivation of Maximum Acceptable Value

No MAV.

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# Spinosad dt

Spinosad is the International Organization for Standardization’s approved name for a mixture of spinosyns A and D, with A:D proportions in the range 50:50 to 95:5. CAS No. 168316-95-8. Spinosad DT and spinosad EC are intended only for mosquito larviciding and the specification is, therefore, restricted to WHO. Other varieties exist, eg, spinosad TC, SC and GR.

### Spinosyn A

CAS No. 131929-60-7. The IUPAC name for spinosyn A is (2R,3aS,5aR,5bS,9S,13S,14R,16aS,16bR)-2-(6-deoxy-2,3,4-tri-O-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-14-methyl-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione. The CAS name is (2R,3aS,5aR,5bS,9S,13S,14R,16aS,16bR)-2-[(6-deoxy-2,3,4-tri-O-methyl-α-L-mannopyranosyl)oxy]-13-[[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-14-methyl-1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione.

### Spinosyn D

CAS No. 131929-63-0. The IUPAC name for spinosyn D is (2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-2-(6-deoxy-2,3,4-tri-O-methyl-α-L-mannopyranosyloxy)-13-(4-dimethylamino-2,3,4,6-tetradeoxy-β-D-erythropyranosyloxy)-9-ethyl-2,3,3a,5a,5b,6,7,9,10,11,12,13,14,15,16a,16b-hexadecahydro-4,14-dimethyl-1H-as-indaceno[3,2-d]oxacyclododecine-7,15-dione. The CAS name is (2S,3aR,5aS,5bS,9S,13S,14R,16aS,16bS)-2-[(6-deoxy-2,3,4-tri-O-methyl-α-L-mannopyranosyl)oxy]-13-[[(2R,5S,6R)-5-(dimethylamino)tetrahydro-6-methyl-2H-pyran-2-yl]oxy]-9-ethyl-2,3,3a,5a,5b,6,9,10,11,12,13,14,16a,16b-tetradecahydro-4,14-dimethyl-1H-as-indaceno[3,2-d]oxacyclododecin-7,15-dione.

### Maximum Acceptable Value

The WHO (2010 and 2017) states that it is not appropriate to set a formal guideline value for spinosad DT for use to control vectors breeding in drinking-water containers.

### Sources to water

Spinosad is a spinosyn insecticide, and is a natural product derived from soil fermentation with the naturally occurring actinomycete (bacterium) Saccharopolyspora spinosa. It has been described as a macrocyclic lactone insecticide (JMPR 2008), often used on caterpillars, thrips, beetle and fly pests in a range of fruit and vegetable crops, ornamentals, turf, and stored grains, with contact activity on all life stages of insects, including eggs, larvae and adults.

Spinosad appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

It is used for mosquito control in potable water in containers. Spinosad DT 7.48 percent is specified for use as a vector control agent in drinking-water sources against Aedes aegypti by the World Health Organization under the WHO Pesticide Evaluation Scheme (WHOPES). Formulations for control of vectors are specified by WHO at a dose of  
0.25–0.5 mg/L. The expected duration of efficacy under field conditions is four to six weeks.

### Forms and fate in the environment

Spinosad has a relatively high log Kow of 4.0 and would be expected to adsorb to particles, sediment and the sides of containers. In a study by the manufacturers of the formulation developed for use in potable water designed to simulate normal product usage, the maximum concentration observed was 0.52 mg/L after three days. Spinosyn B is a degradation product of spinosyn A.

Spinosad is relatively short-lived in the field and photodegrades rapidly, with half-lifes less than a day. Spinosad and its residues are not expected to leach in the soil (USEPA 1997). This is greatly exceeded in the dark due to its very slow hydrolysis.

In soil laboratory incubations under aerobic conditions in the dark, spinosyn A exhibited low to moderate persistence, forming the major (>10 percent applied radioactivity (AR)) metabolite spinosyn B (maximum 67 percent AR), which exhibited moderate to high persistence. Spinosyn D exhibited moderate to medium persistence, forming the major (>10 percent AR) metabolite N‐demethyl spinosyn D (maximum 68 percent AR), which exhibited moderate to high persistence. Spinosyn A and D exhibited low mobility to immobility in soil. Metabolite spinosyn B exhibited low mobility to immobility, and metabolite N‐demethyl spinosyn D exhibited medium mobility to immobility in soil. It was concluded that the adsorption of spinosyn A and D and its metabolites was not pH dependent (EFSA 2018).

In laboratory incubations in dark aerobic natural sediment water systems, spinosyn A and spinosyn D exhibited medium to high persistence, forming the major metabolites spinosyn B (maximum 17.3 percent in sediment and maximum 7.4 percent in water) and N‐demethyl spinosyn D (maximum 14.5 percent in sediment and maximum 6.1 percent in water) respectively. The unextractable sediment fraction accounted for  
8.7–68.8 percent AR at study end (150–120 days). The potential for groundwater exposure from the representative uses by spinosad above the parametric drinking water limit of 0.1 μg/L was concluded to be low (EFSA 2018).

Water solubility is about 230 mg/L (spinosyn A) and 0.35 mg/L (spinosyn D) at pH 7. At pH 5: about 290 mg/L (spinosyn A) and 30 mg/L (spinosyn D), and at pH 9: 16 and 0.05 mg/L respectively.

### Recommended analytical techniques

#### Referee method

See JMPR (2008).

### Health considerations

Spinosad was evaluated for toxicology by the FAO/WHO JMPR in 2001. The JMPR concluded that spinosad has low acute toxicity. In studies with repeated doses, no acute toxicological alerts were observed that might indicate the need for establishing an acute reference dose (acute RfD). An ADI of 0–0.02 mg/kg bw was established on the basis of a NOAEL of 2.4 mg/kg bw per day in a two-year study of toxicity and carcinogenicity in rats and a 100-fold safety factor. The Swiss authorities assigned an ADI of 0–0.02 mg/kg bw/d, based on a NOEL of 2.4 mg/kg bw/d in the two-year study on rats. This range is in agreement with the ADI assigned by the JMPR. The JMPR concluded that it was not necessary to assign an acute reference dose (ARfD). These values were reaffirmed in JMPR (2011). The definition of the residue (for compliance with the MRL and for estimation of dietary intake) sum of spinosyn A and spinosyn D.

Although spinosad at the approved application rate could apparently exceed the ADI for children and infants, the use of a slow-release tablet formulation for mosquito control in water means that this would not be possible. The maximum concentration actually achieved with the slow-release formulation was approximately 0.052 mg/L.

The intake would therefore be:

* 39 μg for a 5 kg bottle-fed infant assuming consumption of 0.75 litre = 7.8 μg/kg body weight
* 52 μg for a 10 kg child assuming consumption of 1 litre = 5.2 μg/kg body weight
* 104 μg for a 60 kg adult assuming consumption of 2 litres = 1.7 μg/kg body weight.

This means that the exposure is well below the ADI for all sectors of the population. Even the application of a double dose would result in exposure below the ADI. The ADI is set for lifetime, and the average exposure over time will be lower than the exposures indicated above.

USEPA (1997) reports a NOEL of 4.9 mg/kg/d for spinosad when evaluated in a subchronic 13-week test on dogs; a chronic RfD of 0.0268 mg/kg/d was derived. There was no evidence of carcinogenicity or mutagenicity. The same cRfD was quoted in USEPA (2002); an acute RfD was unnecessary. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0249 mg/kg/d for both spinosad and spinetoram. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for spinetoram and spinosad is 0.174 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia for spinosad is 0.02 mg/kg body weight, with a NOEL of 2.4 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EC (2006) established an ADI of 0.024 mg/kg/d, and considered that an ARfD was unnecessary due to the low toxicity of the active substance. These values were reaffirmed by EFSA (2011 and 2013). EFSA (2018) confirmed the ADI, but introduced an ARfD of 0.1 mg/kg based on the maternal NOAEL of 10 mg/kg bw per day for early maternal body weight changes in the developmental toxicity study in rabbits, UF of 100.

### Derivation of Maximum Acceptable Value

No MAV.

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# Spiromesifen

CAS No. 283594-90-1. The IUPAC name for spiromesifen is 3-mesityl-2-oxo-1-oxaspiro[4.4]non-3-en-4-yl 3,3-dimethylbutyrate. The CAS name 2-oxo-3-(2,4,6-trimethylphenyl)-1-oxaspiro[4.4]non-3-en-4-yl 3,3-dimethylbutanoate.

### Maximum Acceptable Value

Spiromesifen does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Spiromesifen is a contact tetronic acid insecticide/miticide used on various vegetable crops and strawberries. The mode of action is through lipid inhibition.

Spiromesifen appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

The technical material contains N,N-dimethylacetamide, which has to be regarded as a relevant impurity the maximum content is 4 g/kg (EFSA 2012).

### Forms and fate in the environment

Spiromesifen is not expected to persist in the environment because it readily undergoes both biotic and abiotic degradation; however, its primary degradate is persistent. Spiromesifen strongly sorbs to sediment so is not likely to be mobile; however, its main degradates do not sorb and may migrate to groundwater. Half-lifes in the field range from 2 to 10 days. Spiromesifen was generally retained in the top 15 cm of soil in the terrestrial field dissipation studies; however, the transformation products BSN2060-enol and BSN2060-carboxy were generally detected at the lowest depths of the field studies (CDPR 2005).

Hydrolysis of spiromesifen is pH dependent, being faster at alkaline pH and produces the major metabolite M01 that does not hydrolyse further (EFSA 2002).

Water solubility is about 0.13 mg/L.

### Recommended analytical techniques

#### Some alternative methods

See EFSA (2012).

### Health considerations

The chronic reference dose (cRfD) of 0.022 mg/kg/d was established for spiromesifen based on the NOAEL of 2.2 mg/kg/day and uncertainty factor of 100, from a two generation reproduction study in rats. An acute RfD was unnecessary. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.022 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for spiromesifen is 0.154 mg/L (no acute one-day value available.)

JMPR (2016) established an ADI of 0–0.03 mg/kg bw for spiromesifen on the basis of a NOAEL of 3.3 mg/kg bw per day for macroscopic and histopathological effects on the adrenal glands in an 18-month mouse study and a NOAEL for parental toxicity of 3.3 mg/kg bw per day, based on decreased body weights in F1 males and F1 females and decreased absolute spleen weights in F1 males in a two-generation reproductive toxicity study in rats. This ADI is supported by a NOAEL for offspring toxicity of 3.8 mg/kg bw per day, based on decreased body weights in male and female F1 and F2 pups during lactation and on decreased absolute spleen and thymus weights in male F1 pups observed in a two-generation reproductive toxicity study in rats. A safety factor of 100 was used. The meeting concluded that the ADI would apply to spiromesifen and the metabolites spiromesifen-enol (M01), 4-hydroxymethyl-spiromesifen-enol (M02) and its glucoside and 4-carboxy-3-hydroxy-spiromesifen-enol (M07). The meeting concluded that it was not necessary to establish an ARfD for spiromesifen in view of its low acute oral toxicity and the absence of any toxicological effects, including developmental toxicity, that would likely be elicited by a single dose.

Spiromesifen has been classified as “not likely to be carcinogenic to humans” (USEPA 2010).

Spiromesifen did not show any genotoxic or carcinogenic potential. The relevant repeat dose No Observed Adverse Effect Level (NOAEL) is 3 mg/kg bw per day. The Acceptable Daily Intake (ADI) is 0.03 mg/kg bw per day, based on the relevant long-term toxicity NOAEL of 3 mg/kg bw per day applying an uncertainty factor of 100; the Acute Reference Dose (ARfD) is 2 mg/kg bw based on the acute neurotoxicity NOAEL and an uncertainty factor of 100 (EFSA 2012).

### Derivation of Maximum Acceptable Value

No MAV.

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# Spirotetramat

CAS No. 203313-25-1. The IUPAC name for spirotetramat is cis-4-(ethoxycarbonyloxy)-8-methoxy-3-(2,5-xylyl)-1-azaspiro[4.5]dec-3-en-2-one. The CAS name cis-3-(2,5-dimethylphenyl)-8-methoxy-2-oxo-1-azaspiro[4.5]dec-3-en-4-yl ethyl carbonate.

There are two possible stereoisomers of spirotetramat, cis- and trans-isomers; the cis-isomer is the active material. The ratio of the cis- to trans-isomers is about 98:2.

### Maximum Acceptable Value

Spirotetramat does not have a MAV in the DWSNZ, and it is not mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.2 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Spirotetramat is a tetramic acid (or ketoenole) systemic, long-acting, leaf insecticide used against a broad spectrum of sucking insects. The pesticidal mechanism of action is disruption of lipogenesis as a result of inhibition of acetyl CoA carboxylase.

Spirotetramat appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Spirotetramat has a host of metabolites and degradation products; see USEPA (2008). For drinking water, the residues of concern for risk assessment purposes are spirotetramat, BYI 08330-enol, and BYI 08330-ketohydroxy; the degradates are assumed to be no more toxic than the parent.

The parent spirotetramat and its major metabolites spirotetramat-enol and spirotetramat-ketohydroxy may be of concern in soils and water due to their high concentrations found in laboratory studies (for the parent and spirotetramat-enol) or to their relative persistence (for spirotetramat-ketohydroxy). The soils may also be repositories of toxic residues since high levels of non-extracted residues were observed in metabolism studies. The total residues of spirotetramat, spirotetramat-enol, spirotetramat-ketohydroxy and non-extracted residues are much more persistent than the parent or spirotetramat-enol alone. Half-lifes of 161–204 days were estimated from the aerobic soil metabolism studies for spirotetramat-enol + spirotetramat-ketohydroxy + non-extracted residues; while half-lifes of 141–693 days were estimated from the aerobic aquatic metabolism studies for spirotetramat + spirotetramat-enol + spirotetramatketohydroxy + non-extracted residues.

EFSA (2013) states that according to the soil degradation field studies, the maximum DT90 value for spirotetramat accounts for 3.5 days. The DT90 value for the sum of spirotetramat-enol and spirotetramat-ketohydroxy was calculated to be 105 days; for the sum of spirotetramat, spirotetramat-enol, spirotetramat-ketohydroxy and spirotetramat-MA-amide a DT90 of 77.8 days was reported.

Due to their higher persistence, moderate to high solubility, and relatively low levels of binding, spirotetramat residues of concern (ie, spirotetramat, spirotetramat-enol, spirotetramat-ketohydroxy and non-extracted residues) have a potential to contaminate adjacent bodies of water for periods of weeks to several months post-treatment due to run-off events (both via dissolution or erosion). In addition, there is some potential to move sub-surface and contaminate groundwater.

New York State (2009) states: Even though spirotetramat has a low Koc and is considered mobile, it will probably not leach significantly to groundwater on sandy Long Island soils because of the very short half-life and low application rate. The degradate spirotetramat-ketohydroxy is also not expected to leach to groundwater given the low application rate and fairly short half-life. Modelling results support this determination.

The test substance was unstable under acidic and alkaline conditions (half-lifes of 32.5 days (25°C) and 48 days (20°C) at pH 4) and degraded with a half-life of 7.6 hours at pH 9 (25°C). The hydrolytic degradation was strongly temperature dependent (JMPR 2008). See JMPR for discussion on metabolites.

Water solubility is pH 4: 33.5 mg/L; pH 7: 29.9 mg/L; pH 9: 19.1 mg/L.

### Removal methods

The concentration of spirotetramat and most of its metabolites should be reduced to some extent by treatment processes that remove particulate matter, depending on the soil type; activated carbon treatment may assist. Some newer advanced oxidation processes may be more effective.

### Recommended analytical techniques

#### Some alternative methods

See USEPA (2008) and JMPR (2008).

### Health considerations

The short-term and long-term toxicity of spirotetramat is well understood. The thyroid and thymus glands were target organs in oral subchronic toxicity studies in the dog; whereas, the testes-epididymides were the target organs following subchronic oral treatment of rats. Long-term toxicity studies reflected the short-term toxicological profile of spirotetramat with the thymus and thyroid as target organs following one-year oral exposure of dogs. Chronic exposure of rats to spirotetramat also reflected the subchronic pattern of testicular toxicity. No evidence of tumour formation was found following long-term studies of rodents, and spirotetramat was also negative for mutagenicity and clastogenicity in several standard in vivo and in vitro assays. The reproductive and developmental toxicity potential of spirotetramat was tested in rats and rabbits. In addition to testicular histopathology observed following subchronic and chronic exposure of rats to spirotetramat, male reproductive toxicity was recorded in the two-generation reproductive toxicity study. However, development of the sexual organs of offspring (balano-preputial separation, vaginal opening) was unaffected. In a study designed to explore the time of onset of testicular toxicity in rats, decreased epididymal sperm counts were noted after 10 days of exposure. Therefore, repeated dosing with spirotetramat is necessary to produce male reproductive toxicity in rats. Similar effects were observed after repeated dosing with the enol metabolite of spirotetramat. Developmental toxicity was not observed with spirotetramat in the absence of maternal toxicity in either the rat or rabbit. There was no evidence of carcinogenicity in tests on rats.

The dietary acute reference dose (aRfD) of 1.0 mg/kg/d for the general population, including females 13–49 years of age, was established based on the NOAEL of 100 mg/kg/day from the acute neurotoxicity study in rats. The LOAEL of 200 mg/kg/day is based on clinical signs of toxicity in males and females and decreased motor activity in males.

The dietary chronic reference dose (cRfD) of 0.05 mg/kg/d was established based on the NOAEL (5 mg/kg/day) from the one-year toxicity study in the dog. The LOAEL of 20 mg/kg/day is based on thymus involution in males. The NOAEL of 5 mg/kg is the lowest in the database.

The 2008 JMPR meeting established an ADI of 0–0.05 mg/kg bw per day based on a NOAEL of 5 mg/kg bw per day identified on the basis of thymus involution in a one-year study in dogs and with a safety factor of 100. The meeting established an ARfD of 1 mg/kg bw, based on a NOAEL of 100 mg/kg bw identified on the basis of altered motor and locomotor activity and FOB changes in a single-dose study in rats treated by gavage and with a safety factor of 100. This ARfD provides adequate protection from maternal toxicity and abortion observed at 160 mg/kg bw per day in the study of developmental toxicity in rabbit, even in the unlikely event that the observed effect could be attributed to a single dose (FAO/WHO 2008).

These JMPR values are reaffirmed by EFSA (2011 and 2013) and JMPR (2013, 2015).

The Acceptable Daily Intake (ADI) adopted in Australia for spirotetramat is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg from a one-year study in dogs. This NOEL is based on decreased thyroid hormone triiodothyronine and thyroxine levels and thymus involution. The ADI incorporates a safety factor of 100. The ARfD is 1 mg/kg bw based on a NOEL of 100 mg/kg bw/day from an acute neurotoxicity study in rats. The ARfD incorporates a safety factor of 100.

EC (2013) quote an ADI of 0.025 mg/kg/d, and an ARfD of 0.1 mg/kg bw. However, EFSA (2013) established an ADI of 0.05 mg/kg bw/d, and an ARfD of 1 mg/kg bw.

Spirotetramat is classified by the USEPA as “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Spiroxamine

CAS No. 118134-30-8. The IUPAC name for spiroxamine is 8-tert-butyl-1,4-dioxaspiro[4.5]decan-2-ylmethyl(ethyl)(propyl)amine. The CAS name is 8-(1,1-dimethylethyl)-N-ethyl-N-propyl-1,4-dioxaspiro[4.5]decane-2-methanamine. Technical spiroxamine is a mixture of diastereomers A and B roughly 50:50; both are pesticidally active.

### Maximum Acceptable Value

Spiroxamine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Spiroxamine is a foliar spiroketalamine fungicide which inhibits sterol biosynthesis, and is used on crops such as barley, wheat and rye; also used on grapes.

Spiroxamine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Spiroxamine shows no hydrolysis at pH 5 or 7 and slight hydrolysis at pH 9. The photolytic half-life is about 50 days.

The half-life of spiroxamine in aquatic situations (aerobic water and sediment) was found to be 28 to 106 days for the whole systems, but dissipation from the water column is much faster (12 to 13 hours), reflecting the rapid adsorption to sediment of spiroxamine and its metabolites. Laboratory studies indicate that spiroxamine is unlikely to leach, and field studies suggest that even in extreme situations, spiroxamine and its major metabolites are unlikely to leach deeply into soil so are unlikely to contaminate groundwater.

The octanol/water partition coefficient Log(Kow) is: Diastereomer A: 610 (log Pow = 2.79) at pH 7 @20°C, and Diastereomer B: 960 (log Pow = 2.98 at pH 7 @20°C (USEPA 2004).

According to the soil degradation studies evaluated in the framework of the peer review, the DT90field value of spiroxamine is 466 days which is higher than the trigger value of 100 days (EFSA 2010). The major soil metabolites were identified as M01 and M02 (DT90field values of 321 and 318 days, respectively) (EFSA 2015).

Spiroxamine water solubility is above 200 g/L (>20 percent) at pH 3 (diastereomers A and B); pH 7 at 20°C: 470 mg/L (A), 340 mg/L (B); pH 9 at 20°C: 14 mg/L (A), 10 mg/L (B).

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of spiroxamine in water.

### Recommended analytical techniques

#### Some alternative methods

See <http://www.epa.gov/pesticides/methods/ecmmethods/450904-07-S.pdf> and EFSA (2009).

### Health considerations

The target organ and critical of spiroxamine are the liver and irritant effects on the mucosal epithelium of the oesophagus and fore-stomach.

EC (1999) quoted a short-term oral NOAEL for spiroxamine of 2.5 mg/kg bw/d from a 12‑month test on dogs, and 4.2 mg/kg/d for long-term toxicity and carcinogenicity (based on two-year oral rat testing). The rat LD50 oral acute toxicity is 374 mg/kg bw. The ADI is reported at 0.005 mg/kg/d with an ARfD not being required.

The Acceptable Daily Intake (ADI) adopted in Australia for spiroxamine is 0.02 mg/kg body weight, with a NOEL of 2.5 mg/kg bw based on a 12‑month dog dietary study and using a 100-fold safety factor in recognition of the extensive toxicological database available for spiroxamine, and the ARfD is 0.2 mg/kg bw using a 100-fold safety factor.

USEPA (2004) quoted a chronic dietary endpoint (cRfD) of 0.0083 mg/kg/day, based on a NOAEL of 2.5 mg/kg/day based on hepatocytomegaly, cataracts, and decreased albumin in males and females; liver discoloration and decreased triglycerides in females; and increased alanine aminotransferase in males at a LOAEL of 28.03 mg/kg/day in a chronic oral toxicity study in dogs. A 300-fold uncertainty factor (10X for interspecies extrapolation, 10X for intraspecies variations, and 3X UFDB for the lack of an acceptable two-generation reproduction study) was applied. An acute RfD of 0.1 mg/kg was derived.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.10 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for spiroxamine is 1.0 mg/L.

EFSA (2015) established an ADI and an ARfD at 0.025 mg/kg bw per day and 0.1 mg/kg bw, respectively.

Lifetime studies in mice at up to 250 mg/kg bw/day and rats at doses of up to 43 mg/kg bw/day did not reveal any evidence of carcinogenicity. The reproductive performance of rats fed spiroxamine at up to 42 mg/kg bw/day continuously over two generations was unaffected. USEPA (2004) states that spiroxamine is “not likely” to be a human carcinogen based on the lack of evidence of carcinogenicity in both the rat and the mouse.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Streptomycin

CAS No. 57-92-1 for streptomycin. CAS No. 128-46-1 for dihydrostreptomycin. After that there seems to be some confusion.

CAS No. 1425-61-2, CAS No. 3810-74-0 and CAS No. 5490-27-7 have been used for dihydrostreptomycin sulphate (sesquisulfate).

CAS No. 3810-74-0 and CAS No. 5490-27-7 have also been used for streptomycin sulfate.

CAS No. 5490-27-7 has also been used for dihydrostreptomycin sulphate (sesquisulfate).

### Maximum Acceptable Value

Streptomycin is not mentioned in DWSNZ, or in the WHO Guidelines.

### Sources to water

Streptomycin is an [antibiotic](http://en.wikipedia.org/wiki/Antibiotic) ([antimycobacterial](http://en.wikipedia.org/wiki/Antimycobacterial)) drug, the first of a class of drugs called [aminoglycosides](http://en.wikipedia.org/wiki/Aminoglycoside) to be discovered, and it was the first cure for [tuberculosis](http://en.wikipedia.org/wiki/Tuberculosis). It is derived from the [actinobacterium](http://en.wikipedia.org/wiki/Actinobacteria) [Streptomyces griseus](http://en.wikipedia.org/wiki/Streptomyces_griseus).

Dihydrostreptomycin is formed by reduction of streptomycin. As a result, pharmacokinetic properties, toxicological profiles, and spectrum of antimicrobial and biological activity of the two compounds are similar. Therefore, data on the two compounds are usually considered together for the purpose of establishing a single ADI. Their main use is for treatment of bacterial infections in food-producing animals.

Streptomycin is a general use pesticide registered overseas for use on fruits and vegetables, and to control PSA on kiwifruit in New Zealand. Streptomycin and dihydrostreptomycin sulphate appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)), and are registered for use as antibiotics.

### Forms and fate in the environment

NPIC (1994) quotes for streptomycin sulfate a soil half-life of one day, water solubility of 2 percent and a sorption coefficient (soil Koc) of 339. This resulted in a pesticide movement to groundwater rating of extremely low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In animals and humans dihydrostreptomycin and streptomycin are poorly absorbed from the gastrointestinal tract and the majority of the oral dose is recovered in the faeces (EMEA 2005).

Streptomycin is practically non-toxic. The USEPA (1988) stated that streptomycin has been used since the late 1940s to treat bacterial infections in humans. As a result of this use as a human drug, there is an extensive body of toxicological data available on streptomycin. Thus, all toxicological data requirements (for use as a pesticide) have been waived. This was updated (USEPA 2006), resulting in the USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for streptomycin and streptomycin sesquisulfate being set at 0.35 mg/L. (No acute one day value available.) This is based on a chronic RfD of 0.05 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted in Australia for streptomycin and dihydrostreptomycin is 0.05 mg/kg body weight with a NOEL of 5 mg/kg bw. EXTOXNET quotes an ADI of 0.05 mg/kg/d for streptomycin.

EMEA (2005) quotes for both streptomycin and dihydrostreptomycin an ADI of 0.025 mg/kg bw, calculated using the NOEL of 5 mg/kg bw/day derived from the two-year rat study with dihydrostreptomycin by applying a safety factor of 200, due to the limited data on reproductive toxicity.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Strychnine

CAS No. 57-24-9. The IUPAC and CAS name for strychnine is strychnidin-10-one. Strychnine sulphate: CAS No. is 60-41-3.

### Maximum Acceptable Value

Strychnine does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Strychnine is classed as an avicide and botanical rodenticide. It was commonly used to kill pests such as birds and rodents. In the US it can only be used underground for control of pocket gophers, and use of the sulphate and nitrate products is banned due to their much higher solubilities.

Strychnine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 where it is described as a “nutrient – oral, medicated/antibiotic” (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Strychnine was the first alkaloid (a terpene indol alkaloid) to be identified in plants of the genus [Strychnos](http://en.wikipedia.org/wiki/Strychnos), Family [Loganiaceae](http://en.wikipedia.org/wiki/Loganiaceae). Strychnos, named by [Carl Linnaeus](http://en.wikipedia.org/wiki/Carl_Linnaeus) in 1753, is a genus of trees and climbing shrubs of the gentian order. The genus contains 196 various species and is distributed throughout the warm regions of Asia (58 species), America (64 species), and Africa (75 species). The seeds and bark of many plants in this genus contain the powerful poison strychnine. In some Strychnos plants a 9,10‑dimethoxy derivative of strychnine, the alkaloid [brucine](http://en.wikipedia.org/wiki/Brucine), is also present. [Brucine](http://en.wikipedia.org/wiki/Brucine) was used in the colorimetric analysis of nitrate in water; it is not as poisonous as strychnine.

The US Forest Service reported two instances in which strychnine was detected in water at concentrations ranging from 13 to 23 ppb after strychnine applications of approximately 0.33 lb a.i./acre USDA 2010).

Occasionally strychnine is found mixed with “street” drugs such as LSD, heroin, and cocaine. It is used under medical supervision as a stimulant for the treatment of cardiac disorders.

### Forms and fate in the environment

The majority of data indicate that strychnine is persistent, but not mobile, the parent is adsorbed to organic matter and clay. The hydrolysis and soil photolysis studies reveal that neither process produces a significant transformation of the parent molecule. Greater than 90 percent is biodegraded in soil within approximately 40 days. Available data satisfy the environmental fate requirements for below-ground uses. With the present below-ground use pattern, strychnine is not likely to reach groundwater or surface water (USEPA 1996).

Strychnine water solubility is reported to about 140 mg/L. Solubility of the sulphate is nearer 2 percent.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of strychnine in water.

### Health considerations

The usual fatal dose for humans is 60–100 mg strychnine and is fatal after a period of 1–2 hours, though lethal doses vary depending on the individual. In smaller doses it has been used as a stimulant. Chronic poisoning is not known.

USEPA (1987) refers to an oral RfD of 0.0003 mg/kg/day or 0.02 mg/day for a 70-kg person. Because of the high acute toxicity via the oral and ocular routes, subchronic and chronic data were not required (USEPA 1996).

Strychnine has not been reviewed by the Joint FAO/WHO pesticide committee.

In the absence of an acute RfD or an acceptable chronic RfD, the current US Forest Service risk assessment bases both surrogate acute and chronic RfDs on the threshold limit value (TLV) recommended by ACGIH, which has been in effect for more than 50 years. This TLV is equivalent to a dose of 0.02 mg/kg bw and is intended to be protective in both acute and longer-term exposures. This TLV is based on human data and is consistent with the information available on the mechanism of action and pharmacokinetics of strychnine so is used as a surrogate acute RfD. USDA (2010) notes however that strychnine doses ranging from 0.02 to 0.1 mg/kg bw/day have been used therapeutically for members of the general public.

### Derivation of Maximum Acceptable Value

No MAV.

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# Sulfentrazone

CAS No. 122836-35-5. The IUPAC name for sulfentrazone is 2′,4′-dichloro-5′-(4-difluoromethyl-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl)methanesulfonanilide. The CAS name for sulfentrazone is N-[2,4-dichloro-5-[4-(difluoromethyl)-4,5-dihydro-3-methyl-5-oxo-1H-1,2,4-triazol-1-yl]phenyl]methanesulfonamide.

### Maximum Acceptable Value

Sulfentrazone does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Sulfentrazone is classed as a selective post-emergence anilide or triazolone or triazolinone herbicide, used to control a variety of broadleaf weeds and sedges amongst grass and a range of crops.

Sulfentrazone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Some commercial products comprise 6 percent toluene; some may be sold mixed with other pesticides.

### Forms and fate in the environment

Sulfentrazone can contaminate surface water through spray drift. Under some conditions, sulfentrazone may also have a high potential for run-off into surface water (primarily via dissolution in run-off water), for several to many months post-application. Based on the current environmental fate data base, sulfentrazone has the following characteristics:

1 moderately soluble

2 not susceptible to hydrolysis

3 extremely susceptible to direct photolysis in water

4 very stable to photolysis on soil

5 aerobic half-life of 1.5 years

6 anaerobic half-life of nine years

7 very high mobility in soil (average Koc = 43, Kd < 1)

8 low volatility from soils and water.

With these properties, it appears that sulfentrazone is highly mobile and persistent, and has a strong potential to leach into groundwater and move offsite to surface water. It also indicates that most sulfentrazone will be partitioned in the water column instead of in the suspended and bottom sediments (USEPA 1997).

Health Canada (2011) says sulfentrazone can enter aquatic ecosystems through spray drift and/or run-off from treated fields. In surface water ecosystems, sulfentrazone remains in the water column and is very susceptible to aerobic phototransformation. Based on field studies, it is not expected to persist in surface waters. Sulfentrazone is persistent in soil and groundwater.

Sulfentrazone water solubility is reported to about 240 to 800 mg/L; the variation may depend on the formulation.

### Health considerations

A 90-day feeding study in dogs resulted in a NOEL of 28 mg/kg/day and a LOEL of 57 mg/kg/day for males and 73 mg/kg/day for females. Evidence of treatment-related developmental toxicity consisted of decreased foetal viability, decreased foetal body weight, and increased incidence of foetal alterations, comprised, for the most part, of skeletal malformations and variations. A supplementary prenatal oral developmental toxicity study in rats confirmed the maternal and foetal findings of the previously conducted study and did not alter the study conclusions. The developmental (foetal) NOEL is 10.0 mg/kg/day (USEPA 1997). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.1 mg/kg/d, and an ARfD of 0.14 mg/kg/d. USEPA (2014) quotes an acute RfD and aPAD of 0.14 mg/kg/d based on females 13-49 years old, and cRfD and cPAD of 0.14 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for sulfentrazone is 4.62 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for sulfentrazone is 0.05 mg/kg body weight, with a NOEL of 12 mg/kg bw, and the ARfD is 0.1 mg/kg bw.

Sulfentrazone is not likely to be carcinogenic. However, under the conditions of the studies reviewed, sulfentrazone caused developmental and reproductive toxicity. The results of these studies elicited a high level of concern, since the developmental toxicity studies demonstrated embryo/foetal toxicity at treatment levels that were not maternally toxic, and significant toxic effects were observed primarily in the second generation animals of the reproduction study. Because these animals had been exposed to sulfentrazone in utero, the possibility that the observed reproductive toxicity resulted from a developmental and/or genotoxic mechanism was suggested (USEPA 1997).

USEPA (2014) classified sulfentrazone as not likely to be carcinogenic to humans.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Sulfoxaflor

CAS No. 946578-00-3. The IUPAC name for sulfoxaflor is [methyl(oxo){1-[6-(trifluoromethyl)-3-pyridyl]ethyl}-λ6-sulfanylidene]cyanamide. The CAS name is N‑[methyloxido[1-[6-(trifluoromethyl)-3-pyridinyl]ethyl]-λ4-sulfanylidene]cyanamide.

Sulfoxaflor contains 2 tetrahedral stereogenic atoms (the sulfur atom, and the carbon atom attached to position 3 of the pyridine ring), and is a mixture of the four possible stereoisomers. Both (E)- and (Z)-isomers (involving the S=N double bond and the cyano group) exist, but they rapidly interconvert at ambient temperatures.

### Maximum Acceptable Value

Sulfoxaflor does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Sulfoxaflor, a systemic sulfoximine insecticide used against sap-sucking insects, acting as an insect neurotoxin, appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2015 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

Application is often recommended when pollinators are not likely to be present in an area as sulfoxaflor is highly toxic to bees.

### Forms and fate in the environment

In soil laboratory incubations under aerobic conditions in the dark, sulfoxaflor exhibited very low persistence. Laboratory experiments demonstrated that sulfoxaflor and metabolite X11719474 were stable to photolysis at the soil surface. Sulfoxaflor and X11719474 exhibited very high to high mobility in soil; X11519540 and X11579457 exhibited very high soil mobility. It was concluded that the adsorption of all these substances was not pH dependent. In satisfactory field dissipation studies carried out at four sites (one each in Germany, northern France, Spain and Italy, spray application of sulfoxaflor at N and 2N rates to the soil surface on bare soil plots in May), sulfoxaflor exhibited low persistence and X11719474 exhibited moderate to high persistence (EFSA 2014).

In laboratory incubations in dark aerobic natural sediment water systems, sulfoxaflor exhibited moderate to medium persistence, forming the major metabolite X11719474 (maximum 35–48 percent AR in water and 10–30 percent AR in sediment, as sum of isomers), with no decline of X11719474 being apparent. The potential for groundwater exposure from the representative uses by sulfoxaflor above the parametric drinking water limit of 0.1 μg/L was concluded to be low (EFSA 2014).

Solubility in water at 20°C: pH 5: 1,380 mg/L; pH 7: 568 mg/L; pH 9: 551 mg/L. Henry’s Law constant at 20°C: pH 5: 2.81 x 10-7 Pa.m3/mol; pH 7: 6.83 x 10-7 Pa.m3/mol; pH 9: 7.05 x 10-7 Pa.m3/mol. Partition coefficient at 20°C: pH 5: Log Pow = 0.806; pH 7: Log Pow = 0.802; pH 9: Log Pow = 0.799.

APVMA (2013) reports half-lifes of 84 to 261 days in water, 103–382 days in the whole system and undetectable degradation in sediment. Sulfoxaflor was mainly bound as non-extractable residues in the sandy clay loam system.

JPMR (2011) reports a soil half-life of 0.3 to 0.6 days, and describes the main metabolites, some of which have very long half-lifes (up to a year).

### Recommended analytical techniques

#### Some alternative methods

See JMPR (2011), USEPA (2013) and EFSA (2014).

### Health considerations

Sulfoxaflor is almost completely absorbed after oral administration and poorly metabolised; more than 93 percent is rapidly excreted unchanged in urine and faeces. Sulfoxaflor showed no genotoxic potential, but liver tumours occurred in both rats and mice, as well as Leydig cell tumours and preputial gland tumours in rats only. The weight of evidence suggests that liver tumours in mice and rats are not relevant to humans. After the peer review meeting, ECHA concluded that sulfoxaflor should not be classified as carcinogen (EFSA 2014).

Exposure to sulfoxaflor and its major metabolites resulted in hepatotoxicity in several guideline studies. For example, sulfoxaflor caused liver weight and enzyme changes, hypertrophy, proliferation, and tumours in subchronic and chronic studies. Short-term studies with metabolites resulted in similar liver effects. For sulfoxaflor, hepatoxicity occurred at lower doses in long-term studies compared to short-term studies. Developmental/offspring toxicity, manifested as skeletal abnormalities and neonatal deaths, was observed in rats only (USEPA 2013).

USEPA (2013) developed a chronic RfD of 0.05 mg/kg/d based on a NOAEL of 5.13 mg/kg/d, and an acute RfD of 0.06 mg/kg/d for females aged 13 to 50.

The JMPR meeting established an acceptable daily intake (ADI) for sulfoxaflor of  
0–0.05 mg/kg bw, based on a NOAEL of 5.13 mg/kg bw per day for hepatocellular degeneration in female rats in a two-year toxicity and carcinogenicity study and application of a safety factor of 100. The ADI is supported by the NOAEL of 6.07 mg/kg bw per day for systemic toxicity (increased vacuolisation/fatty change of centrilobular hepatocytes in F0 males) and offspring toxicity (reduced neonatal survival) at 24.6 mg/kg bw per day in a two-generation rat study, the NOAEL of 6.36 mg/kg bw per day, based on effects in the liver (increased serum cholesterol, vacuolisation/fatty change of hepatocytes) in a 13-week study in rats, and the overall NOAEL of 6 mg/kg bw per day in the 90-day and one-year dog studies. The meeting established an acute reference dose (ARfD) for sulfoxaflor of 0.3 mg/kg bw, based on the NOAEL of 25 mg/kg bw for decreased motor activity at 75 mg/kg bw in an acute neurotoxicity study in rats. A 100-fold safety factor was applied. Sulfoxaflor is unlikely to pose a carcinogenic risk to humans at levels of dietary exposure (JMPR 2011 and 2014).

EFSA (2014) reports the relevant short-term toxicity oral NOAEL to be 6.36 mg/kg/d based on a 90-day dietary study, and the long term toxicity and carcinogenicity NOAEL to be 4.24 mg/kg bw per day based on non-neoplastic liver effects. From these values they developed an ADI of 0.04 mg/kg/d and an ARfD of 0.25 mg/kg bw. APVMA (2013) had derived these values too.

The Acceptable Daily Intake (ADI) adopted in Australia for sulfoxaflor is 0.04 mg/kg body weight, with a NOEL of mg/kg bw. The ARfD is 0.25 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2013. *Public Release Summary on the Evaluation of the New Active Constituent Sulfoxaflor in the Product Transform Insecticide*. APVMA Product Number 64101 [76 pp]. http://apvma.gov.au/sites/default/files/publication/14041-prs-sulfoxaflor.pdf

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# Sulphaquinoxaline

CAS No. 59-40-5. The IUPAC name for sulphaquinoxaline is 4-amino-N-2-quinoxalinylbenzenesulfonamide) or 4-amino-N-quinoxalin-2-yl-benzenesulfonamide. Also called 2-(p-aminobenzene)sulfonamidoquinoxaline. Sometimes referred to as sulfaquinoxaline or SQ. It is usually supplied as the sodium salt, CAS No. 967-80-6. Sometimes sold mixed with other products, eg, amprolium hydrochloride (CAS No. 137-88-2).

### Maximum Acceptable Value

Sulphaquinoxaline does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Sulphaquinoxaline is a sulphonamide antibiotic used to prevent and treat coccidiosis in poultry, usually dosed into their drinking-water or food, eg, sulphaquinoxaline is used prophylactically at 125 mg/kg feed, or therapeutically at higher concentrations in the mash or in drinking-water (up to 0.04 percent solution). It also has uses mixed with bromadiolone (qv) a rodenticide. Sulphaquinoxaline can also be used for prevention and control of fowl typhoid in chickens and turkeys. Coccidiosis is mainly caused the oocysts of some species of the Eimeria protozoa, not unlike the way Cryptosporidium oocysts affect various birds and mammals.

Sulphaquinoxaline appears as an antibiotic and coccidiostat on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

In the UK, sulphaquinoxaline had also been used on pigs, cattle and sometimes sheep. The Swann Committee (Swann 1969) drew attention to some therapeutic uses of antibiotics which can be regarded as unwise, especially attempts to control by mass medication the spread of intestinal diseases caused by the Enterobacteriaceae which rapidly become resistant, and it called for more studies of epidemiology, which might lead to better long-term methods of control through husbandry practices (Lucas 1972).

In 1991 the USEPA cancelled the registration of products containing N-(2-quinoxalinyl) sulfanilamide (sulfaquinoxaline) used as a rodenticide.

### Forms and fate in the environment

With all hormones, antibiotics and other pharmaceutical agents administered either orally or by injection to animals, the major route of entry of the product into the environment is probably via excretion following use and the subsequent dispersal of contaminated manure on to land. As well as contaminating the soil column, it is possible for veterinary medicines to leach to shallow groundwater from manured fields or even reach surface water bodies through surface run-off. Sulphonamides generally have half-lifes of 30 days or lower, and are therefore likely to be significantly degraded during manure/slurry storage (although no data is available on the fate of the degradation products). See Boxall et al (2002).

Water solubility of the sodium salt is about 5 percent, so is expected to be mobile in soils. The half-life of sulfonamides in water is >21 days.

### Health considerations

Sulphonamides have been used widely at subtherapeutic and therapeutic concentrations in food animal production, but increasing concern about their carcinogenic and mutagenic potential and their thyroid toxicity has lead to decreased use, longer withdrawal times and tighter residue monitoring. Those sulphonamides approved for use in food animals are sulfamethazine, sulfadimethoxine, sulfaquinoxaline, sulfachlorpyridazine, sulfathiazole, sulfacetamide and sulfanilamide (FAO 2005).

The Acceptable Daily Intake (ADI) adopted in Australia for sulfaquinoxaline is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

Boxall et al. 2002. *Review of Veterinary Medicines in the Environment*. R&D Technical Report P6-012/8/TR [251 pp]. <http://publications.environment-agency.gov.uk/pdf/SP6-012-8-TR-e-p.pdf>

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# 2,4,5-T

CAS No. 93-76-5. The IUPAC and CAS name for 2,4,5-T is 2,4,5-trichlorophenoxyacetic acid.

### Maximum Acceptable Value

Based on health considerations, the concentration of 2,4,5-T in drinking-water should not exceed 0.01 mg/L.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.07 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

Under good manufacturing conditions, a typical production lot of the technical material assayed about 95 percent 2,4,5-trichlorophenoxyacetic acid, about 5 percent homologous and isomeric acids and less than 0.1 ppm (mg/kg) of 2,3,4,7,8-tetrachlorodibenzo-p-dioxin (TCDD). Under poorly controlled manufacture TCDD had been reported to be present in one commercial sample of 2,4,5-T at a level of approximately 27 ppm. Current production specifications limit TCDD to 0.1 ppm (WHO 1975).

### Sources to water

2,4,5-T may enter source waters as a result of its use for the control of gorse and other brush weeds. The total annual usage of 2,4,5-T in New Zealand has been above 700,000 kg in the past and was averaging around 500,000 kg in the late 1980s. Most of the usage was in the North Island, with about 250,000 kg being used in the Rangitikei county. In 1990 it was voluntarily withdrawn from use. There was additional concern about 2,4,5-T because of impurities of dioxins in the product, including the highly toxic tetra-chlorinated dioxin; 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) was not to exceed 0.01 mg/kg. 2,4,5-T is a plant growth regulator (a synthetic hormone in the auxin family).

2,4,5-T no longer appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register).

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. 2,4,5-T appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

### Forms and fate in the environment

2,4,5-T can be made as either amine salts or butyl esters. The esters hydrolyse rapidly into the acid and the salts dissociate in water. The acid undergoes degradation to produce 2,4,5-trichlorophenol. The half-life of 2,4,5-T in soil ranges from 12–59 days with a recommended average half-life of 24 days.

The water solubility of the acid is 150 mg/L; the ester is practically insoluble and the solubility of the amine salts range from 189,000 to 500,000 mg/L (19 to 50 percent).

NPIC (1994) quotes for 2,4,5-T acid a soil half-life of 30 days, water solubility of 278 mg/L and a sorption coefficient (soil Koc) of 80. This resulted in a pesticide movement to groundwater rating of high.

If released in soil, 2,4,5-T can biodegrade and its mobility is expected to vary from highly mobile in sandy soil to slightly mobile in muck (due to adsorption to humic acids and other organic matter). Removal by biodegradation apparently limits the extent of leaching, however, and groundwater contamination is likely only by rapid flow through large channels and deep soil cracks. 2,4,5-trichlorophenol and 2,4,5‑trichloroanisole are the primary microbial degradation products of 2,4,5-T. Chemical hydrolysis in moist soils and volatilisation from dry and moist surfaces should not be significant. The persistence of 2,4,5-T in soil is reported to vary between 14 to 300 days, but usually does not exceed one full growing season regardless of the application rate. Degradation under anaerobic conditions in flooded soils is much slower (half-life less than or equal to 48 weeks) than in field moist soils. If released to water, photochemical decomposition, volatilisation and biodegradation of 2,4,5-T appear to be the dominant removal mechanisms. The primary degradation product of 2,4,5-T in water is 2,4,5-trichlorophenol. The aquatic near surface half-life for direct photolysis has been calculated to be 15 days during summer at latitude 40 degrees. Humic substances can photosensitise 2,4,5-T and humic induced photoreactions may dominate photodegradation processes when humic substance concentrations exceed 15 mg/L of organic C/L. Primary photodegradation products are 2,4,5-trichlorophenol and 2-hydroxy-4,5-dichlorophenoxyacetic acid. Adsorption of 2,4,5‑T to humic acids in suspended solids and sediments may be significant. Oxidation, chemical hydrolysis, volatilisation and bioaccumulation should not be significant (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

Of 230 source water samples obtained from 212 supplies in New Zealand between 1988 and 1992, four samples contained detectable levels of 2,4,5-T. The concentrations ranged from 0.00005 mg/L (0.05 g/L) to 0.00019 mg/L (0.19 g/L). 2,4,5-T was detected on one occasion in a well near Gisborne at a concentration of 0.0001 mg/L (0.1 g/L). The P2 programme in 2001 found a sample with 2,4,5-T at 1 percent of its MAV.

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, found 2,4,5-T in one zone at a concentration of 0.0002 mg/L, with the median concentration being “nd” (limit of detection = 0.0001 mg/L) (ESR 2001).

MAF (2006) reports that 2,4,5-T has been found in groundwater in Poverty Bay, at 0.0001 mg/L.

Five water utilities in the US reported detecting 2,4,5-T in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, the highest being 0.0076 mg/L.

Chlorophenoxy herbicides are not frequently found in drinking-water; when detected, concentrations are usually no greater than a few micrograms per litre (WHO 2004).

### Removal methods

Available information indicates that 2,4,5-T can be removed effectively from water by adsorption on to granular, or powdered, activated carbon; GAC should reduce the concentration down to about 0.001 mg/L. Approximately 90 percent removal has been reported for ion exchange, and 63 percent for removal by coagulation/clarification/ filtration.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (APHA 6640B; EPA 515.3).

#### Some alternative methods

1. High Performance Liquid Chromatography with a Photoiodide Array Ultraviolet Detector (EPA 555).

### Health considerations

In general, chlorophenoxy herbicides are absorbed rapidly from the gastrointestinal tract and distributed evenly throughout the body. Accumulation in human tissues is not expected, and a steady-state level in the human body will be achieved within  
3–5 days of exposure. Elimination occurs primarily in the urine, mostly in the unchanged form. Biological half-lifes of chlorophenoxy herbicides in mammals range from 10 to 33 hours. Metabolic conversions occur only at high doses. The salt and ester forms are hydrolysed rapidly and follow the same pharmacokinetic pathways as the free acid forms.

2,4,5-T is considered to be moderately acutely toxic. Symptoms of high oral doses include nausea, vomiting, drowsiness, fever, increases in pulse and respiration, shock, coma and death.

Animals subject to long-term exposure to high doses of 2,4,5-T experienced symptoms including reduced body weight gain, elevated urinary excretion of porphyrins, heptacellular swelling, paleness and increased relative liver and kidney weights.

The reference dose or RfD (USEPA 1989/2006/2009/2011) is 0.01 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.35 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for 2,4,5-T been deleted.

Results of various reproductive studies indicate that 2,4,5-T, without appreciable dioxin contamination, caused teratogenic effects (cleft palate and kidney malformations) in only mice at doses above 20 mg/kg body weight.

Chlorophenoxy herbicides as a group, including 2,4-D and MCPA, have been classified by the International Agency for Research on Cancer in Group 2B (possibly carcinogenic to humans). However, based on the available data from studies on exposed populations and on animals, it is not possible to assess the carcinogenic potential of any specific chlorophenoxy herbicide. Therefore, drinking-water guidelines for these compounds are based on a threshold approach for other toxic effects.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV for 2,4,5-T in drinking-water. The calculation was based on reduced body weight gain, increased liver and kidney weights, and renal toxicity in a two-year study in rats.

The MAV for 2,4,5-T in drinking-water was derived as follows:

3 mg/kg body weight/day x 70 kg x 0.1 = 0.01 mg/L

2 L/day x 1,000

where:

* no observable adverse effect level = 3 mg/kg body weight per day based on reduced body weight gain, increased liver and kidney weights and renal toxicity in a two-year study in rats, with an uncertainty factor of 1,000 (100 for interspecies and intraspecies variation and 10 to take into consideration the suggested association between 2,4,5-T and soft tissue sarcoma and non-Hodgkin lymphoma in epidemiological studies)
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 1,000 (100 for inter and intra-species variation and 10 for the suggested association between 2,4,5-T and soft tissue sarcoma and non-Hodgkin lymphoma in epidemiological studies).

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The chronic health risk limit (exposure greater than 10 percent of a lifetime) for 2,4,5-T is 0.07 mg/L.

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# Tau-fluvalinate

CAS No. 102851-06-9. The IUPAC name for tau-fluvalinate is (RS)-α-cyano-3-phenoxybenzyl N-(2-chloro-α,α,α-trifluoro-p-tolyl)-D-valinate. The CAS name is cyano(3-phenoxyphenyl)methyl N-[2-chloro-4-(trifluoromethyl)phenyl]-D-valinate. Tau-fluvalinate represents a 1:1 mixture of the two isomers R-α-cyano and s-α-cyano isomers.

The unresolved isomeric mixture of this substance has the ISO common name [fluvalinate](http://www.alanwood.net/pesticides/fluvalinate.html) (CAS No. 69409-94-5), which consists of four active diastereoisomers; its use has been discontinued.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for tau-fluvalinate; the WHO Guidelines do not refer to tau-fluvalinate.

### Sources to water

Tau-fluvalinate is a Type II synthetic pyrethroid ester miticide, insecticide and acaricide. In the US, the majority of the usage is in commercial greenhouses and on outdoor field- and container-grown ornamentals. It is also used for the topical treatment of honey bees for against the parasitic mite Varroa jacobsoni.

Tau-fluvalinate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). Fluvalinate does not appear in the list.

Tau-fluvalinate was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in tomatoes.

### Forms and fate in the environment

If released to soil, tau-fluvalinate is expected to have no mobility based upon Koc value of 135,000. Volatilisation from moist soil surfaces is not expected to be an important fate process based on an estimated Henry’s Law constant of 1.20 x 10-4 Pa m3 /mole at 25°C. Tau-fluvalinate will not volatilise from dry soil surfaces based upon its vapour pressure. Tau-fluvalinate is expected to degrade rapidly under aerobic conditions (half-lifes of 6.8 to 8.0 days in an agricultural soil) but be persistent under anaerobic conditions. Laboratory tests have shown that tau-fluvalinate photodegrades rapidly (half-life of 1 day) on glass, soil and plant surfaces exposed to sunlight. Given this profile, the main routes of exposure from use of tau-fluvalinate are expected to be due to run-off and spray drift. This synthetic pyrethroid has a high organic carbon partitioning coefficient (Koc), and like other pyrethroids, will accumulate in sediment in aquatic systems.

Solubility in water is about 0.002 mg/L. If released into water, fluvalinate is expected to adsorb to suspended solids and sediment based on its Koc values. Aqueous hydrolysis half-lifes of fluvalinate at 25°C of 30 days at pH 3 and 6, and one to two hours at pH 9 have been reported. Laboratory tests have shown that fluvalinate photodegrades rapidly (half-life of one day) in aqueous solutions exposed to sunlight. An agricultural water-sediment persistence study found that fluvalinate was undetectable after 15 days in the water-phase; however, it persisted beyond 20 days in the sediment.

NPIC (1994) quotes for fluvalinate a soil half-life of seven days, water solubility of 0.005 mg/L and a sorption coefficient (soil Koc) of 1,000,000. This resulted in a pesticide movement to groundwater rating of extremely low.

Tau-fluvalinate and the metabolite haloaniline have DT90 values of 296 and 515 days respectively.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of tau-fluvalinate in water.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

Tau-fluvalinate is moderately acutely toxic, being classified in USEPA Toxicity Category II for oral toxicity. Tau-fluvalinate dietary risks from food and drinking water sources are low and not of concern to the USEPA.

Although tau-fluvalinate is added to beehives, its concentration is quite low because it is very soluble in beeswax. However, honey is still the main source of tau-fluvalinate for humans.

A chronic dietary exposure analysis was performed for tau-fluvalinate using a reference dose (RfD) of 0.01 mg/kg-bwt/day based on a no-observable effect level (NOEL) of 1.0 mg/kg- bwt/day from a two-year rat feeding study with an uncertainty factor of 100. The end point effect of concern was decreased body weight gain in both sexes (USEPA 1996). Subsequently USEPA (2005) quotes both an acute RfD and a chronic RfD of 0.005 mg/kg/d, both based on a NOAEL of 0.5 mg/kg/d and uncertainty factors of 100. In 1991, USEPA had an oral RfD for fluvalinate of 0.01 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.005 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tau-fluvalinate is 0.05 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for fluvalinate is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

EC (in <http://ec.europa.eu/sanco_pesticides/public/index.cfm>) refers to an ADI of 0.005 mg/kg/d and an ARfD of 0.05 mg/kg/d for tau-fluvalinate, quoting an EFSA source. These values are repeated in EFSA (2017).

Cancer endpoints were not selected, since no evidence of carcinogenicity was seen in rat and mouse carcinogenicity studies with tau-fluvalinate, and the available mutagenicity/genetic toxicity data do not indicate a concern. Tau-fluvalinate may be classified as “not likely to be a human carcinogen” (USEPA 2005). Fluvalinate appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

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# Tebuconazole

CAS No. 107534-96-3. The IUPAC name for tebuconazole is (RS)-1-p-chlorophenyl-4,4-dimethyl-3-(1H-1,2,4-triazol-1-ylmethyl)pentan-3-ol. The CAS name is α-[2-(4-chlorophenyl)ethyl]-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol.

### Maximum Acceptable Value

Tebuconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The USEPA concluded on 22 September 2009 that tebuconazole is known or anticipated to occur in PWSs and may require regulation. Therefore they added tebuconazole to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

EPA established an environmental exposure limit of 0.00024 mg/L (0.24 µg/L) for tebuconazole in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Tebuconazole is a systemic conazole (triazole) fungicide used on a wide range of crops around the world, and as a seed dressing. The compound acts as an ergosterol biosynthesis inhibitor; the lack of normal sterol production inhibits the growth of the fungus, thereby effectively preventing further infection and/or invasion of host tissues. It is often mixed with other products.

Tebuconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is used on onions.

### Forms and fate in the environment

The half-life of tebuconazole in soils is very long (up to or exceeding one year). Water solubility is about 30 to 40 mg/L. Henry’s Law constant 1 x 10-5 Pa.m³ / mol at 20°C. Octanol/water partition coefficient log POW = 3.7 at 20°C, pH 7.

JMPR (2011) reports: vapour pressure is about 2 x 10-6 Pa. Henry’s Law constant = 1 x 10-5 Pa.m3/mol at 20°C. Water solubility = 36 mg/L at 20°C for pH 5 to 9. Partition coefficient n-octanol/water = Pow = 3.7 at 20°C and 3.1 at 25°C. Hydrolytically stable at 5, 7 and 9 sterile, aqueous phosphate buffers, in the dark at 25°C. No degradation was observed over a 28 day period, half-life >1 year. Photolytically stable at pH 7, photolysis products were not observed after 30 days of irradiation. Soil half-lifes were measured in Europe between 20 to 90 days and 8 to 912 days in North America. Metabolites are listed.

Tebuconazole shares common metabolites with other triazole-derivative chemicals, including free triazole (1,2,4-triazole) and triazole-conjugated plant metabolites (such as triazole alanine and triazole acetic acid). These common metabolites have been the subject of separate risk assessments (see below). See EFSA (2011) for a list of metabolites.

Tebuconazole exhibits high to low mobility in soil; 1,2,4-triazole exhibits very high to high mobility in soil. It was concluded that it was unlikely that adsorption of tebuconazole was pH dependent. The adsorption of 1,2,4-triazole was not pH dependent (EFSA 2014).

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

The toxicity of tebuconazole was first evaluated by the 1994 Joint FAO/WHO Meeting on Pesticide Residues (JMPR). That meeting established an acceptable daily intake (ADI) of 0–0.03 mg/kg body weight (bw) on the basis of a no-observed-adverse-effect level (NOAEL) of 2.9 mg/kg bw per day for histopathological alterations in the adrenal glands seen at 4.4 mg/kg bw per day and above in two 52-week toxicity studies in dogs and using a safety factor of 100.

The USEPA (2005) considers acute and chronic dietary exposures are below their level of concern for all population groups. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.029 mg/kg/d, and an ARfD of 0.029 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tebuconazole is 0.29 mg/L.

The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite.

The JMPR 2010 meeting reaffirmed the ADI of 0–0.03 mg/kg bw on the basis of an overall NOAEL of 2.9 mg/kg bw per day in two one-year dietary toxicity studies in dogs, based on histopathological alterations in the adrenals seen at the LOAEL of 4.4 mg/kg bw per day, and using a safety factor of 100. The meeting established an acute reference dose (ARfD) of 0.3 mg/kg bw on the basis of a maternal and developmental toxicity NOAEL of 30 mg/kg bw per day in studies of developmental toxicity in rats and rabbits based on maternal toxicity manifested as decreases in body weight gains in the early treatment period and visceral and skeletal anomalies seen at higher doses. The increased incidence of the number of small fetuses, defined on the basis of low body weights, was considered unlikely to be due to a single exposure or a small number of exposures. The ARfD is supported by the NOAEL of 30 mg/kg bw per day observed in a 28-day oral (gavage) toxicity study in rats based on changes in haematological parameters seen at the LOAEL of 100 mg/kg bw per day, which might be produced by a single dose (FAO/WHO 2010, JMPR 2011, 2015, 2017).

The acceptable daily intake (ADI) for humans had been estimated at 0.03 mg/kg bw (IPCS 1994).

The Acceptable Daily Intake (ADI) adopted in Australia as at December 2008 was 0.01 mg/kg body weight, with a NOEL of 1.5 mg/kg bw. By Jul 2011 this had changed to an ADI of 0.03 mg/kg body weight, with a NOEL of 2.96 mg/kg bw.

EC (2008) established an ADI and ARfD of 0.03 mg/kg/d. Reaffirmed in EFSA (2013, 2014 and 2015). Metabolites 1,2,4-triazole, triazole acetic acid(a), triazole lactic acid: ADI 0.02 mg/kg/d and ARfD of 0.06 mg/kg/d. Metabolite: triazole alanine ADI 0.1 mg/kg/d and ARfD of 0.1 mg/kg/d. See datasheet for triazole metabolites for latest ADI and ARfD.

As at September 2008 the USEPA has classified tebuconazole in Group C: a possible human carcinogen, based on a statistically significant increase in the incidence of hepatocellular adenoma, carcinoma, and combined adenoma/carcinomas in both sexes of NMRI mice. The chronic RfD value is 0.029 mg/kg/day which is approximately 9,600‑fold lower than the dose that would induce liver tumours (279 mg/kg/day). Oral administration of tebuconazole caused developmental toxicity in all species evaluated (rat, rabbit, and mouse), with the most prominent effects seen in the developing nervous system. In the available toxicity studies on tebuconazole, there was no toxicologically significant evidence of endocrine disruptor effects. USEPA (2015) concluded that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for tebuconazole since additional testing will not impact the current EPA established regulatory endpoints for human health risk assessments.

The 2010 JMPR meeting concluded that tebuconazole caused developmental toxicity and teratogenic effects at doses that were maternally toxic in rats and rabbits, and the meeting concluded that tebuconazole is unlikely to be genotoxic. In view of the absence of genotoxic potential, the absence of carcinogenicity in rats and no carcinogenicity in mice relevant to human dietary exposure levels, the meeting concluded that tebuconazole is unlikely to pose a carcinogenic risk to humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Tebufenozide

CAS No. 112410-23-8. The IUPAC name for tebufenozide is N-tert-butyl-N′-(4-ethylbenzoyl)-3,5-dimethylbenzohydrazide. The CAS name is 3,5-dimethylbenzoic acid 1-(1,1-dimethylethyl)-2-(4-ethylbenzoyl)hydrazide.

### Maximum Acceptable Value

Tebufenozide does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The USEPA concluded on 22 September 2009 that tebufenozide is known or anticipated to occur in PWSs and may require regulation. Therefore they added tebufenozide to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

EPA established an environmental exposure limit of 0.0007 mg/L (0.7 µg/L) for tebufenozide in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Tebufenozide is a diacylhydrazine insecticide (a moulting hormone agonist), used on many fruits. Tebufenozide is a fat-soluble insecticide used to control Lepidoptera pests in fruits, vegetables and other crops. It has a novel mode of action in that it mimics the action of the insect moulting hormone, ecdysone. Lepidoptera larvae cease to feed within hours of exposure and then undergo a lethal, unsuccessful moult.

Tebufenozide appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Tebufenozide is persistent in soils, with half-lifes of around six or 12 months, for anaerobic and aerobic soils respectively. It degrades photolytically with a half-life of about two months in pond water. EFSA (2014) states that the degradation rate of tebufenozide is soils with pH of 5.5–6.4 was moderate; the DT90 from field studies ranged from 34 to 106 days.

Water solubility is about 1 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

#### Some alternative methods

See FAO.

### Health considerations

Tebufenozide was first evaluated by the 1996 JMPR, which established an ADI of  
0–0.02 mg/kg on the basis of NOAELs for haematotoxicity (main action) of 1.8 mg/kg bw per day in a one-year study in dogs, and 1.6 mg/kg bw per day in a two-generation study of reproductive toxicity in rats, using a safety factor of 100 (FAO 1996, JMPR 2003).

The 2001 JMPR evaluated the acute toxicity of tebufenozide on the basis of the available data. The meeting established an acute reference dose (RfD) of 0.05 mg/kg bw, on the basis of a NOAEL of 5 mg/kg bw per day for haematotoxicity in a two-week study in dogs. The meeting noted that it might be possible to refine this estimate using the results of a study designed specifically for this purpose. On the basis of a study better suited to assess acute toxic effects, the acute RfD of 0.05 mg/kg bw was revised to 0.9 mg/kg bw (JMPR 2003).

USEPA (1996) refers to and discusses benzoic acid (3,5-dimethyl-1-(1,1-dimethylethyl)-2-(4-ethylbenzoyl) hydrazide) without using the word tebufenozide. Tebufenozide is used in USEPA (1999, 2000). The reference dose (RfD), for chronic toxicity as defined in a one-year chronic dog study is 0.018 mg/kg/day based upon a NOEL of 1.8 mg/kg/day in male dogs and applying an uncertainty factor of 100. The agency did not identify an acute dietary toxicological endpoint, therefore, the risk from this route of exposure is negligible. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.018 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tebufenozide is 0.126 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 1.8 mg/kg bw.

EFSA (2014) quotes an ADI of 0.02 mg/kg/d; no ARfD was deemed necessary.

Tebufenozide was not carcinogenic in mice or rats under the conditions of the studies. Tebufenozide and its metabolites have been adequately tested for genotoxicity in a range of assays both in vitro and in vivo. The FAO/WHO meeting concluded that neither tebufenozide nor its metabolites were genotoxic.

As at June 2008 the USEPA classified tebufenozide in Group E: having evidence of non-carcinogenicity for humans. In studies evaluated previously by the JMPR meeting, it had been concluded that tebufenozide and its metabolites are not genotoxic. It was also concluded that tebufenozide is not embryotoxic or fetotoxic, or teratogenic in rats or rabbits at doses of up to 1,000 mg/kg bw per day.

### Derivation of Maximum Acceptable Value

No MAV.

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# Tebuthiuron

CAS No. 34014-18-1. The IUPAC name for tebuthiuron is 1-(5-tert-butyl-1,3,4-thiadiazol-2-yl)-1,3-dimethylurea. The CAS name is N-[5-(1,1-dimethylethyl)-1,3,4-thiadiazol-2-yl]-N,N′-dimethylurea.

### Maximum Acceptable Value

Tebuthiuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.5 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

### Sources to water

Tebuthiuron is a broad spectrum, non-selective, systemic thiadiazolylurea or urea herbicide.

Tebuthiuron does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 2 (Pesticides that are manufactured for export) of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Pesticides) Transfer Notice 2006 (with amendments), as at 24 June 2008, see: (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Pesticides).

### Forms and fate in the environment

Tebuthiuron has all the characteristics of a material with a high potential for groundwater contamination. It is highly soluble in water, adsorbs only weakly to soil particles and is highly persistent in soils (soil half-life = 360 days). Tebuthiuron is easily moved with moisture in the soil. In areas receiving 40 to 60 inches of annual rainfall, the time that it takes for half of the tebuthiuron to break down in soil is 12 to 15 months; it takes longer for the herbicide to break down in areas that have less rainfall. No degradation was observed in a 33-day study of photolysis of tebuthiuron in water. The USEPA considers tebuthiuron to be one of a group of pesticide compounds that have the greatest potential for leaching into, and contaminating, groundwater. However, it was not found in groundwater in a US groundwater survey conducted by the USEPA (EXTOXNET 1993).

Up to 42 percent of the herbicide applied was still present after 11 years on lands where the mean annual rainfall is low (<430 mm). Nine years after application, up to 73 percent was found at depths of 60 to 90 cm (CEQG 1999).

Water solubility is about 2,000 mg/L.

NPIC (1994) quotes for tebuthiuron a soil half-life of 360 days, water solubility of 2,500 mg/L and a sorption coefficient (soil Koc) of 80. This resulted in a pesticide movement to groundwater rating of very high.

USGS (2006) give the following values: log Kow = 1.79; log Koc (where Koc is in mL/g) = 2.1; water solubility = 2,400 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = -4.88; half-life in aerobic soil = 1,050 days; half-life in water = >2,700 days.

### Typical concentrations in drinking-water

Four water utilities in the US reported detecting tebuthiuron in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.076 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

EXTOXNET (1993) quotes an ADI of 0.20 mg/kg based on a two-year rat feeding study (NOEL of 20 mg/kg/day) and using 100-fold safety factor. USEPA (1992) and EXTOXNET (1996) quote an oral reference dose (RfD) of 0.07 mg/kg/d.

The Acceptable Daily Intake (ADI) adopted for tebuthiuron in Australia is 0.07 mg/kg body weight, with a NOEL of 7 mg/kg bw.

The USEPA established a Lifetime Health Advisory (LHA) level of 0.5 mg/L for tebuthiuron in drinking water, meaning that water containing tebuthiuron at or below this level is acceptable for drinking every day over the course of one’s lifetime, without posing any health concerns (EXTOXNET 1993).

The reference dose or RfD for tebuthiuron (USEPA 2006/2009/2011) is 0.07 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 2 mg/L.

It is unlikely that tebuthiuron causes reproductive effects or birth defects, and does not appear to be mutagenic or carcinogenic (Group D human carcinogen) (EXTOXNET 1996).

### Derivation of Maximum Acceptable Value

No MAV.

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# Temephos

CAS No. 3383-96-8. The IUPAC name for temephos is O,O,O’O’-tetramethyl O,O’‑thiodi-p-phenylene bis(phosphorothioate), or O,O,O′,O′-tetramethyl O,O′-thiodi-p-phenylene diphosphorothioate. The CAS name is O,O′-(thiodi-4,1-phenylene) bis(O,O-dimethyl phosphorothioate). Sometimes called temefos, or in the early days of its use: difenphos.

### Maximum Acceptable Value

WHO (2011 and 2017) state that it is not considered appropriate to set guideline values for pesticides used for vector control in drinking-water.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; excursions above this level even for a short period are of concern, because the health-based guideline is based on short-term effects.

### Sources to water

Temephos is a non-systemic organophosphorus insecticide, mainly used as a larvicide to control mosquito, midge, black fly and other insects in public health applications, and to control fleas on dogs and cats. It is sometimes mixed with other insecticides for broader spectrum control. It is also used for mosquito control in potable water. It is specified for use as a vector control agent in drinking-water sources by WHO under WHOPES. The recommendation for the use of temephos in potable water is that the dosage should not exceed 1 mg/L (WHO 2017).

The main formulation types available are GR and EC – common names are Abate and Abathion. Temephos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. The temephos-oxon content shall not exceed 3 g/kg. The iso-temephos content shall not exceed 13 g/kg.

### Forms and fate in the environment

Temephos has no acidic or basic characteristics; it is stable to hydrolysis (half-life >30 days at pH 4 to 9 at 25ºC), and photolysis occurs only slowly (half-life 15 days, continuous irradiation with artificial sunlight).

Weekly application of temephos at twice the normal application rates on pond water resulted in the rapid disappearance of the compound from the water and from the sediments. At even higher application rates to pond water there were still only traces of the compound detected one week after application (EXTOXNET 1996).

It is not very soluble: solubility only 0.03 to 0.04 mg/L at 25°C in distilled water. The major transformation products of temephos are temephos sulfoxide and temephos sulfone, which are more water soluble (WHO 2009). The octanol/water partition coefficient is Log Pow = 4.41 at 25°C ± 1°C, pH not stated (WHO 2011a).

NPIC (1994) quotes for temephos a soil half-life of 30 days, water solubility of 0.001 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

For the purposes of vector control, temephos is used at a concentration of up to 1 mg/L in drinking-water (JMPR 2006, WHO 2011).

### Removal methods

The low aqueous solubility and high octanol-water partition coefficient (0.03 mg/L and 4.9, respectively; WHO 2005) suggest that temephos should be removed by adsorption on to activated carbon and possibly removed during coagulation. Some newer advanced oxidation processes may also be effective.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

### Health considerations

Two impurities, O-{4-[(4-{[methoxy(methylthio)phosphoryl]oxy}phenyl)thio]phenyl}O,O-dimethylthiophosphate (CL78791, for ease of reference here termed “iso-temephos”) and 4‑({4‑[(dimethoxyphosphorothioyl)oxy]phenyl} thio)phenyl dimethyl phosphate (CL52828, for ease of reference here termed “temephos oxon”) qualified for designation as relevant impurities. No data were available on the toxicity of these impurities but, by inference from the data of Gallo and Lawryk (1991), they were considered likely to be appreciably more acutely toxic than temephos itself.

USEPA (2001) quotes a NOAEL of 0.3 mg/kg/day for the short-term, intermediate-term, and long-term or chronic occupational risk assessments. This endpoint is based on inhibition of cholinesterase in the red blood cells of rats of both sexes at 0.9 mg/kg/day (LOAEL) in a 90-day feeding study. The toxic effect was observed within one week after initiation of treatment, and thus is considered to be appropriate for a short-term (1–7 day) assessment. Use of this same endpoint for the chronic assessment is supported by similar doses and endpoints seen in another subchronic toxicity study in rats, as well as a chronic study in dogs where red blood cell and plasma cholinesterase inhibition occurred from one week onward.

WHO (2017) quotes a NOAEL of 2.3 mg/kg bw per day. Temephos is recommended by WHO for addition to potable water as larvicide treatment at an application rate not exceeding 1 mg/L. Assuming that an adult weighing 60 kg would consume two litres per day of drinking-water containing temephos at 1 mg/L, this would be equal to an oral exposure of 0.033 mg/kg bw. However, given the limited solubility of temephos in water, incomplete dissolution in drinking-water would be expected and this could result in actual exposures being appreciably less than this estimate. Consequently, 0.033 mg/kg bw per day was regarded as a worst-case upper limit of exposure (JMPR 2006). The meeting considered that the database was insufficiently robust to serve as the basis for establishing an ADI or an ARfD for temephos. The meeting concluded that the relevant NOAEL for human risk assessment is 2.3 mg/kg bw per day on the basis of inhibition of brain acetylcholinesterase activity in rats. This NOAEL provides a margin of exposure (MoE) from the estimated oral exposure derived from drinking-water treated with temephos of about 70. Consideration should be given to using alternative sources of water for small children and bottle-fed infants for a period after an application of temephos, where this is practical.

No clinical symptoms attributable to temephos were observed among members of a village in which water storage containers were treated monthly with 1 percent temephos granules over a 19-month period. Monthly treatment in this fashion should maintain a level of 0.5 mg/L temephos in the water.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.1 mg/kg body weight, with a NOEL of 1 mg/kg bw from a four-week dietary study in humans. This NOEL is based on serum cholinesterase inhibition. The ADI incorporates a safety factor of 10.

As at May 2002 the USEPA concluded that there was no evidence of carcinogenicity with temephos and that temephos formulations should be classified as slightly toxic end use products (EPA toxicity class III).

### Derivation of Maximum Acceptable Value

No MAV.

Temephos is specified for use as a vector control agent in drinking-water sources by WHO under the WHO Pesticides Evaluation Scheme. Formulations for control of vectors are specified by WHO (2005, 2006). The recommendation for the use of temephos in potable water is that the dosage should not exceed 1 mg/L.

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# Tepraloxydim

CAS No. 149979-41-9. The IUPAC name for tepraloxydim is (5RS)-2-{(EZ)-1-[(2E)-3-chloroallyloxyimino]propyl}-3-hydroxy-5-perhydropyran-4-ylcyclohex-2-en-1-one. The CAS name is 2-[1-[[[(2E)-3-chloro-2-propenyl]oxy]imino]propyl]-3-hydroxy-5-(tetrahydro-2H-pyran-4-yl)-2-cyclohexen-1-one. A commercial product used in New Zealand is called Aramo.

### Maximum Acceptable Value

Tepraloxydim is included in the [plan of work of the rolling revision](http://www.who.int/entity/water_sanitation_health/gdwqrevision/en/index.html) of the WHO *Guidelines for Drinking-water Quality*. It is not mentioned in their 2011 Guidelines.

### Sources to water

Tepraloxydim is a cyclohexene oxime or cyclohexadione-oxime post-emergence broad spectrum herbicide, used to control grasses around onions and other crops (it is an acetyl coA carboxylase inhibitor).

Tepraloxydim appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2010 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The expiry date of the EU approval for the graminicide, tepraloxydim, is to be restored to its original date of 31 May 2015, following the decision of the applicant BASF not to further pursue its renewal.

### Forms and fate in the environment

The half-life of tepraloxydim in aerobic soils has been reported between 10 and 80 days (IUPAC 2010). The aerobic soil biodegradation of tepraloxydim was fairly rapid with half-lifes of 4.6 to 10.1 days. In a sterile aerobic soil, the half-life was estimated at 167 days. When incubated in an anaerobic soil, the DT50 and DT90 values for both isomers of tepraloxydim were 41 and 135 days, respectively.

In two natural pond water/sediment systems, tepraloxydim biodegraded with DT50 and DT90 values of 49 to 171 and ≥162 days, respectively, in the whole system and 41 to 129 and ≥136 days in the aerobic surface water only (APVMA 2003).

Tepraloxydim was stable to hydrolysis at pH 7 to 8.8, but degraded at pH 4 with a half-life of 6.6 days at 22°C with the oxazole DP-2 and DP-8 as the major degradates. The compound is also expected to be stable at pH >8.8. Photodegradation in water was relatively rapid with half-lifes of 0.72, 1.5 and 1.6 days at pH 5, 7 and 9, respectively (APVMA 2003).

See EFSA (2011) for a list of metabolites.

Solubility in distilled water is about 430 mg/L; water solubility at pH 4 is also about 430 mg/L, and 7,250 mg/L at pH 9 (EC 2004). Adsorption/desorption studies on nine soils indicated high to very high mobility in soil for parent tepraloxydim and generally high mobility for the metabolites DP-1 and DP-2 in six soils, with some exceptions. This indicates the possibility of leaching to groundwater (APVMA 2003).

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

#### Some alternative methods

See APVMA (2003).

### Health considerations

APVMA (2003) quotes an ADI for tepraloxydim of 0.05 mg/kg/day based on a NOAEL of 5 mg/kg/day in two-year rat dietary studies and using a 100-fold safety factor in recognition of the extensive toxicological database available for tepraloxydim In February 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

EC (2004) established an ADI of 0.025 mg/kg/d and an ARfD of 0.4 mg/kg/d.

NZFSA proposes a maximum residue limit for tepraloxydim of 0.1 mg/kg in onions (see: <http://www.nzfsa.govt.nz/consultation/mrl-2009-amdt-1/discussion-doc/page-14.htm>).

The acceptable daily intake (ADI) is 0.025 mg/kg/d and the acute reference dose (ARfD) is 0.4 mg/kg/d (IUPAC 2010). These values were reaffirmed by EFSA (2011/2014).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.50 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tepraloxydim is 50 mg/L.

The USEPA (2007) considers data are inadequate for an assessment of human carcinogenic potential because there was some evidence of liver tumours in female rats at the high dose in the carcinogenicity phase of the study, but not in the chronic phase of the study. Female mice developed liver tumours at an excessively toxic dose. Male mice had non-neoplastic liver changes similar to or exceeding those seen in female mice at the same dose, though there was no increase in liver tumour incidences. Tepraloxydim was not mutagenic in a battery of assays. Considering all of this evidence, tepraloxydim is not expected to pose a cancer risk for humans, and a quantitative cancer risk assessment was not conducted.

### Derivation of Maximum Acceptable Value

No MAV.

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# Terbacil

CAS No. 5902-51-2. IUPAC name for terbacil is 3-tert-butyl-5-chloro-6-methyluracil. The CAS name is 5-chloro-3-(1,1-dimethylethyl)-6-methyl-2,4(1H,3H)-pyrimidinedione.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of terbacil in drinking-water should not exceed 0.04 mg/L.

The WHO Guidelines (2004 and 2011) do not mention terbacil.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.09 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.2 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Terbacil is a selective uracil herbicide usually used for control of both annual weeds and perennial grasses. It is sprayed on soil surfaces preferably just before, or otherwise during, the period of active weed growth. Terbacil works in plants by interfering with photosynthesis. It is part of a family of chemicals called substituted uracils.

Terbacil appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

In most soil types, terbacil has a relatively low tendency to be adsorbed to soil particles (Koc = 55 g/mL). It is highly soluble in water and highly persistent in soils. Soil half-lifes of 120 days or two to five months have been reported. This information indicates that terbacil is likely to be moderately mobile in soil and potentially can pollute groundwater so should not be used on sandy or gravelly soils. In moist soils, terbacil is subject to microbial degradation.

Contamination of surface waters near terbacil-treated areas, and subsequent exposure of humans and non-target organisms, is possible due to terbacil’s mobility in soil and its high water solubility. Terbacil is stable in water and does not readily undergo hydrolysis or photodegradation. The water solubility of terbacil is 710 mg/L and the log Kow is 1.89 (TOXNET). Thus, terbacil is likely to be highly mobile in soil and potentially pollute groundwater. Because of this, it should not be used on sandy or gravelly soils that have less than 1 percent organic matter, particularly if the water table is near the soil surface.

NPIC (1994) quotes for terbacil a soil half-life of 120 days, water solubility of 710 mg/L and a sorption coefficient (soil Koc) of 55 (log Koc = 9.0; USEPA 2008). This resulted in a pesticide movement to groundwater rating of very high. Its GUS score is 5.06, indicating that it will leach to groundwater.

See USEPA (1998) for discussion on metabolites.

### Typical concentrations in drinking-water

Terbacil has been found 4 times in Waikato groundwaters, ranging from 0.00008 to 0.006 mg/L (MAF 2006).

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Terbacil occurred at 4.0 µg/L, ie, 0.004 mg/L.

Terbacil was found in two bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.00054 to 0.0025 mg/L. The bores were in the Waikato region.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Terbacil was found in two wells, from 0.048 to 0.051 µg/L, ie, up to 0.000051 mg/L.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Terbacil was found in one sample, at 0.84 µg/L, ie, 0.00084 mg/L.

### Removal methods

No information available. The weak soil adsorption and high water solubility suggest that treatment processes that remove particulate matter will be ineffective at reducing the concentration of terbacil in water. However, some newer advanced oxidation processes are expected to be effective.

### Analytical methods

### Health considerations

Terbacil has low acute toxicity in humans and other animals. In general, the uracil herbicides are rapidly excreted in urine by mammals. This may account for their reportedly low toxicity. The oral LD50 of terbacil for rats is 5,000 to 7,500 mg/kg. Signs of acute terbacil poisoning in rats include weight loss, paleness, lack of movement and rapid respiration. Six out of six male rats survived ten daily doses of 1,000 mg/kg. No evidence of toxicity was seen in two-year feeding studies of rats fed doses as high as 12.5 mg/kg or in dogs fed doses as high as 6.25 mg/kg of terbacil. At 125 to 500 mg/kg there was a lower rate of weight gain, liver enlargement and other liver changes in rats. The high dose produced a slight increase in liver weight in dogs.

Terbacil is a USEPA General Use Pesticide, in class IV – practically nontoxic. The USEPA has established a Lifetime Health Advisory (LHA) level of 90 micrograms per litre (0.09 mg/L) for terbacil in drinking-water. This means that EPA believes that water containing terbacil at or below this level is acceptable for drinking every day over the course of one’s lifetime, and does not pose any health concerns.

USEPA (2005) states that the reference dose (RfD) for systemic toxicity was determined for terbacil as 0.013 mg/kg/day, by the USEPA’s RfD committee in 1986. The RfD was calculated from a two-year feeding study in dogs in which the NOAEL was 1.25 mg/kg/day (based on increased relative liver weights and increased serum alkaline phosphatase, seen at 7.25 mg/kg/day), and an uncertainty factor of 100. The RfD of 0.013 mg/kg/day was reaffirmed by the USEPA’s RfD Committee on 1 September 1994. The parent molecule is the only moiety of toxicological significance appropriate for regulation in plant and animal commodities. For acute drinking water risk, the Drinking Water Levels of Concern (DWLOCs) were calculated using an aRfD (acute) endpoint of 0.125 mg/kg and compared to surface water or ground water EEC (estimated environmental concentration) values of 0.154 mg/L and 0.125 mg/L, respectively. The acute DWLOC for the most sensitive group (infants and children) is 1.1 mg/L; the chronic DWLOC is 0.1 mg/L, again DWLOC for the most sensitive group (infants and children). In assessing the potential risk from cumulative effects of terbacil and other chemical substances, the USEPA considered structural similarities that exist between terbacil and other substituted uracil compounds such as bromacil; a comparison of the available toxicological database for terbacil and bromacil revealed no clear common mode of toxicity for these chemicals.

The reference dose or RfD (USEPA 2006/2009/2011) is 0.01 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.4 mg/L; this was based on increased liver weights and serum alkaline phosphatase in dogs at the next highest dose level, and an uncertainty factor of 100.

The Health Reference Level for terbacil is 0.09 mg/L based on the RfD of 0.013 mg/kg/d, a 70 kg person drinking 2 L/d, and water being 20 percent of the intake (USEPA 2008). This value is derived much the way we derive our MAVs.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.06 mg/kg body weight, with a NOEL of 6.25 mg/kg bw from a long-term (two-year) dietary study in dogs. The NOEL is based on increased relative liver weight and elevated serum alkaline phosphatase at the highest dose tested of 60 mg/kg bw/day. The ADI incorporates a safety factor of 100.

Terbacil is not mutagenic and has given no evidence of carcinogenicity. As at September 2008 the USEPA has classified terbacil in Group E: evidence of non-carcinogenicity for humans. This chemical appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

The provisional MAV for terbacil in drinking-water was derived by the MoH as follows:

1.25 mg/kg body weight per day x 70 kg x 0.1 = 0.044 mg/L (rounded to 0.04 mg/L)

2 L x 100

where:

* no observable adverse effect level = 1.25 mg/kg-day based on the absence of increase in thyroid/body weight ratio, a slight increase in liver weights, and an elevated alkaline phosphatase level, in a two-year dog feeding study
* average weight of an adult = 70 kg
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult per day = 2 L
* uncertainty factor = 100.

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# Terbufos

CAS No. 13071-79-9. The IUPAC name for terbufos is S-tert-butylthiomethyl O,O‑diethyl phosphorodithioate. It can also be called S‑[[(1,1‑dimethylethyl)thio]methyl] O,O-diethyl phosphorodithioate.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for terbufos; the WHO Guidelines do not refer to terbufos.

The maximum acceptable concentration for terbufos in drinking-water in Canada is 0.001 mg/L, based on analytical achievability.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.0009 mg/L.

The USEPA concluded on 22 September 2009 that terbufos is known or anticipated to occur in PWSs and may require regulation. Therefore they added terbufos to their CCL 3 (Drinking Water Contaminant Candidate List 3). They added the degradation product terbufos sulfone (CAS No. 56070-16-7) to the list as well (USEPA 2009a).

The USEPA (2006a/2009/2011) established a lifetime health advisory of 0.0004 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

### Sources to water

Terbufos is a systemic organophosphate insecticide and nematicide, often used on grain crops.

Terbufos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). After 1 July 2023 terbufos will no longer able to be manufactured in or imported into New Zealand.

This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

Terbufos was not detected in Canadian surface water samples from either the Grand or the Thames river basins, which are located in areas heavily used for agriculture (detection limit <0.0001 mg/L).

### Forms and fate in the environment

Terbufos is moderately persistent in the soil. Terbufos metabolites have similar or lower toxicity than the parent compound. Terbufos and its metabolites quickly degrade during the first 15–30 days after application, then gradually stabilise. Terbufos is generally immobile and is therefore unlikely to leach or contaminate groundwater. See JMPR (2005) for discussion on metabolites.

JMPR (2005) states that under conditions favourable to microbial growth, the linear metabolic half-life in aerobic soil is approximately 27 days (5.6 days for non-linear) and in anaerobic soil is 67 days (21 days for non-linear). Under abiotic conditions, the hydrolysis half-life is 12.3–13.7 days in the typical range of environmental pH values (pHs 5, 7, and 9). The important metabolites terbufos sulfoxide and terbufos sulfone are more mobile and persistent than parent terbufos. The sulfoxide and sulfone half-lifes are 116 and 96 days, respectively. These metabolites are also mobile in all tested soils and may reach groundwater when terbufos is used in a location where irrigation or rain water moves through the soil profile to groundwater. In addition, terbufos and its metabolites may enter surface water as a result of run-off events. Volatilisation may be a major dissipation route for the portion of parent terbufos that remains on the surface of soil after incorporation.

The solubility of terbufos in water is about 5.5 mg/L in buffers ranging from pH 4 to 9 at 25°C. Water solubilities of the two major soil/water degradates at 25°C are 3,214 mg/L and 407 mg/L for terbufos sulfoxide and terbufos sulfone, respectively.

In water, terbufos hydrolyses rapidly. At a concentration of 4.6 mg/L, its hydrolysis half-lifes were 4.5, 5.5 and 8.5 days at pH 5, 7, and 9 respectively. In another study, terbufos hydrolysed with a half-life of 2.2 weeks at pH 5, 7 and 9. Formaldehyde was the major degradate detected.

Health Canada (1987, edited 1995) states that the vapour pressure of terbufos is 34.6 mPa at 25ºC, and its water solubility is 10–15 mg/L at 25ºC. Terbufos is hydrolysed under alkaline conditions in soil or water. Terbufos has some residual action in soil. It was not considered in either the Canadian or US ranking schemes for pesticides deemed to have the potential to leach from soil to water.

NPIC (1994) quotes for terbufos a soil half-life of five days, water solubility of 5 mg/L and a sorption coefficient (soil Koc) of 500. This resulted in a pesticide movement to groundwater rating of very low.

USGS (2006) give the following values: log Kow = 4.48; log Koc (where Koc is in mL/g) = 2.70; water solubility = 5 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 0.39; half-life in aerobic soil = 5 days; half-life in water = 1.9 days.

### Typical concentrations in drinking-water

In a 1986 study of municipal water in Manitoba, terbufos was not detected in 49 samples (detection limit 0.0002 mg/L), and was not detected in surface water samples from either the Grand or the Thames river basins, which are located in areas heavily used for agriculture (Health Canada 1987, edited 1995).

### Removal methods

No information available. The fairly strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of terbufos in water, however, some of the degradation products may not be removed.

### Recommended analytical techniques

#### Referee method

No MAV so not needed.

#### Some alternative methods

See JMPR (2005).

### Health considerations

When rats were fed approximately 0, 0.01, 0.02, 0.046 or 0.09 mg/kg/day for 90 days, the NOAEL was 0.02 mg/kg/day; similar results were obtained in a one-year study with rats (EXTOXNET 1996). A no-observed-adverse-effect level (NOAEL) of 0.0025 mg/kg bw for cholinesterase inhibition was observed in a 28-day dog study (Health Canada 1987, edited 1995).

The USEPA established a Lifetime Health Advisory (LHA) of 0.001 mg/L of terbufos in drinking-water. This means that the USEPA believes that water containing terbufos at or below this concentration is acceptable for drinking every day over the course of one’s lifetime, and does not pose any health concerns. Consumption of terbufos at high levels well above the LHA level over a long period of time has caused damage to the eye and stomach, disturbances in foetal development and cholinesterase inhibition in animals.

The JMPR toxicological review was conducted in 2003, which established an ADI of 0.0006 mg/kg bw/day and an acute RfD of 0.002 mg/kg bw/day.

The Acceptable Daily Intake (ADI) adopted in Australia and New Zealand for terbufos is 0.0002 mg/kg body weight, with a NOEL of 0.0025 mg/kg bw from a short-term (six-month dietary) study. The NOEL is based on decreased serum cholinesterase activity in dogs. The ADI incorporates a safety factor of 10.

The reference dose or RfD (USEPA 2006a/2009/2011) is 0.00005 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006a/2009/2011) is 0.002 mg/L. USEPA (2006) quotes a chronic PAD for terbufos of 0.00005 mg/kg/day (0.005 mg/kg/day ÷ 100) based on plasma ChE observed in a 28-day oral toxicity study in dogs (NOAEL = 0.005 mg/kg/day) and a one-year oral toxicity study in dogs.

As at September 2008 the USEPA has classified terbufos in Group E: evidence of non-carcinogenicity for humans.

### Derivation of Maximum Acceptable Value

No MAV.

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# Terbumeton

CAS No. 33693-04-8. The IUPAC name for terbumeton is N2-tert-butyl-N4-ethyl-6-methoxy-1,3,5-triazine-2,4-diamine. The CAS name is N-(1,1-dimethylethyl)-N′-ethyl-6-methoxy-1,3,5-triazine-2,4-diamine. Also called 2-amino-4-tert-butylamino-ethyl-6-methoxy-1,3,5-triazine-2,4-diamine, terbutone and terbuthylon.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for terbumeton; WHO does not refer to terbumeton in their Guidelines.

### Sources to water

Terbumeton, a methoxytriazine selective herbicide (triazine) commonly used to control annual and perennial grasses and broad-leaved weeds; often used with terbuthylazine in New Zealand, and with atrazine in parts of Europe. It has been banned in France since 1998; it had been used in vineyards and been found in groundwater up to 0.00007 mg/L.

Terbumeton does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals (or pesticides)).

### Forms and fate in the environment

The half-life in organic-rich soil is about 300 days, ie, persistent, but moderately mobile in the absence of organic matter. The major metabolites are terbumeton-desethyl, terbumeton-2-hydroxy and terbumeton-deisopropyl.

Water solubility is about 130 mg/L.

### Removal methods

No information available.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See Conrad et al (2007).

### Health considerations

Terbumeton was positive for mammary gland tumours, it is not marketed in the United States. Following oral administration, terbumeton is rapidly absorbed; more than 95 percent is eliminated within 96 hours, predominantly in the urine, with about 25 percent in the faeces (Crop Protection Compendium).

The acceptable daily intake (ADI) is stated in Sitem to be 0.075 mg/kg/d.

### Derivation of Maximum Acceptable Value

No MAV.

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# Terbuthylazine

CAS No. 5915-41-3. The IUPAC name for terbuthylazine is N2-tert-butyl-6-chloro-N4-ethyl-1,3,5-triazine-2,4-diamine. The CAS name is 6-chloro-N-(1,1-dimethylethyl)-N’-ethyl-1,3,5-triazine-2,4-diamine. Also called TBA. May be misspelt as terbutylazine.

### Maximum Acceptable Value

Based on health considerations, the concentration of terbuthylazine in drinking-water should not exceed 0.008 mg/L.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.01 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Terbuthylazine, a herbicide that belongs to the chlorotriazine family, may enter source waters as a result of its application as a pre- or post-emergence selective herbicide for the control of grass and broadleaf weeds in forestry, maize, sweetcorn, peas, certain orchard crops, and long-term non-selective weed control in non-crop situations. The herbicidal effects take about three weeks to appear. Terbuthylazine was introduced as an atrazine substitute due to the latter’s persistence.

Propazine and simazine are relevant impurities in terbuthylazine technical material of Syngenta origin with maximum limits of 10 g/kg and 30 g/kg respectively, while atrazine and simazine are relevant impurities in technical material of Oxon origin with maximum limits of 1 g/kg and 5 g/kg respectively (EFSA 2011).

Terbuthylazine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The total annual usage of terbuthylazine in New Zealand in the late 1980s was 39,000 kg. ERMA notes that 223.8 tonnes of terbuthylazine were used in New Zealand in 2004, at an application rate of 10,000 grams of active ingredient per hectare.

### Forms and fate in the environment

If released to soil, terbuthylazine is expected to have only slight mobility based on field observations. Although Koc values of 151 to 514 suggest moderate to low mobility, terbuthylazine interacts in soil to form strongly bound residues. Volatilisation from moist soil surfaces is not expected to be an important fate process based on an estimated Henry’s Law constant of 1.64 x 10-6 Pa.m3/mole at 25°C and results of soil volatilisation tests. Some sensitised photodegradation may occur on soil surfaces exposed to sunlight. Its GUS score is 2.95, indicating intermediate leaching potential to groundwater.

In soil, microbial degradation occurs via dealkylation of the side chain, hydroxylation resulting from hydrolysis of the chlorine atoms and of the dealkylated amino group, and ring cleavage.

If released to water, terbuthylazine is expected to adsorb to suspended solids and sediment based on its Koc. There are sufficient data (USEPA 1995) to conclude that terbuthylazine degrades very slowly under aerobic aquatic conditions. Terbuthylazine degraded slowly with registrant calculated half-life of 38.8 days in flooded loam sediment that was incubated aerobically in darkness for 30 days at 25°C. The degradate 2-tert-butylamino-4-chloro-6-amino-5-triazine persisted after 22 days.

James et al (1998) found terbuthylazine residues were reduced within six months to  
1–5 percent of that applied with half-lives of 23 and 37 days in a sandy and clay soil respectively. No residues were detected below 10 cm. Soil water content had very little effect. Under normal conditions of use, terbuthylazine residues should not carry over to the next growing season and are unlikely to contaminate groundwater. FAR (2007) stated that the rate of degradation of terbuthylazine in soil has been found to be influenced by temperature. Residual life of the chemical has been found to increase in low temperatures and one such study shows residual life could be as much as five times longer when two temperature (10°C and 30°C) were compared.

In soil laboratory incubations under aerobic conditions in the dark, terbuthylazine exhibits medium to high persistence forming the major metabolites desethylterbuthylazine and hydroxy-terbuthylazine. The persistence of these two metabolites ranged from moderate to high for desethyl-terbuthylazine and high to very high for hydroxy-terbuthylazine. For terbuthylazine the potential for groundwater exposure from the representative uses above the parametric drinking water limit of 0.1 μg/L was concluded to be low. The potential for groundwater exposure by the metabolites desethyl-terbuthylazine, hydroxy-terbuthylazine and desethyl-hydroxyterbuthylazine was however concluded to be high over a wide range of geoclimatic conditions (EFSA 2011).

Water solubility is about 7–12 mg/L.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, found terbuthylazine in two zones at concentrations of 0.0002 to 0.002 mg/L (25 percent of the MAV), with the median concentration being “nd” (limit of detection = 0.0002 mg/L). The P2 programme in 2001 found a sample with terbuthylazine at 2.5 percent of its MAV (ESR 2001).

Terbuthylazine has been found 71 times in groundwaters throughout New Zealand, ranging from 0.00001 to 0.002 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Terbuthylazine occurred at 0.05 to 0.3 µg/L, ie, up to 0.0003 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Terbuthylazine occurred at 0.01 to 3.5 µg/L, ie, up to 0.0035 mg/L.

In their fourth Pesticides in Groundwater Survey, ESR detected pesticides in 28 of the 133 wells tested; 13 wells had more than one pesticide. No pesticides were found above their MAV. Nineteen pesticides and two triazine metabolites were detected; 67 percent of the detections were of pesticides in the triazine group (Close and Flintoft 2004). Terbuthylazine occurred at 0.01 to 2.0 µg/L, ie, up to 0.002 mg/L.

Terbuthylazine was found in eight bores during the fifth national survey of pesticides in groundwater in New Zealand (Gaw et al 2008); the concentration range was 0.000011 to 0.00042 mg/L. The bores were in the Manawatu, Wellington, Marlborough, Canterbury, Otago and Southland regions.

In their sixth Pesticides in Groundwater Survey (in 2010), ESR sampled 162 wells, detecting 22 pesticides and metabolites. They were found in 38 wells, of which 15 had more than one pesticide. All pesticide detections were from unconfined aquifers (23 wells) or from aquifers with unknown status (15 wells). No pesticides were detected in wells from semi-confined or confined aquifers. Again, mean nitrate concentrations were significantly higher for wells with pesticide detections than for wells without pesticide detections. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Skinner 2012). Terbuthylazine was detected in 17 wells from six regions, ranging from 0.014 to 5.8 mg/m3 (µg/L), which was 73 percent of the MAV.

In their seventh Pesticides in Groundwater Survey, ESR tested for 80 pesticides in 165 wells, detecting 21 pesticides and metabolites. They were found in 28 wells, of which 10 had more than one pesticide. One pesticide, diedrin, was found above its MAV. Sixty-one percent of the detections were of pesticides in the triazine group (Close and Humphries 2016). Terbuthylazine was found in 16 samples (10 percent of all wells sampled), from 0.012 to 1.39 µg/L, ie, up to 0.0014 mg/L.

Concentrations in water seldom exceed 0.0002 mg/L, although higher concentrations have been observed (WHO 2004).

### Removal methods

WHO (2011/2017) states that a concentration as low as 0.0001 mg/L of terbuthylazine should be achievable using GAC particularly following conventional coagulation/ filtration. Some newer advanced oxidation processes are likely to be effective too.

### Recommended analytical techniques

#### Referee method

No referee method has been given for terbuthylazine because no method meets the required criteria. See WHO (2003) for further information.

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with a Nitrogen Phosphorus Detector (Chlorophenoxy acidic herbicides, trichlorobenzoic acid, chlorophenols, triazines and glyphosate in water 1985) (HMSO 1986).

2. TBA is extracted from water by solid-liquid extraction on reversed phase-C18 material, eluted with a solvent and then separated, identified and quantified by high-performance liquid chromatography using ultraviolet detection at 220 nm. The limit of detection is about 0.0001 mg/L (ISO 1997).

3. See EFSA (2011).

### Health considerations

In long-term dietary studies in rats, effects on red blood cell parameters in females, an increased incidence of non-neoplastic lesions in the liver, lung, thyroid and testis and a slight decrease in body weight gain, were observed.

USEPA (1995) quoted a RfD of 0.00035 mg/kg/day for terbuthylazine. This was based on an NOEL of 0.35 mg/kg/day from the chronic toxicity study in rats, where effects on body weight and food consumption were observed in males and females at 1.6 mg/kg/day. An uncertainty factor of 100 was used to account for inter- and intra-species variability, with an additional factor of 10 to compensate for lack of non-rodent chronic toxicity data and reproductive toxicity data.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.003 mg/kg body weight, with a NOEL of 0.35 mg/kg bw from a 24-month dietary study in rats showing a decrease in bodyweight gain and food consumption. The ADI incorporates a safety factor of 100. An ARfD is not necessary.

EC (in <http://ec.europa.eu/sanco_pesticides/public/index.cfm>) reports an ADI of 0.004 mg/kg/d and an ARfD of 0.008 mg/kg/d, quoting an EFSA source. These values are confirmed in EFSA (2011).

As at September 2008 the USEPA has classified terbuthylazine in Group D: not classifiable as to human carcinogenicity.

There is no evidence that terbuthylazine is carcinogenic or mutagenic. In long-term dietary studies in rats, effects on red blood cell parameters in females, an increased incidence of non-neoplastic lesions in the liver, lung, thyroid and testis and a slight decrease in body weight gain were observed (WHO 2017).

### Derivation of Maximum Acceptable Value

The MAV for terbuthylazine was calculated as follows:

0.22 mg/kg x 70 kg x 0.1 = 0.0077 mg/L (rounded to 0.008 mg/L)

2 L x 100

where:

* no observable adverse effect level = 0.22 mg/kg body weight for decreased body weight gain at the next higher dose in a two-year toxicity/carcinogenicity study in rats
* average weight of adult = 70 kg
* proportion of acceptable daily intake allocated to drinking-water = 0.1
* average quantity of water consumed by an adult = 2 L/day
* uncertainty factor = 100 (for inter- and intra-species variation).

In the 1995 DWSNZ, the MAV for terbuthylazine had been calculated by the MoH as follows:

0.003 mg/kg x 70 kg x 0.2 = 0.02 mg/L

2 L

where:

* average daily intake = 0.003 mg/kg body weight
* average weight of adult = 70 kg
* proportion of acceptable daily intake allocated to drinking-water = 0.2
* average quantity of water consumed by an adult = 2 L/day.

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# Terbutryn

CAS No. 886-50-0. The IUPAC name for terbutryn is N2-tert-butyl-N4-ethyl-6-methylthio-1,3,5-triazine-2,4-diamine. The CAS name is N-(1,1-dimethylethyl)-N′-ethyl-6-(methylthio)-1,3,5-triazine-2,4-diamine. Also called 2-(tert-butylamino)-4-(ethylamino)-6-(methylthio)-s-triazine. Sometimes called terbutryne.

### Maximum Acceptable Value

The DWSNZ do not include a MAV for terbutryn; the WHO Guidelines do not refer to terbutryn.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.4 mg/L; excursions above this level even for a short period are of concern, as the health-based guideline is based on short- to medium-term effects.

### Sources to water

Terbutryn is a selective triazine herbicide which acts as an inhibitor of photosynthesis, often used on grain crops. It is often sold mixed with other compounds. It is approved in the UK (MAFF 1985) for direct application to water for the control of many submerged weeds, algae and some floating weeds; the maximum concentration allowed in water is 0.1 mg/L. See also CEH (2004).

Terbutryn appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008. As at 2014 it is no longer registered in the EU under Annex I of 91/414/EEC, but it still has biocidal uses.

### Forms and fate in the environment

Terbutryn is readily adsorbed in soils with high organic or clay content, with a half-life of 14–28 days.

The solubility of terbutryn in water is about 25 mg/L at 25°C.

In water, terbutryn is not volatile. It will adsorb to sediment and suspended particulate matter. Half-lifes of 180–240 days have been reported for degradation of terbutryn in pond and river sediment. It may be subject to very slow hydrolysis and biodegradation in water.

NPIC (1994) quotes for terbutryn a soil half-life of 42 days, water solubility of 22 mg/L and a sorption coefficient (soil Koc) of 2,000. This resulted in a pesticide movement to groundwater rating of low.

If released to soil, terbutryne is expected to have moderate mobility to no mobility based upon Koc values of 366 to 41,757. Terbutryne volatilised <1 percent to 6 percent in two different soils at 15 and 25°C. Terbutryne may be susceptible to biodegradation based upon half-lifes of 2 and 11 weeks in unfumigated and fumigated soil, respectively. If released into water, terbutryne is expected to adsorb to suspended solids and sediment based upon the Koc values. Terbutryne had degradation half-lifes of 6.9 to 30 days under different conditions in pond and river waters. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant of 2.1 x 10-8 atm-cu m/mol. A BCF of 25 for catfish suggests that bioconcentration in aquatic organisms is low (EAWAG accessed February 2015).

### Removal methods

No information available. The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of terbutryn in water. Oxidation processes (including chlorine) will break down the terbutryn molecule, but use of activated carbon is advisable to remove the degradation products.

### Recommended analytical techniques

#### Referee method

No MAV so not needed..

### Health considerations

The ADI for terbutryn is 0.01 mg/kg (provisional), and the RfD is 0.001 mg/kg/d (EXTOXNET 1996, USEPA 1988)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 10 mg/kg bw from short-term dietary studies in rats (13-week) and dogs (six months). The NOEL is based on clinical signs of toxicity in a six-month dietary study in dogs, and evidence of liver and thyroid toxicity in a 16-week dietary study in rats. The ADI incorporates a safety factor of 100.

The USEPA has classified terbutryn as Toxicity Class III – slightly toxic. In a two-year feeding study of rats, doses of 150 mg/kg of terbutryn caused cancerous tumour growth. However, there is no evidence of carcinogenicity in mice. As at September 2008, terbutryn is classified by the USEPA in Class C: a possible human carcinogen. No mutagenic effects were observed.

### Derivation of Maximum Acceptable Value

No MAV.

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# Tetrachlorvinphos

CAS No. 961-11-5 for the mixed (Z)- + (E)-isomers, or 22248-79-9 for the Z-isomer, and 22350-76-1 for the analogous (E)-isomer. The IUPAC name for tetrachlorvinphos is (Z)-2-chloro-1-(2,4,5-trichlorophenyl)vinyl dimethyl phosphate. The CAS name is (1Z)‑2-chloro-1-(2,4,5-trichlorophenyl)ethenyl dimethyl phosphate. Has been called stirofos and CVMP, TCVP and dimethyl 2,4,5-trichloro-α-(chloromethylene)benzyl phosphate. The technical product typically contains 98 percent Z-stereoisomer and 2 percent E‑stereoisomer.

### Maximum Acceptable Value

Tetrachlorvinphos does not have a MAV in the DWSNZ, and it is not mentioned in the WHO Guidelines.

### Sources to water

Tetrachlorvinphos is a selective phenyl organophosphate acaricide and insecticide, used as an ectoparasiste on animals. It is registered in the US to control fleas, ticks, various flies, lice and pest larvae and is primarily applied to horses, poultry and household dogs/cats.

US cattle producers applied 2.16 million pounds of insecticides to beef and dairy cattle in 1999. Applications made to beef cattle accounted for 72 percent of the total while insecticide use on dairy cattle accounted for 28 percent. Xylene was the top active ingredient in total quantity used at 459,700 pounds followed by tetrachlorvinphos at 287,300 pounds and piperonyl butoxide at 154,300 pounds. These three active ingredients accounted for 42 percent of the US total. See <http://www.nass.usda.gov/Statistics_by_State/Montana/Publications/Press_Releases_Livestock/historic/livagchm.htm>

Tetrachlorvinphos appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

The half-life of tetrachlorvinphos in soil is about two days, so it is not particularly persistent, and will not be expected to be found in groundwater.

Tetrachlorvinphos is fairly stable in acidic and neutral water. Water solubility is about 12 mg/L. The major metabolite is 2,4,5-trichlorophenacyl chloride.

NPIC (1994) quotes for tetrachlorvinphos a soil half-life of two days, water solubility of 11 mg/L and a sorption coefficient (soil Koc) of 900. This resulted in a pesticide movement to groundwater rating of very low. IARC (2017) quotes vapour pressure (Z‑isomer) = 4.2 × 10−8 mm Hg (20°C) so not expected to volatilise from dry soil surfaces. Octanol/water partition coefficient (P): log P, 3.53. Henry’s Law: 1.8 × 10−9 atm m3 mol–1 at 25°C so not expected to volatilise from water.

### Typical concentrations in drinking-water

No drinking water exposure is anticipated from current uses in the US (USEPA 2006).

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

GC/MS methods can measure down to 11 ng/L (0.011 µg/L).

### Health considerations

The acute and chronic reference dose (RfD) was estimated to be 0.067 mg/kg/d body weight, where the RfD is an estimate of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime (USEPA 2006). The oral RfD had earlier been 0.03 mg/kg/d (USEPA 1992) based on reduced body weight gain, increased liver and kidney weights, and RBC ChE inhibition in a two-year dog feeding study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0423 mg/kg/d, and an ARfD of 0.067 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tetrachlorvinphos is 0.67 mg/L.

Subject to correct usage, the dietary risks from eating food items containing residues of tetrachlorvinphos are below the level of concern for the entire US population, including infants and children. Drinking water is not a significant source of exposure (USEPA 2002).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw.

As at September 2008 the USEPA has classified tetrachlorvinphos as likely to be carcinogenic to humans (earlier it had been in group C: a possible human carcinogen). Tetrachlorvinphos produced effects in three carcinogenicity studies involving rats and mice as test animals. Effects included increased incidences of adrenal cortical adenomas and thyroid C-cell adenomas, high incidences of thyroid C-cell hyperplasia, hepatocellular carcinoma, hepatocellular adenomas, and granulomatous lesions of the liver. The risk to humans by ingestion is considered slight in the US because no currently registered tetrachlorvinphos end-use product is labelled for use on any plant commodity (USEPA 1995). The highest health risk is to children who have direct contact with dosed pets.

Tetrachlorvinphos is on the EU endocrine disruptor list. USEPA (2015) concluded that based on the weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for TCVP since additional testing will not impact current EPA established regulatory point of departure or endpoint for human health risk assessments.

IARC (1983) stated that the available data provide no evidence that tetrachlorvinphos is likely to present a carcinogenic risk to humans, ie, Group 3. IARC (2017) revised this. There is inadequate evidence in humans for the carcinogenicity of tetrachlorvinphos. There is sufficient evidence in experimental animals for the carcinogenicity of tetrachlorvinphos. The overall evaluation is that tetrachlorvinphos is possibly carcinogenic to humans (Group 2B).

### Derivation of Maximum Acceptable Value

No MAV.

An upper limit of 0.03 mg/L in drinking-water has been suggested (Shijun et al 1982).

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# Thiabendazole

CAS No. 148-79-8. The IUPAC name for thiabendazole is 2-(thiazol-4-yl)benzimidazole, or 2-(1,3-thiazol-4-yl)benzimidazole. The CAS name is 2-(4-thiazolyl)-1H-benzimidazole. Also called 2-(1,3-thiazol-4-yl)-1H-benzoimidazole. Occasionally referred to as TBZ.

Thiabendazole is also sold as the hypophosphite salt, CAS 28558-32-9.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of thiabendazole in drinking-water should not exceed 0.4 mg/L (400 μg/L).

The WHO Guidelines (2004 and 2011) do not mention thiabendazole.

### Sources to water

Thiabendazole is used as a systemic benzimidazole fungicide for spoilage control of citrus fruit; for treatment and prevention of Dutch elm disease in trees; for control of fungal diseases of seed potatoes. It is also used therapeutically for cats as an anthelmintic (against nematode worms).

Thiabendazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and is available in a variety of formulations, some of which contain other active ingredients (fosetyl-aluminium, thiram, metalaxyl).

Thiabendazole is also used as a [food additive](http://en.wikipedia.org/wiki/Food_additive), a [preservative](http://en.wikipedia.org/wiki/Preservative) with [E number](http://en.wikipedia.org/wiki/E_number) E233. For example, it is applied to [bananas](http://en.wikipedia.org/wiki/Bananas) to ensure freshness. Trade names include: Aliette Super, Apron Combi, Apron TZ, Tecto SC, Tecto.

No information is available on the annual usage of specific active ingredients in New Zealand, although thiabendazole is understood to be likely to constitute only minor use in the agricultural sector (Holland, personal communication).

Thiabendazole is used for veterinary and human medical purposes. In this usage, thiabendazole is listed as a medicine notified as having been supplied under Section 29 of the Medicines Act. Section 29 of the Medicines Act 1981 permits the supply of an unapproved medicine to a medical practitioner for use by a named patient. Medicinally, thiabendazole is also a [chelating agent](http://en.wikipedia.org/wiki/Chelating_agent), which means that it is used medicinally to bind metals in cases of metal poisoning, such as [lead poisoning](http://en.wikipedia.org/wiki/Lead_poisoning), [mercury poisoning](http://en.wikipedia.org/wiki/Mercury_poisoning) or [antimony poisoning](http://en.wikipedia.org/wiki/Antimony). As an antiparasitic, it is able to control [roundworms](http://en.wikipedia.org/wiki/Roundworm), [hookworms](http://en.wikipedia.org/wiki/Hookworm), and other [helminth](http://en.wikipedia.org/wiki/Helminth) species which attack wild animals, [livestock](http://en.wikipedia.org/wiki/Livestock) and humans. In dogs and cats thiabendazole is also used to treat ear infections.

### Forms and fate in the environment

Thiabendazole is not very soluble in water (RSocC 1987); USEPA (2002) and EC (2001) quote 30 mg/L at pH 7 with EC adding 160 mg/L at pH 4.

Thiabendazole binding in soil increases with increasing soil acidity. It is quite persistent. In one study, nine months following application, most of the residues (85–95 percent) were recovered from soil. It is not expected to leach readily from soil (EXTOXNET 2001). USEPA (2002) states that thiabendazole appears to be extremely persistent in the environment. Extrapolated half-lifes ranged from 833–1,100 days in cropped plots and from 1,093–1,444 days in bare-ground plots.

Three degradates were identified in the aqueous photolysis study (benzimidazole-2-carboxamide as a major degradate; benzimidazole and benzimidazole-2-carboxylic acid as minor degradates), two minor degradates in the aerobic soil (bendimidazole). The only degradate that was analysed for in the terrestrial dissipation studies is benzimidazole, since it is the major metabolite in a soil study (anaerobic soil metabolism). Test results showed that benzimidazole was not detected in any soil layers (USEPA 2002).

Thiabendazole is stable in aqueous suspension and acidic media. Its low water solubility will make it unlikely to be in solution, and it will most likely be bound to sediment.

NPIC (1994) quotes for thiabendazole a soil half-life of 403 days, water solubility of 50 mg/L and a sorption coefficient (soil Koc) of 2,500. This resulted in a pesticide movement to groundwater rating of low.

EFSA (2014) reports that aerobic soil degradation studies have indicated that thiabendazole exhibited very high persistence (DT50 >1 year). In dark aerobic sediment water systems (two systems investigated) thiabendazole partitioned to the sediment to a significant extent (maximum 44.3–76.1 percent AR after 42 days). Degradation was slow in both systems and a default DT50 whole system of 1,000 days was used for the exposure assessment calculations. No major metabolites were identified in these experiments.

### Typical concentrations in drinking-water

No Ministry of Health drinking-water surveys have included thiabendazole, so typical concentrations in New Zealand drinking-waters are unknown.

No information is available on concentrations of thiabendazole in international drinking-waters.

### Removal methods

No information is available on the removal of thiabendazole from water. However, since it binds strongly to soil, water treatment processes that remove particulate matter should remove a lot of the thiabendazole.

Trace organic substances can be expected to adsorb on to activated carbon to some extent, and therefore activated carbon is likely to achieve some removal of thiabendazole, although a guide to the efficiency of the process cannot be provided.

Nanofiltration and reverse osmosis may also provide a means of removing this compound from water, but no data are available to support this.

### Recommended analytical techniques

#### Referee method

High pressure liquid chromatography – Fluorescence (EPA 641).

#### Some alternative methods

None.

### Health considerations

There is no information available regarding the greatest source of exposure to thiabendazole for New Zealanders (eg, dermal contact, inhalation, diet: food, water), although dietary intake would be expected to be important because of thiabendazole’s use to protect fruit from fungal damage.

Excretion of thiabendazole in the urine and faeces is rapid in most species and is almost complete after 48 hours in rats and 96 hours in sheep. The excretion products are metabolites reaching peak levels in the blood stream one hour after administration to rats, one to two hours in humans, and four hours after administration in cattle. These metabolites are distributed throughout most body tissues in sheep but detectable in only a few tissues at low levels (less than 0.2 mg/L) in 16 days and at very low levels (0.06 mg/L or less) after 30 days. No evidence of bioaccumulation in animal tissues was found (EXTOXNET 2001).

#### Acute poisoning

The acute oral LD50 for mice is 3,810 mg/kg. For rats it is 3,330 mg/kg and rabbits 3,850 mg/kg (RSocC 1987). These levels suggest a moderate to low acute oral toxicity when compared with other pesticides.

Effects of acute over-exposure to the fungicide include dizziness, anorexia, nausea and vomiting. Other symptoms such as itching, rash, chills and headache occur less frequently. The symptoms are brief and are related to the dose level (EXTOXNET 2001).

#### Chronic exposure

Dogs autopsied after a two-year feeding study showed incomplete development of bone marrow, a wasting away of lymph tissue, and other abnormalities. Most dogs tested at around 100 mg/day for two years developed anemia. The dogs recovered at the end of the study (EXTOXNET 2001).

JMPR (2006) quotes an ADI of 0.1 mg/kg bw (established in 1997). EC (2001) established an ADI of 0.1 mg/kg/d, and considered that an ARfD was unnecessary due to low acute toxicity.

USEPA (2002) quotes both the acute and chronic PAD (population adjusted dose) to be 0.1 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.033 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thiabendazole is 0.23 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.3 mg/kg body weight, with a NOEL of 3 mg/kg bw.

JMPR (2006) estimated two ARfDs for thiabendazole: one for general population; and the other for women of child-bearing age. The ARfD for general population is 1 mg/kg bw. The ARfD for women of child-bearing age is 0.3 mg/kg bw.

EFSA (2014) report the Acceptable Daily Intake (ADI) of 0.1 mg/kg bw per day is based on the NOAEL of the two-year study in rats, with the application of an uncertainty factor (UF) of 100. The Acute Reference Dose (ARfD) of 0.1 mg/kg bw was set based on the maternal NOAEL of the developmental study in rats, taking into account reduction of body weight gain at mid and high dose after the first three doses, with the application of a standard UF of 100.

The USEPA said (in 2002 and again in their 2008 list) that thiabendazole was likely to be carcinogenic to humans at high doses, but not likely to be carcinogenic at low doses. The International Agency for Research on Cancer has not classified thiabendazole for its ability to cause cancer. Thiabendazole is a USEPA General Use Pesticide (GUP), in toxicity class III – slightly toxic.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach was used by the MoH for the derivation of the provisional MAV for thiabendazole in drinking-water, as follows:

3 mg/kg body weight per day x 70 kg x 0.1 = 0.35 mg/L (rounded to 0.4 mg/L)

2 L x 30

where:

* no observable adverse effect level = 3 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 10 percent
* uncertainty factor = 30.

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# Thiacloprid

CAS No. 111988-49-9. The IUPAC name for thiacloprid is (Z)-3-(6-chloro-3-pyridylmethyl)-1,3-thiazolidin-2-ylidenecyanamide. The CAS name is (Z)-[3-[(6-chloro-3-pyridinyl)methyl]-2-thiazolidinylidene]cyanamide.

The meeting (JMPR 2010) noted that thiacloprid is inadequately described by the IUPAC and CA names, which do not distinguish whether thiacloprid is the E-isomer at the C=N group, or the Z-isomer, or a mixture of the two. The manufacturer stated that thiacloprid is the Z-isomer and has provided the new IUPAC and CA names, ie:

* IUPAC – N-{(2Z)-3-[(6-chloro-3-pyridinyl)methyl]-1,3-thiazolan-2-yliden}cyanamide
* CAS – N-[(2Z)-3-[(6-chloro-3-pyridinyl)methyl]-2-thiazolidinylidene]-cyanamide.

### Maximum Acceptable Value

Thiacloprid is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Thiacloprid is described as a [pyridylmethylamine](http://www.alanwood.net/pesticides/class_insecticides.html#pyridylmethylamine_insecticides) or thiazolidine or chloronicotinoid insecticide or [molluscicide](http://www.alanwood.net/pesticides/class_molluscicides.html), which disrupts the nervous system by acting as an inhibitor at nicotinic acetylcholine receptors. It is commonly used for aphid control on roses; it seems to have been used on kiwifruit and citrus trees in New Zealand too. Thiacloprid is closely related to imidacloprid (see datasheet).

Thiacloprid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). See generic note on pages 5/6.

Thiacloprid was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in cucumbers.

JMPR (2010) states that thiacloprid may be co-formulated with beta-cyfluthrin, buprofezin, deltamethrin and ethiprole.

### Forms and fate in the environment

The main route for dissipation of thiacloprid in soil is through microbial degradation (from 1 to 20 days half-life). In an aerobic soil system, the calculated half-life for the degradation product YRC-2894-amide is about 32 to 142 days. In anaerobic soils, the half-life can exceed one year. Thiacloprid is hydrolytically stable in the pH range 5 to 9 and undergoes photolysis only very slowly.

EFSA (2013) states that the DT90 value of thiacloprid is expected to be lower than the trigger value of 100 days. However, soil metabolites of thiacloprid were more persistent in soil. In particular, the metabolites M02 with DT90 values ranging from 106 to 1,047 days, M30 with a highest DT90 of 262 days, and M34 with a highest DT90 of 175 days.

It is stable in anaerobic aquatic conditions (half-life of over one year), and degrades under aerobic aquatic conditions with a half-life of 10 to 63 days. The only two major degradates (greater than 10 percent of applied parent) are the amide [(3-[(6-chloro-3-pyridinyl)methyl]-2-thiazolidinylidene) urea] which is the metabolite of concern in drinking-water, and the sulfonic acid.

Water solubility of thiacloprid is about 185 mg/L, over the range from pH 4 to pH 9. Thiacloprid does not readily leach, however, the sulfonic acid metabolite is expected to be mobile and more persistent so may enter groundwater.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See JMPR (2010).

### Health considerations

The USEPA (2003) NOAEL of 1.2 mg/kg/day was based on chronic feeding studies in rats producing a LOAEL of 2.5 mg/kg/day based on hepatic hypertrophy and cytoplasmic change and thyroid hypertrophy and retinal degeneration, and an uncertainty factor of 300. A chronic RfD of 0.004 mg/kg/d was derived, being considered a safe lifetime intake. New York State (2006) claims the USEPA cRfD of 0.004 mg/kg/d was based on the NOEL of 1.2 mg/kg/day in the chronic feeding/ oncogenicity study in rats and an uncertainty factor of 300 (10-fold each to account for inter- and intra-species differences, and a three-fold factor for the lack of morphometric analysis at lower dose groups in the developmental neurotoxicity study). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.004 mg/kg/d, and an ARfD of 0.01 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thiacloprid is 0.10 mg/L.

EC (2004) established an ADI of 0.01 mg/kg/d and an ARfD of 0.03 mg/kg/d.

APVMA (2001) adopted an ADI for thiacloprid of 0.01 mg/kg bw/day based on a NOEL of 1.2 mg/kg bw/day in a two-year dietary study in rats and using a 100-fold safety factor in recognition of the extensive toxicological database available for thiacloprid. APVMA (2001) adopted an acute reference dose (ARfD) of 0.03 mg/kg bw on the basis of this NOEL and using a 100-fold safety factor. JMPR (2006) also adopted the 0.01 mg/kg/d ADI and 0.03 mg/kg/d ARfD.

JMPR (2010) repeats the ADI of 0–0.01 mg/kg bw and the ARfD of 0.03 mg/kg bw. EFSA (2013 and 2015) reaffirmed those values.

As at September 2008 the USEPA classified thiacloprid as “likely to be carcinogenic to humans”, based on thyroid tumours and uterine tumours in rats and ovary tumours in mice. However, they do not expect that the general population would be exposed to levels that would exceed a negligible cancer risk over a lifetime (USEPA 2003). APVMA (2001) considered these tumours not to be predictive of an increased likelihood of cancer development in humans. In addition, a range of tests showed that thiacloprid did not damage genetic material. JMPR (2006) concluded that the probable mode of action for the luteomas seen in mice is exclusively a high-dose phenomenon that is not relevant for human exposure at the levels of residues found in food. JMPR (2010) concluded that the increased tumour incidences associated with exposure to thiacloprid are threshold phenomena and unlikely to pose a carcinogenic risk to humans at exposure levels relevant to residues found in food. The EC concluded there was no evidence of genotoxicity in a standard battery of in vitro and in vivo tests (data included in the DAR for EU registration).

Thiacloprid up to now is not classified and labelled by the European Chemicals Bureau (ECB). However, on a national level in most of the European countries thiacloprid is classified as a carcinogen category 3: harmful after acute oral and inhalation exposure as well as dangerous for the environment and harmful to aquatic organisms. Currently, thiacloprid is under evaluation in the ECHA process for classification and labelling as a biocide.

### Derivation of Maximum Acceptable Value

No MAV.

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# Thiamethoxam

CAS No. 153719-23-4. The IUPAC name for thiamethoxam is (EZ)-3-(2-chloro-1,3-thiazol-5-ylmethyl)-5-methyl-1,3,5-oxadiazinan-4-ylidene(nitro)amine. The CAS name is 3-[(2-chloro-5-thiazolyl)methyl]tetrahydro-5-methyl-N-nitro-4H-1,3,5-oxadiazin-4-imine.

Thiamethoxam is described as an EZ mixture. It is generally believed that the activation energy for the E↔Z interconversion for the C = N bond is low and that an equilibrium mixture is rapidly established at ambient temperature (JMPR 2010).

### Maximum Acceptable Value

Thiamethoxam is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

EPA established an environmental exposure limit of 0.00035 mg/L (0.35 µg/L) for thiamethoxam in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Thiamethoxam is described as a broad spectrum, systemic [nitroguanidine](http://www.alanwood.net/pesticides/class_insecticides.html#nitroguanidine_insecticides) or [thiazole or neonicotinoid insecticide](http://www.alanwood.net/pesticides/class_insecticides.html#thiazole_insecticides), often used on maize, sweetcorn, sorghum, and several vegetables, to control early season sucking and chewing pests.

Thiamethoxam appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). See generic note on pages 5/6.

Thiamethoxam was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in bok choi.

EFSA (2015) states that the uses as seed treatment and soil treatment of plant protection products containing clothianidin, thiamethoxam or imidacloprid have been prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing these active substances have been prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering.

### Forms and fate in the environment

Under field conditions, the half-life of thiamethoxam is about 7 to 109 days and it does not show any significant leaching in soil despite being expected to be persistent and mobile in terrestrial and aquatic environments. JMPR (2010) quotes half-lifes of 34 to 280 days in five aerobic soils, and 365 days in a sandy loam.

EFSA (2015) reports the soil DT50 of thiamethoxam ranges from 34 to 276 days under laboratory conditions.

Thiamethoxam is stable in water under acid conditions, hydrolysed under alkaline conditions. Aqueous photolysis occurs rapidly. The half-life in water has been measured at 20–50 days. Water solubility is about 4000 mg/L over a wide range of pH (2 to 12).

Thiamethoxam produces a metabolite known as CGA 322704 (also known as clothianidin). Note that clothianidin also appears on ERMA’s Full List of ACVM approved veterinary medicines and pesticides, as at 2009. While some of the toxic effects observed following testing with thiamethoxam and clothianidin are similar, the available information indicates that thiamethoxam and clothianidin have different toxicological effects in mammals and should be assessed separately. Clothianidin is not a significant degradate of thiamethoxam in surface water or groundwater sources of drinking water. Clothianidin drinking water residues only result from uses of clothianidin. There is a separate datasheet for clothianidin.

See JMPR (2010) for discussion on metabolites.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See APVMA (2001) and JMPR (2010).

### Health considerations

In repeat-dose feeding studies in mice, rats and dogs, bodyweight gains were generally lower and the target organs associated with toxicity were the liver and kidney. Changes in the liver included an increased weight and size due to the presence of masses and nodules, some pigmentation, death of some individual liver cells and the presence of scavaging cells to remove the dead cells. In the kidneys there was damage to the process involved in urine production. In dogs there was also an indication of changes within the reproductive organs.

The lowest reported NOELs in long-term studies were 2.6 mg/kg bw/day (mice) and 4.1 mg/kg bw/day (dogs), and 2 mg/kg bw/day for reproductive studies on weaned pups. The acceptable daily intake (ADI) for thiamethoxam is 0.02 mg/kg bw/day based on a NOEL of 2 mg/kg bw/day in a two-generation reproduction study in rats and a safety factor of 100. The safety factor was selected based on the presence of an adequate toxicology database.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw.

EC (2006) and EFSA (2012) established an ADI of 0.026 mg/kg/d, and an ARfD of 0.5 mg/kg/d.

The 2010 JMPR meeting established an acceptable daily intake (ADI) of 0–0.08 mg/kg bw on the basis of a NOAEL of 8.23 mg/kg bw per day in a 90-day study of toxicity in dogs, based on prolonged thromboplastin time. A safety factor of 100 was applied. This ADI is protective of the hepatotoxic and hepatocarcinogenic effects observed in mice, which were not observed in rats because of marked species differences in metabolism. It is also protective of the marginally toxic effects observed in a multigeneration study in rats at 46 mg/kg bw per day. An acute reference dose (ARfD) of 1 mg/kg bw was established on the basis of a NOAEL of 100 mg/kg bw in a single-dose study of neurotoxicity in rats. A safety factor of 100 was applied. The transient functional changes in rats appeared to be mild signs of overt toxicity rather than neurotoxicity. The neurotoxicity study was supported by a single-dose study of toxicity in mice, in which clinical signs of toxicity were observed at 500 mg/kg bw, the lowest dose tested (FAO/WHO 2010). These values were reaffirmed in JMPR (2014).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.012 mg/kg/d, and an ARfD of 0.35 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thiamethoxam is 3.5 mg/L.

In June 2000 the USEPA had classified thiamethoxam as “likely to be carcinogenic to humans”, but in 2005, changed this to “not likely to be carcinogenic to humans”. Clothianidin is also “not likely to be carcinogenic to humans”.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Thidiazuron

CAS No. 51707-55-2. The IUPAC name for thidiazuron is 1-phenyl-3-(1,2,3-thiadiazol-5-yl)urea. The CAS name is N-phenyl-N′-1,2,3-thiadiazol-5-ylurea.

### Maximum Acceptable Value

Thidiazuron is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Thidiazuron is described as a [phenylurea](http://www.alanwood.net/pesticides/class_herbicides.html#phenylurea_herbicides) or thiadiazolylurea herbicide, often used as a plant growth regulator or defoliant by influencing cytokinin activities in plants. Usually used on cotton and fruits. Overseas it has been used to improve post-harvest life of potted plants and cut flowers.

Thidiazuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

In soil, thidiazuron is persistent, as evidenced by laboratory and field half-lifes of approximately one year. It has intermediate soil adsorption coefficients. Such persistence and intermediate mobility would allow some year-to-year accumulation and the potential for run-off from application sites to occur. Based on its solubility, vapour pressure, and other laboratory evidence, thidiazuron is considered to be non-volatile. In addition, based on its relatively low octanol/water partitioning coefficient, thidiazuron is not expected to bioconcentrate. When thidiazuron reaches surface water, photolysis is expected to be the major route of transformation. Aqueous photolysis rapidly yields two photoproducts. One of the photodegradates (photothidiazuron) is a structural isomer of the parent, while the other has a substantially altered chemical structure (1-cyano-3-phenylurea).

Groundwater is not impacted by these degradates because all field studies show that the parent is long-lived in soil. Water solubility is about 20 mg/L.

NPIC (1994) quotes for thidiazuron a soil half-life of 10 days, water solubility of 20 mg/L and a sorption coefficient (soil Koc) of 110. This resulted in a pesticide movement to groundwater rating of low.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of thidiazuron in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Thidiazuron is considered to have low acute toxicity. Thidiazuron is placed in the following acute Toxicity Categories: oral III; dermal IV; inhalation IV; eye irritation IV; and, dermal irritation IV. Thidiazuron is classified as “not likely to be carcinogenic to humans” (USEPA 2005). The USEPA determined that there is reasonable certainty that no harm to any population subgroup will result from aggregate exposure to thidiazuron when considering dietary (food and water) exposure.

Both subchronic and chronic toxicity studies in rats show that thidiazuron causes decreased body weight gains and food consumption. In addition, chronic toxicity studies showed bilateral vesicle atrophy in rats, and dilated tubules of epididymis in mice. In the subchronic toxicity study, small seminal vesicles and prostate were also reported. The data from the developmental toxicity studies in rats and rabbits and of the two-generation reproduction study indicated no increase in susceptibility of fetuses and pups to the in utero and/or postnatal exposure to thidiazuron (USEPA 2005a).

The chronic RfD (= cPAD) is 0.039 mg/kg/d, based on a NOAEL of 3.93 mg/kg/d (UF = 100) from a dog chronic toxicity study where the LOAEL = 11.1 mg/kg/day based on increased incidence of anaemia, changes in haematological parameters, and marked haemosiderosis in liver and spleen. USEPA (2005a). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.0393 mg/kg/d. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thidiazuron is 0.275 mg/L (no acute one-day value available.)

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2.5 mg/kg bw.

No neurotoxicity was reported in any of the studies. Carcinogenicity studies in both rats and mice produced no treatment-related increase in tumour incidence. The standard battery of genotoxicity tests was negative. Therefore, thidiazuron has been classified as “not likely to be carcinogenic to humans” (USEPA 2005a).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

NPIC. 1994. *OSU Extension Pesticide Properties Database*. National Pesticide Information Centre. <http://npic.orst.edu/ingred/ppdmove.htm>

USEPA. 2005. Thidiazuron. *RED Facts*. EPA-738-F-04-012 [5 pp]. See: <http://www.epa.gov/oppsrrd1/REDs/thidiazuron_factsheet.pdf>

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# Thifensulfuron-methyl

CAS No. 79277-27-3. The IUPAC name for thifensulfuron-methyl is methyl 3‑(4‑methoxy-6-methyl-1,3,5-triazin-2-ylcarbamoylsulfamoyl)thiophene-2-carboxylate. The CAS name for thifensulfuron-methyl is methyl 3-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)amino]carbonyl]amino]sulfonyl]-2-thiophenecarboxylate. This substance is a derivative of [thifensulfuron](http://www.alanwood.net/pesticides/thifensulfuron.html), CAS No. 79277-67-1. Known in the US as Harmony. Sometimes applied with metsulfuron-methyl.

### Maximum Acceptable Value

Thifensulfuron-methyl is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Thifensulfuron-methyl is a selective systemic triazinylsulfonylurea herbicide.

Thifensulfuron-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)).

### Forms and fate in the environment

Thifensulfuron-methyl hydrolyses readily at high and low pH, with half-lifes of 28.8 and six hours at pH 4 and pH 10 respectively, in sterile buffers at 28°C. It is much more stable at neutral pH; the half-life at pH 7 at 45°C is 250 hours. Photolytic degradation of thifensulfuron-methyl is slow. The half-life in aerobic soils has been reported at  
3–20 days. The half-life in anaerobic soil is about 27 days, and ranges from 20 to 90 days in water. EFSA (2012 and 2015) list the main metabolites.

Thifensulfuron-methyl degrades rapidly in water due to photolysis, forming the major degradation products IN-A4098, IN-V7160 and a metabolite identified as IN-D8858 (maximum 15.3 percent AR). In laboratory incubations in dark aerobic natural sediment water systems, thifensulfuron-methyl exhibited moderate persistence, forming the major metabolites IN-JZ789 (maximum 21 percent AR), IN-L9223 (maximum 39 percent AR), IN-V7160 (maximum 25 percent AR), IN-A4098 (maximum 20 percent AR) and IN‑L9225 (maximum 55 percent AR) in the water phase. This assessment assumed a default worst-case DT50 of 1,000 days in soil and water sediment systems (EFSA 2015).

EC (2001) states “Particular attention should be given to the potential for groundwater contamination, when the active substance is applied in regions with vulnerable soil and/or climatic conditions”.

Water solubility is about 220 mg/L at pH 5; 2,200 mg/L at pH 7; and 8,800 mg/L at pH 9.

NPIC (1994) quotes for thifensulfuron-methyl a soil half-life of 12 days, water solubility of 2,400 mg/L and a sorption coefficient (soil Koc) of 45. This resulted in a pesticide movement to groundwater rating of moderate.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

LC-MS/MS methods are available (EFSA 2015).

### Health considerations

The lowest relevant NOAEL is estimated (EC 2001) to be 0.96 mg/kg bw/d, based on a two-year study using rats, and thifensulfuron-methyl tested negative for carcinogenicity. An ADI of 0.01 mg/kg bw was derived using a safety factor of 100; an ARfD was considered to be unnecessary.

USEPA (2010) quotes a cPAD and chronic RfD of 0.043 mg/kg/d. The oral RfD had earlier been 0.013 mg/kg/d (USEPA 1991). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.043 mg/kg/d, and an ARfD of 1.59 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thifensulfuron methyl is 52.5 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia for thifensulfuron is 0.01 mg/kg body weight, with a NOEL of 1.25 mg/kg bw.

Thifensulfuron-methyl has not been evaluated by the FAO/WHO JMPR and WHO/IPCS (JMPR 2011).

EFSA (2012) states that an ADI was established at 0.02 mg/kg bw per day. An ARfD was not deemed necessary. EFSA (2015) revised these values: the agreed acceptable daily intake (ADI) is 0.01 mg/kg bw per day, on the basis of the relevant long-term NOAEL of 1.3 mg/kg bw in the two-year study in rats based on mammary gland tumours at 26 mg/kg bw per day. An uncertainty factor of 100 was applied. This ADI also applies to its metabolites thifensulfuron (IN-L9225) and IN-JZ789. The agreed acute reference dose (ARfD) is 2 mg/kg bw based on the NOAEL of 200 mg/kg bw per day for slight reduced body weight gain during the first days of dosing observed at 800 mg/kg bw per day in the developmental toxicity study in rats. An uncertainty factor of 100 was applied. This ARfD also applies to its metabolites thifensulfuron (IN-L9225) and IN‑JZ789.

Thifensulfuron methyl is classified as (USEPA 2010) “not likely to be carcinogenic to humans”, based on acceptable chronic/carcinogenicity studies in rats and mice at doses that are considered to be adequate, and not excessive for the determination of carcinogenic potential. The available mutagenicity studies in vivo and in vitro show that thifensulfuron methyl is neither mutagenic nor clastogenic.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# 2-(thiocyanomethylthio) benzothiazole

CAS No. 21564-17-0. The IUPAC name for 2-(thiocyanomethylthio)benzothiazole is 2‑(thiocyanatomethylthio)-1,3-benzothiazole. The CAS name is (2‑benzothiazolylthio)methyl thiocyanate. Also called TCMTB or 2-(cyanomethylthio) benzothiazole. Has a trade name of Busan.

### Maximum Acceptable Value

2-(Thiocyanomethylthio)benzothiazole is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

2-(Thiocyanomethylthio)benzothiazole is a thiazole (or mercaptobenzothiazole) biocide. As an antimicrobial pesticide, TCMTB has several uses. TCMTB is used as a wood preservative for antisapstain control, a microbiocide/microbiostat and bactericide/bacteriostat in industrial processes and non-potable water systems (eg, pulp and paper mill systems, sewage systems) and in industrial/residential materials preservatives (eg, pulp/paper products, leather products and hides, paint, latex, carpet, textiles, wallpaper). It is used at concentrations up to 6.2 percent w/w in association with copper or other active ingredients in antifouling products.

TCMTB is used as an agricultural pesticide for seed treatment, eg, barley, oats, rice, wheat, safflower, cotton and sugar beets. TCMTB is also used as a slimicide and paper coating preservative for controlling bacteria, fungi and yeasts that cause deterioration of paper and paperboard products and used to preserve paper-adhesive formulations (USEPA 2006).

2-(Thiocyanomethylthio)benzothiazole does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Timber Preservatives, Antisapstains and Antifouling Paints) Transfer Notice 2004 (as amended), as at 14 March 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select timber preservatives …).

### Forms and fate in the environment

TCMTB is hydrolytically stable under abiotic and buffered conditions at pH 5 and slowly degrades at pH 7. Under more alkaline conditions, hydrolysis proceeds more rapidly with a calculated half-life ranging from 1.8 to 2.1 days. Photolytically, TCMTB degrades in pH 5 buffered aqueous solutions with a calculated half-life of 1.5 hours. Based on its degradation in the environment, TCMTB is not likely to pose a concern for surface water run-off. Aquatic metabolism under aerobic and anaerobic conditions, as well as aerobic soil metabolism, are major routes of dissipation for TCMTB. TCMTB’s calculated degradation half-life in flooded lake sediment is 6.9 days; however, the apparent half-life occurs between two and four days. Similarly, TCMTB shows a tendency of degrading anaerobically in flooded sediment within 2.7 days. Under aerobic conditions in sandy loam soil, a representative agricultural soil, TCMTB degrades with a calculated half-life of 1.4 days. TCMTB’s tendency to bind with agricultural soils varies according to soil type. TCMTB is mobile to very mobile in various soils; however, because of its tendency to biodegrade in water and soils, TCMTB is not likely to contaminate surface and ground waters.

TCMTB is environmentally unstable; therefore, it is important to evaluate the toxicity of the more persistent degradation products 2-mercaptobenzothiazole (2-MBT), 2‑(methylthio)benzothiazole (MTBT), benzothiazole (BT), and 2-hydroxybenzothiazole (HOBT). TCMTB was the most toxic compound evaluated in both the acute and chronic tests with EC50s of 15.3 and 9.64 microgram/L, respectively. 2-MBT, the first degradation product, was the second most toxic compound with acute and chronic EC50s of 4.19 and 1.25 mg/L, respectively. The toxicity of MTBT and HOBT were similar with acute EC50s of 12.7 and 15.1 mg/L and chronic EC50s of 6.36 and 8.31 mg/L, respectively. The least toxic compound was BT with acute and chronic EC50s of 24.6 and 54.9 mg/L, respectively. TCMTB was orders of magnitude more toxic than its degradation products (Nawrocki et al 2005).

TCMTB has several metabolites, including 2-mercaptobenzothiazole (2-MBT) and 2‑benzothiazolesulfonic acid (2-BTSA). The USEPA’s Risk Assessment Review Committee met and determined that the residue of concern for tolerance expression and risk assessment is TCMTB in/on plants. 2-MBT and other TCMTB metabolites were not found at significant levels to be considered residues of concern. The determination of the residues of concern in plant commodities was based on tomato and melon metabolism studies and available toxicity data. 2-BTSA was found at significant levels (62 percent in tomato fruit); however, it was determined that it should be excluded as a residue of concern because it is expected to be less toxic than the parent TCMTB. 2‑BTSA does not contribute significantly to the chronic toxicity of the parent. This decision is considered preliminary pending the results of confirmatory metabolism data that are required to support the currently registered uses of TCMTB.

The Henry’s Law constant of 6.5 x 10-12 atm-m3/mole indicates that thiocyanic acid (2‑benzothiazolylthio) methyl ester is expected to be essentially non-volatile from water and soil surfaces.

For drinking water, the residues of concern included TCMTB and 2-MBT, based on an available aerobic soil metabolism study (MRID 43532201). Although 2-MBT is distinctly less toxic than the parent, it was conservatively included in the drinking water assessment because it is a toxic metabolite of concern. All other metabolites were not found at significant levels; and are not to be considered residues of concern.

2-Thiocyanomethylthio)benzothiazole water solubility is about 10 mg/L; partition coefficient, log Pow, is 3.26 at 20°C (DEFRA 2005). EPA [(http://www.epa.govt.nz/search-databases/Pages/ccid-details.aspx?SubstanceID=3104](file:///C:\Users\sgilbert\AppData\Local\Microsoft\Windows\INetCache\Content.Word\(http:\www.epa.govt.nz\search-databases\Pages\ccid-details.aspx%3fSubstanceID=3104)) quotes 33 mg/L. Other sources say it is about  
100–125 mg/L.

### Typical concentrations in drinking-water

USEPA (2006) considers for surface drinking water, the peak (acute) concentration of TCMTB and its degradates is not likely to exceed 0.001 mg/L and that the average annual (chronic) concentration is not likely to exceed 0.0007 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The main toxicological effects of TCMTB are inhalation toxicity, point of contact irritation (skin and eye) and skin sensitisation. TCMTB is a site of contact toxicant and as would be expected the stomach is the target organ following oral administration (DEFRA 2005).

The acute dietary (all populations, including infants and children) toxicological limit is a PAD (population adjusted dose) of 0.25 mg TCMTB/kg/day, based on a NOAEL of 25.1 mg/kg/d and a uncertainty factor of 100, from a developmental toxicity study in rats.

The chronic dietary (all populations) toxicological limit is a PAD (population adjusted dose) of 0.01 mg TCMTB/kg/day, based on a LOAEL of 3.8 mg/kg/d and a uncertainty factor of 300, from a chronic toxicity study in dogs. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.01 mg/kg/d, and an ARfD of 0.25 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for TCMBT (Busan 72) is 2.5 mg/L.

Well-conducted studies in rats and mice indicate that TCMTB is unlikely to act as a potential carcinogen following oral administration. NOAELs for carcinogenic effects in rats of >20 mg/kg/d and in mice of >150 mg/kg/d are apparent following chronic dietary administration of TCMTB. DEFRA (2005).

The USEPA concluded that TCMTB should be classified as Group C – possible human carcinogen – and recommended that for the purpose of risk characterisation, the Reference Dose (RfD) approach should be used for quantitation of human risk. This was based on statistically significant increases in tumours in both sexes of the Sprague-Dawley rat: testicular interstitial cell adenomas in males and thyroid C-cell adenomas in females. Although these adenoma results were not seen as statistically significant, they may indicate an association with endocrine disruption.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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USEPA. 2006*. Re‑registration Eligibility Decision for 2-(Thiocyanomethylthio)-benzothiazole (TCMTB)*. EPA 739-R-05-003 [126 pp]. See: <http://www.epa.gov/pesticides/reregistration/status.htm> or <http://www.epa.gov/pesticides/reregistration/REDs/tcmtb_red.pdf>

# Thiodicarb

CAS No. 59669-26-0. The IUPAC name for thiodicarb is (3EZ,12EZ)-3,7,9,13-tetramethyl-5,11-dioxa-2,8,14-trithia-4,7,9,12-tetraazapentadeca-3,12-diene-6,10-dione. The CAS name for thiodicarb is dimethyl N,N′‑[thiobis[(methylimino)carbonyloxy]]bis[ethanimidothioate].

### Maximum Acceptable Value

Thiodicarb is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The USEPA concluded on 22 September 2009 that thiodicarb is known or anticipated to occur in PWSs and may require regulation. Therefore they added thiodicarb to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

Thiodicarb should not contain more than 5 g/kg of methomyl.

### Sources to water

Thiodicarb is a non-systemic oxime carbamate molluscicide and insecticide with a relatively narrow spectrum of activity closely related to its first metabolite, methomyl (qv), which is also an impurity.

Thiodicarb appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Thiodicarb is very stable at pH 6 but unstable in alkaline conditions. It is subject to decomposition by light. The major by-product of photolysis is methomyl. Light textured soils cause more rapid degradation than heavy texture soils. Thiodicarb exhibits low mobility in all soils. Degradation is also influenced by increasing temperature, degree of aeration, and microbial activity. The half-life on soil and plant surfaces is less than one week. The 2001 JMPR meeting concluded that thiodicarb and methomyl degradates persist in soil for at least four months and are taken up by plants and ultimately incorporated into natural products. This apparent variability is somewhat dependent on soil type, eg, in soil under aerobic conditions, thiodicarb degraded rapidly to methomyl, with a half-time based on first-order kinetics of  
0.01–2.0 days, depending of soil type. The half-time of methomyl in sandy loam soil was 27 days.

The route and rate of degradation of thiodicarb under anaerobic conditions was studied in a soil–water mixture. The soil was flooded with deionised water and purged with nitrogen for 42–43 days before treatment to establish anaerobic conditions. A solution of thiodicarb was applied to the water surface at a nominal application rate equivalent to 1 kg ai/ha. During incubation, the system was purged continuously with nitrogen to maintain anaerobic conditions. Within 16 minutes, the concentration of thiodicarb was <1 percent of the applied dose. The concentration of methomyl was constant, at about 2 percent of the applied dose. An intermediate compound, S‑methyl-N-[N-methyl-N-(methylaminothio)-carbamoyloxy] thioacetamidate, was found at ≤17 percent of the applied dose. Acetonitrile was the ultimate degradate, accounting for 88 percent of the applied radiolabel after four hours.

Thiodicarb is non-persistent in the environment. EC (2007) states that thiodicarb should not be included in Annex I to Directive 91/414/EEC because of concerns of possible groundwater contamination.

Water solubility is about 25–30 mg/L.

NPIC (1994) quotes for thiodicarb a soil half-life of seven days, water solubility of 19 mg/L and a sorption coefficient (soil Koc) of 350. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The metabolic pathway of thiodicarb in animals has been demonstrated to be thiolysis to methomyl (USEPA 1998), followed by hydrolysis to the methomyl oxime, and subsequent metabolisation to acetonitrile (see datasheet). Acetonitrile is then metabolised to acetamide, a potential carcinogen, and further hydrolysed to acetic acid, which enters the intermediary metabolism cycle of the animal and is ultimately expired as carbon dioxide.

USEPA (1998) states that the RfD for thiodicarb was calculated to be 0.03 mg/kg/day from a chronic rat toxicity study with a NOEL of 3.3 mg/kg/day for males and 4.5 mg/kg/day for females. The RfD was based on an increased incidence of extramedullary hemopoiesis in males and decreased RBC cholinesterase in females at the LOEL. An uncertainty factor of 100 was used for deriving the RfD and includes 10x for inter-species extrapolation and 10x for intra-species variation. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.03 mg/kg/d, and an ARfD of 0.033 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thiodicarb is 0.33 mg/L.

IPCS proposed a temporary ADI for humans of 0–0.01 mg/kg, and an ADI of 0.03 mg/kg in 1986 which was reaffirmed in 2000 by JMPR (WHO 2000).

The EU (2007) considered the information available is insufficient to satisfy the requirements set out in Annex II and Annex III Directive 91/414/EEC, particularly regarding the acute dietary risk for toddlers resulting from the consumption of treated table grapes and for adults resulting from the consumption of wine produced from treated wine grapes.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.03 mg/kg body weight, with a NOEL of 3 mg/kg bw.

Thiodicarb was not mutagenic in a wide variety of assays. However, it was positive in the mitotic gene conversion assay using Saccharomyces cerevisiae.

JMPR (2000) concluded that thiodicarb was unlikely to pose a carcinogenic risk to humans. As at September 2008 the USEPA has classified thiodicarb in Group B: a probable human carcinogen. The B classification was based on statistically significant increases in tumours in both sexes of the mouse and statistically significant increases in testicular interstitial cell tumours in male rats. Thiodicarb appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

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# Thiophanate-methyl

CAS No. 23564-05-8. The IUPAC name for thiophanate-methyl is dimethyl 4,4′-(o-phenylene)bis(3-thioallophanate). The CAS name for thiophanate-methyl is dimethyl [1,2-phenylenebis(iminocarbonothioyl)]bis[carbamate]. Sometimes called TM. The analogous diethyl ester has the ISO common name [thiophanate](http://www.alanwood.net/pesticides/thiophanate.html).

### Maximum Acceptable Value

Thiophanate-methyl is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The USEPA concluded on 22 September 2009 that thiophanate-methyl is known or anticipated to occur in PWSs and may require regulation. Therefore they added thiophanate-methyl to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.09 mg/L for thiophanate-methyl; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Thiophanate-methyl should not contain more than 0.5 mg/kg of 2,3‑diaminophenazine, or 0.5 mg/kg of 3-hydroxy-2-aminophenazine.

### Sources to water

Thiophanate-methyl is a systemic carbamate (or benzimidazole) fungicide used to control fungal diseases such as mould, spot, mildew, scorch, rot and blight in a variety of crops. It is also used as an insecticide, miticide and anti-sapstain. Its main use in California is on grape vines. It is used in Australia to control soil borne diseases in ornamental plants, but APVMA is reconsidering its registration.

Thiophanate-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Thiophanate appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

ERMA states: Benomyl and thiophanate-methyl that enter the environment are converted to carbendazim, which can be regarded as the environmentally relevant compound. The half-lifes are 2–19 hours for benomyl and 3–4 days for thiophanate-methyl. The carbendazim formed decomposes in the environment with a half-life of months under aerobic and anaerobic conditions in soil and water. Carbendazim partitions from water to soil and sediment. It binds to the mineral component of the soil, probably through the imidazole ring. Adsorption is strong and carbendazim does not leach through the soil profile, despite its low Kow. No contamination of groundwater can be expected, as confirmed by field monitoring of bore water.

Water solubility of thiophanate-methyl is about 20 mg/L in the range of pH 4 to 7.5.

NPIC (1994) quotes for thiophanate methyl a soil half-life of 10 days, water solubility of 3.5 mg/L and a sorption coefficient (soil Koc) of 1,830. This resulted in a pesticide movement to groundwater rating of very low.

Note: carbendazim is also called methyl 2-benzimidazoyl carbamate, or [methyl 2‑benzimidazolecarbamate](http://www.chemindustry.com/chemicals/1010087.html) (CAS No. 63278-70-6).

### Removal methods

Treatment processes that remove particulate matter should be effective in reducing the concentration of thiophanate-methyl and carbendazim. GAC should also be effective.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

A HPLC–MS/MS method exists for monitoring thiophanate-methyl and carbendazim in surface, ground and drinking water with a LOQ of 0.05 μg/L for each compound.

### Health considerations

An ADI of 0.08 mg/kg bw/day was established for thiophanate-methyl on the basis of the NOEL of 8 mg/kg bw/d in a three-generation study of reproductivity toxicity in rats and in a one-year study in dogs, and a safety factor of 100 (JMPR 1998). The 1998 JMPR also concluded that an ARfD was not required because thiophanate-methyl is of low acute toxicity when administered orally or dermally and that the acute intake of residues is unlikely to present a risk to consumers. The 2006 meeting reaffirmed this. The ADI for carbendazim (methyl 2-benzimidazole carbamate or MBC) is 0.03 mg/kg/day established in 1979.

The 2017 JMPR meeting established an ADI of 0–0.09 mg/kg bw for thiophanate-methyl on the basis of a NOAEL of 8.8 mg/kg bw per day based on reduction in body weight gain and clinical chemistry, urine analysis and histopathological changes in the kidney, thyroid, liver and adrenals in a two-year study in rats. This ADI is supported by the overall NOAEL of 10 mg/kg bw per day based on increased thyroid weight and histopathological changes in the thyroid observed in three-month, one-year and two-year toxicity studies in dogs. A safety factor of 100 was used. The meeting established an ARfD of 1 mg/kg bw for thiophanate-methyl on the basis of a NOAEL of 125 mg/kg bw for transient reductions in body weight gains (including body weight losses) and feed consumption in an acute neurotoxicity study in rats, using a safety factor of 100.

USEPA (2005) quotes a chronic RfD for thiophanate-methyl of 0.08 mg/kg/d and a cPAD of 0.027 mg/kg/d, and 0.025 mg/kg/d and a cPAD of 0.0025 mg/kg/d for carbendazim. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0267 mg/kg/d, and an ARfD of 0.20 mg/kg/d for thiophanate-methyl. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thiophanate-methyl is 6.6 mg/L.

EC (2005) derived an ADI of 0.08 mg/kg/d and an ARfD of 0.2 mg/kg/d for thiophanate-methyl. However, since plant and food residues are expressed as carbendazim, its ADI and ARfD of 0.02 mg/kg/d may be more relevant (EFSA 2012). However, EFSA (2018) states that taking into consideration the clastogenic properties of thiophanate-methyl, no threshold for this effect is assumed; therefore, no toxicological reference values (dietary, such as the acceptable daily intake (ADI) and the acute reference dose (ARfD) can be derived; this represents a critical area of concern for the approval of the active substance.

The Acceptable Daily Intake (ADI) adopted in Australia as at December 2008 for thiophanate and thiophanate-methyl was 0.02 mg/kg body weight, with a NOEL of 2 mg/kg bw from a long-term rat study. The NOEL is based on degeneration and atrophy in the testes. The ADI incorporates a safety factor of 100. By July 2011 the Acceptable Daily Intake (ADI) for thiophanate-methyl was 0.08 mg/kg body weight, with a NOEL of 8 mg/kg bw, and the ARfD is 0.2 mg/kg bw. The ARfD only applies to women of child-bearing age. An ARfD for the general population is considered to be unnecessary (<https://apvma.gov.au/>).

JMPR (2006) states that thiophanate-methyl has been adequately tested in a range of assays for genotoxicity. Thiophanate-methyl does not cause gene mutations or structural chromosomal aberrations; however, it causes changes in chromosome number (aneuploidy) both in vitro and in vivo. Induction of micronucleus formation in mice was seen after single high doses (500 mg/kg bw and above), but the response was weak when compared with that for the main metabolite of thiophanate-methyl, carbendazim, which is considered to be responsible for the observed effect. The mechanism by which aneuploidy is induced by carbendazim is clearly understood and there is a clear threshold for this effect. The meeting concluded that the genotoxic effect of thiophanate-methyl is a threshold phenomenon and is related to the production of carbendazim. The European Union (EU) has classified carbendazim as a potential genotoxic chemical. The major metabolite carbendazim, ie, methyl 2‑benzimidizole carbamate (MBC), has the potential to cause mutagenic effects.

As at September 2008 the USEPA has classified thiophanate-methyl as likely to be carcinogenic to humans. Thiophanate-methyl appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

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# Thiram

CAS No. 137-26-8. The IUPAC name for thiram is either tetramethylthiuram disulfide or bis(dimethylthiocarbamoyl) disulfide. The CAS name is tetramethylthioperoxydicarbonic diamide. In some parts of the world, also called tetramethylthiuram bisulfide, thiuram and TMTD.

### Maximum Acceptable Value

Neither the DWSNZ nor WHO Guidelines mention thiram.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for thiram in water (set by an approval under Part 5 of the HSNO Act) of 0.00001 mg/L (0.001 µg/L).

### Sources to water

Thiram is a dimethyl dithiocarbamate, or disulphide, compound used as a broad spectrum, multi-site action fungicide to prevent crop damage in the field (eg, from Botrytis species) and to protect harvested crops from deterioration in storage or transport. It must be used at close intervals due to its short half-life in soil (0.5 days). Thiram is also used as a seed protectant and to protect fruit, vegetable, ornamental, and turf crops from a variety of fungal diseases. In addition, it is used as an animal repellent to protect fruit trees and ornamentals from damage by birds, rabbits, rodents, and deer. It also appears in mixtures with other fungicides and insecticides. However, the major international use of thiram is in rubber processing as an accelerator and vulcanising agent (IARC 1991).

This substance appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 10.6 tonnes of thiram were used in New Zealand in 2004, at an application rate of 4,800 grams of active ingredient per hectare.

In June 2013 the EPA stated that antifouling paints containing thiram can only be used in New Zealand for another 10 years. See EPA (2013).

Thiram has been used in the treatment of human scabies, as a sunscreen, and as a bactericide applied directly to the skin or incorporated into soap. Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007).

### Forms and fate in the environment

Thiram and the metabolite DMCS have of low to moderate persistence: DT90 up to 190 days. Thiram is nearly immobile in clay soils or in soils high in organic matter. Thiram appears to have low mobility in the environment and degrades rapidly (mean half-life = 3.5 days in a hydrolysis study). DMCS has very high mobility. The half-life for the disappearance of thiram from the control in the dark was 15.9 days and in the soil under artificial light 3.7 days. Dimethyl carbamothioperoxoate was found to be the main soil degradate. It reached its maximum level at four days and exceeded the level of the parent compound after 42 days, but 99.8 percent of the parent had disappeared at this time. See JMPR (1996) and EFSA (2017) for a discussion on metabolites.

The initial half-life of thiram was about two days with more than 90 percent disappearance within seven days. Thiram itself was not detectable in solvent extracts of the sediments. Methyl dimethyldithiocarbamate, CS2 and CO2 were identified as products (JMPR 1996). In water, thiram is rapidly broken down by hydrolysis and photodegradation, especially under acidic conditions. Thiram may adsorb to suspended particles or to sediment. Carbon disulphide (which is volatile) is the major metabolite. Dimethyldithiocarbamic acid methyl ester has also been detected in water (EC 2003).

Because it is only slightly soluble in water (about 15–25 mg/L) and has a strong tendency to adsorb to soil particles, thiram is not expected to contaminate groundwater.

NPIC (1994) quotes for thiram a soil half-life of 15 days, water solubility of 30 mg/L and a sorption coefficient (soil Koc) of 670. This resulted in a pesticide movement to groundwater rating of low.

EU (2015) reports the Partition coefficient n-octanol/water (Log Kow) is 1.8 at pH4, 2.1 at pH 7 and 1.9 at pH 10.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of thiram in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2017).

### Health considerations

Thiram and other dithiocarbamates are metabolic poisons. Their acute toxic effects are largely similar to those of carbon disulfide, supporting the conclusion that the common metabolite of these compounds is responsible for their toxicity. This conclusion is supported by the findings that most dithiocarbamates of very low toxicity are poorly absorbed and that a large portion of an oral dose is excreted in the faeces unchanged. In contrast to carbon disulfide, thiram also causes thyroid dysfunctions in vertebrates. Thiram induces an alcohol intolerance either by inhibiting acetaldehyde dehydrogenase or through the formation of a quaternary compound with the ethanol (WHO 1985).

Symptoms of chronic exposure to thiram in humans include drowsiness, confusion, loss of sex drive, incoordination, slurred speech, and weakness, in addition to those due to acute exposure. Repeated or prolonged exposure to thiram can also cause allergic reactions such as dermatitis, watery eyes, sensitivity to light, and conjunctivitis. Except for the occurrence of allergic reactions, harmful chronic effects from thiram have been observed in test animals only at very high doses.

Thiram is not a member of the ethylene(bis)dithiocarbamate (EBDC) chemical family, and thus it should not generate ethylene thiourea. It is classified by the USEPA as toxicity class III – slightly toxic.

When surface water or groundwater are abstracted for drinking water purposes, residues of thiram and the groundwater metabolite DMCS that are potentially present in surface water, or DMCS that has the potential to be present in groundwater, could, following the water treatment processes of chlorination or ozonation, result in the hazardous N,N‑dimethylnitrous amide (NDMA) being present in drinking water. The potential for shallow vulnerable groundwater exposure above the parametric drinking water limit of 0.1 μg/L by the toxicologically relevant metabolite DMCS was predicted to be high over the geoclimatic conditions represented by all the FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use) groundwater scenarios for the representative spray uses assessed. This is a concern for the uses on apple, pear, cherry, strawberry and peach. This concern also applies for half the FOCUS groundwater scenarios (4/8) for the seed treatment use on maize. DMCS is considered of potential concern since it is acutely toxic if swallowed and if inhaled, carcinogenic category 1B and causing damage to organs through prolonged or repeated exposure (EFSA 2017).

A temporary ADI of 0–0.005 mg/kg bw, allocated for thiram in 1974, was extended in 1977 and 1980. The temporary ADI was withdrawn in 1985 because of the inadequacy of the total data base. The studies available to the 1987 Joint Meeting were not adequate for estimating an ADI. JMPR (1992) established an ADI of 0–0.01 mg/kg bw. EFSA (2017) also uses an ADI of 0.01 mg/kg bw and an ARfD of 0.025 mg/kg bw.

USEPA (2004) quotes a chronic RfD (and cPAD) of 0.015 mg/kg/d with a NOAEL of 1.5 mg/kg/d. The oral RfD had earlier been 0.005 mg/kg/d (USEPA 1992) based on neurotoxicity in a two-year rat feeding study. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.015 mg/kg/d, and an ARfD of 0.014 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for thiram is 0.46 mg/L.

EC (2003) established an ADI of 0.01 mg/kg/d, and an ARfD of 0.6 mg/kg/d. EFSA (2015) affirmed these values.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.004 mg/kg body weight, with a NOEL of 0.4 mg/kg bw from a long-term (two-year) dietary study in dogs. The NOEL is based on neurological disturbances, anaemia and changes in the liver. The ADI incorporates a safety factor of 100. The ARfD is 0.1 mg/kg bw.

EU (2015) reports that the lowest NOAEL of 0.84 mg/kg bw/d was observed in a one-year dog study based on increased liver weight, increased blood cholesterol and decreased total protein observed in males at the next dose level of 2.61 mg/kg bw/d. This NOAEL was used by the registrant for the chemical safety assessment of thiram to derive long-term DNELs for systemic effects.

The IARC considered thiram is not classifiable as to its carcinogenicity to humans (Group 3). As at September 2008, the USEPA has classified thiram as “not likely to be carcinogenic to humans”.

Thiram is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

No MAV.

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# Thymol

CAS No. 89-83-8. The IUPAC name for thymol is 2-isopropyl-5-methylphenol or 5‑methyl-2-propan-2-yl-phenol. The CAS name is 5-methyl-2-isopropyl-1-phenol. It is also called isopropyl-m-cresol, hydroxycymene, and several trade names.

The formulated product also contains the active substance eugenol, which contains the relevant impurity methyleugenol. On analysis of the formulated product during storage studies it was found that both the initial and after storage samples contained up to five times higher levels of methyleugenol than would be expected from the technical specification of eugenol. Methyleugenol is a relevant impurity in the formulation because it is a genotoxic carcinogen (EFSA 2012).

### Maximum Acceptable Value

Thymol is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Thymol is a natural monoterpene phenol constituent of oil of thyme, a naturally occurring mixture of compounds in the plant Thymus vulgaris (thyme), and from mandarin and tangerine oils. It is used in beehives to control the varroa mite and other nuisances such as moulds. It is also used as a vertebrate repellent. It has also been used as a bactericide and fungicide.

Thymol is sometimes used as an active antiseptic ingredient in some toothpastes and mouthwashes, and is a common additive in cigarettes. It has USFDA approval when used as a synthetic flavouring, a preservative, and indirect food additive of adhesives. Its first use was probably as a mummy preservative by the Egyptians.

Thymol appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Thymol has a half-life of 16 days in water and five days in soil.

Since thymol is readily biodegradable, and based on its chemical structure, a waiver for studies of the route of degradation in soil was accepted. Neither hydrolysis nor aqueous photolysis of thymol has been investigated (EFSA 2012).

Water solubility is about 900 mg/L.

### Typical concentrations in drinking-water

Unlikely to find its way to water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The USEPA is not aware of any adverse effects to humans or the environment in the scientific literature associated with any thymol related use. Based on available data, no endocrine system-related effects have been identified with consumption of thymol. Information submitted from the public literature and reviewed by the USEPA describes immunological endpoints in relation to short-term and chronic dosing. No effects were seen in the thymus, spleen, lymph nodes, white cell counts, red cell counts, haemoglobin counts, or hematocrits following the dosing of rats with 1,000 or 10,000 mg/kg of food grade thymol for 19 weeks.

The toxicological database was insufficient to derive reference values (acceptable daily intake (ADI), acute reference dose (ARfD) or acceptable operator exposure level (AOEL)). As thymol is a naturally occurring compound in a variety of herbs and food, it is noted that reference values would only be needed if exposure through plant protection uses would exceed the estimated natural background exposure through food items for humans (EFSA 2012).

### Derivation of Maximum Acceptable Value

No MAV.

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# Tolclofos-methyl

CAS No. 57018-04-9. The IUPAC name for tolclofos-methyl is O-2,6-dichloro-p-tolyl O,O-dimethyl phosphorothioate. The CAS name is O-(2,6-dichloro-4-methylphenyl) O,O-dimethyl phosphorothioate. It is sometimes misspelt as toclofos-methyl, or toclophos-methyl, or tolclophos-methyl.

### Maximum Acceptable Value

Tolclofos-methyl is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Tolclofos-methyl is an organophosphorus (or chlorophenyl) fungicide. Tolclofos-methyl is very widely used for the control of seed-borne diseases in potatoes (FAO 1994). The product may be applied to the tubers at planting as a solid formulation or as a dip treatment. In some cases it is applied to the soil before planting, either as an overall incorporated treatment or in the furrow. In the method of use in most countries, pre-harvest intervals are fixed by the growth period of the crop. It can also be used on other vegetables.

Tolclofos-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The estimated soil half-lifes were between 9.3 and 60 days under aerobic and up to 80 days under anaerobic laboratory conditions. In field studies the total residue level in the top 7.5 cm layer of the soils decreased to about 17 percent and 7 percent of the initial concentration within 75 and 150 days after application. Under field conditions the calculated half-lifes in the soil ranged from about 7 to 39 days (FAO 1994). EFSA (2014) stated that according to the soil degradation studies evaluated in the framework of the peer review, DT90 values of tolclofos-methyl and its relevant soil metabolite (DM‑TM) are expected to be lower than 30 days and three days, respectively.

FAO (1994) lists 21 metabolites, but states that 27 metabolites have been detected in various soil types, with the major compounds (from aerobic soils) being 2,6-dichloro-4-methylphenyl dimethyl phosphate, 2,6-dichloro-4-methylphenyl methyl hydrogenphosphate, 2,6-dichloro-4-methylphenol, and O-(2,6-dichloro-4-methylphenyl)-O-methyl-O-hydrogen phosphorothioate. From anaerobic soils, p‑cresol (4-methylphenol), 2-chloro-4-methylphenol were also found. Note that the organic chemicals datasheet for 4-chloro-3-methylphenol states: the 2-chloro-4-methylphenol taste threshold in drinking-water to be <0.00005 mg/L, and the odour threshold to be 0.00015 mg/L.

Batch adsorption/desorption studies indicate a low potential for mobility in soil for tolclofos-methyl so is not expected to exceed the 0.1 μg/L trigger in ground water. In the water/sediment systems, tolclofos-methyl is relatively rapidly partitioned to sediment were it degrades mainly thought biotic processes. The main hydrolysis metabolites in water were 2,6-dichloro-4-methylphenol, and the demethyl derivative O-(2,6-dichloro-4-methylphenyl) O-methyl O-hydrogen phosphorothioate. The half-life in water may exceed a year, but in river and pond water, it is nearer four weeks.

Water solubility is about 1 mg/L.

NPIC (1994) quotes for tolclofos-methyl a soil half-life of 30 days, water solubility of 0.3 mg/L and a sorption coefficient (soil Koc) of 2,000. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

It is unlikely that either parent or degradation products would be present in soil in subsequent years or would reach groundwater when tolclofos-methyl has been applied according to GAP.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of tolclofos-methyl.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

Appropriate HPLC–MS/MS method exists for monitoring of tolclofos-methyl residues in water with a LOQ of 0.1 μg/L (EFSA 2018).

### Health considerations

The Acceptable Daily Intake (ADI) adopted in Australia for tolclofos-methyl is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg.

An ADI of 0.064 mg/kg bw has been developed based on the NOAEL of 6.4 mg/kg bw/day from the two-year toxicity study in mice (EFSA 2005/2014, EC 2006); an ARfD was not allocated.

The JMPR meeting (IPCS 1994) concluded that tolclofos-methyl is not genotoxic and there was no evidence of teratogenicity or carcinogenicity. An ADI of 0.07 mg/kg bw was established on the basis of a NOAEL of 50 ppm, equal to 6.5 mg/kg bw per day, in the 104-week study of toxicity and carcinogenicity study in mice, and a safety factor of 100.

EFSA (2017) deemed the data were sufficient to derive an acceptable daily intake (ADI) of 0.064 mg/kg body weight (bw) per day. No acute reference dose (ARfD) was deemed necessary. But EFSA (2018) adopted an ARfD of 0.14 mg/kg bw based on the NOAEL of 13.8 mg/kg bw per day for cholinesterase inhibition observed at 564 mg/kg bw per day on day 14 in the nine-month toxicity study in mice. An UF of 100 was applied.

### Derivation of Maximum Acceptable Value

No MAV.

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# Toltrazuril

CAS No. 69004-03-1. The IUPAC name for toltrazuril is 1-methyl-3-[3-methyl-4-[4-(trifluoromethylthio)phenoxy]phenyl]-1,3,5-triazinane-2,4,6-trione. The CAS name is (1‑(3-methyl-4`-trifluoromethyl-thiophenoxy)-phenyl)-3-methyl-1,3,5-triazine-2,4,6 (1H, 3H, 5H) trione.

### Maximum Acceptable Value

Toltrazuril is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.004 mg/L; excursions above this level even for a relatively short period are of concern, as the health-based guideline is partially based on short-term effects.

### Sources to water

Toltrazuril is a triazinetrione derivative used as anticoccidial agent. Toltrazuril damages the intracellular development stages of coccidia. It is widely used in chickens, turkeys and pigs for the prevention and treatment of coccidiosis (due to Eimeria), by administration via drinking water at 25 mg/L for continuous administration over 48 hours or at 75 mg/L for eight hours per day on two consecutive days; both treatments correspond to a dose of about 7 mg/kg/d. There are reports of toltrazuril being used to treat cryptosporidiosis, sometimes with monensin.

Toltrazuril appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Toltrazuril is highly water soluble: one formulation is sold as a 2.5 percent solution.

Toltrazuril (Baycox) is a veterinary medicine used to treat broilers and broiler breeders infected with a disease called coccidiosis. Although used to maintain the health of the flock, it also has environmental risks which can be avoided by taking some simple precautions. Toltrazuril is normally added directly to the birds’ drinking water and passes through them, deposited in their manure. If spread on to land the active ingredient will enter groundwater and can cause serious pollution to rivers and drinking water supplies. Spreading is the best environmental option, at a rate not greater than 1.5 tonnes per hectare per year (0.6 tons per acre). This is the maximum safe spreading rate to protect groundwater. This covers manure produced from when the treatment with Baycox® started, up until one week after the treatment has ceased (EA, UK).

The major metabolite is toltrazuril sulfone.

### Removal methods

Some newer advanced oxidation processes are expected to be effective at reducing the concentration of toltrazuril in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

Toltrazuril was assessed by the CVMP and a toxicological ADI of 0.002 mg/kg bw was established based on the threshold dose of 1 mg/kg bw/day for pre-neoplastic lesions retained from a carcinogenicity study in rats and applying a safety factor of 500 (EMEA 2004).

The Acceptable Daily Intake (ADI) adopted in Australia for toltrazuril is 0.01 mg/kg body weight, with a LOEL of 1 mg/kg from a two-year dietary study in rats. The LOEL is based on the occurrence of pre-neoplastic uterine lesions. The ADI incorporates a safety factor of 100.

### Derivation of Maximum Acceptable Value

No MAV.

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# Tolylfluanid

CAS No. 731-27-1. The IUPAC name for tolylfluanid is N-dichlorofluoromethylthio-N′,N′-dimethyl-N-p-tolylsulfamide. The CAS name is 1,1-dichloro-N-[(dimethylamino)sulfonyl]-1-fluoro-N-(4-methylphenyl)methanesulfenamide. Sometimes spelt (or misspelt?) tolyfluanid.

### Maximum Acceptable Value

Tolylfluanid is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

The Environmental Protection Authority of New Zealand ([www.epa.govt.nz](http://www.epa.govt.nz) and go to Substance Exposure Limit Register in Search our Databases) has established an environmental exposure limit (EEL) for tolylfluanid in water (set by an approval under Part 5 of the HSNO Act) of 0.00006 mg/L (0.06 µg/L).

EPA established an environmental exposure limit of 0.00006 mg/L (0.06 µg/L) for tolyfluanid in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Tolylfluanid is a [phenylsulfamide or haloalkylthio fungicide](http://www.alanwood.net/pesticides/class_fungicides.html#phenylsulfamide_fungicides) used for control of fungal disease in apples, grapes, hops and tomatoes. It can also be used against moulds to protect paint film on outdoor wooden surfaces, including pleasure craft (ECHA 2014). Tolylfluanid is closely related to dichlofluanid (qv).

Tolylfluanid appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 14.1 tonnes of tolylfluanid were used in New Zealand in 2004, at an application rate of 3,750 grams of active ingredient per hectare. Tolyfluanid is approved as an ingredient in anti-fouling paints for use in New Zealand (EPA 2013).

Tolylfluanid was one of the commoner agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA Food Residues Surveillance Programme), sometimes above the MRL in strawberries.

Tolylfluanid is no longer registered within the EU (EFSA 2013). It was registered for use in the European Union for use in/on apples, grapes and tomatoes.

### Forms and fate in the environment

A metabolite of tolylfluanid has been named as 4-dimethylaminosulphotoluidide (also called N,N-dimethyl-N’-p-tolylsulphamide or DMST). Another metabolite has been named as dimethylsulftoluidide. The half-life of tolylfluanid is less than a day, with the main metabolite being DMST.

ECHA (2014) discusses N,N-dimethylsulfamide (N,N-DMS), a persistent second degradation product of tolylfluanid. Concentrations of N,N-DMS can exceed the drinking water limit value of 0.1 μg/L. The main concern is related to water treatment and the possible formation of N-nitrosodimethylamine (NDMA, qv) during ozonation of groundwater containing N,N-DMS.

Tolylfluanid is of low water solubility, ie, 0.9 mg/L at 25°C (SRC 2007). It is expected to bind to sediment and suspended solids, based on an experimental log Kow of 3.9 (SRC 2007). Tolyfluanid is not expected to volatilise from water surfaces, based on an estimated Henry’s Law constant of 7.61 x10-7 atm.m3/mole and a vapour pressure of 1.5 x10-6 mm Hg (SRC 2007). Tolyfluanid is reported to be susceptible to hydrolysis, with reported hydrolytic half-lifes of 12 days, 5.6 days and 42.5 hours at pH 4, 7 and 9, respectively (EFSA 2005). Tolyfluanid is not expected to undergo photolysis and is reported not to be readily biodegradable (EFSA 2005). Copied from DWI (2008).

### Typical concentrations in drinking-water

The use of plant protection products containing tolylfluanid may lead to unacceptable concentrations of the metabolite N,N-dimethylsulfamide in groundwater (EFSA 2013). See Health Considerations.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See FAO. Tolylfluanid (162) explanation 381–5.

### Health considerations

The UK Pesticides Safety Directorate (PSD) has received information from the European Commission that the German Regulatory authorities have suspended a tolylfluanid-containing fungicide “Euparen M WG”. The suspension is on the basis that a newly-characterised metabolite of tolylfluanid, namely dimethylsulfamide, may in the course of treatment of water for the public supply, be converted into a nitrosamine. Nitrosamines are harmful to health and the product has been suspended whilst the risk is investigated. In the UK, PSD has been in contact with the approval holder Bayer Crop Science Limited who has voluntarily agreed to suspend sale and supply of the two approved products containing tolylfluanid – ‘Elvaron Multi’ (MAPP No 11422) and ‘Talat’ (MAPP No 11311) until these issues can be resolved. PSD has amended the approval of these products to [suspend approval](http://www.pesticides.gov.uk/uploadedfiles/Web_Assets/PSD/Tolylfluanid-0+0%20COPR%20suspension.doc) for sale, supply, advertisement and use with immediate effect.

JMPR established an ADI in 2002 of 0–0.08 mg/kg bw (INCHEM 2002). An acute reference dose of 0.5 mg/kg bw was established by the 2002 JMPR. JMPR (2003) states that for the estimation of dietary intake and compliance, report the sum of tolylfluanid and N,N-dimethyl-N’-(4-methylphenyl)sulfamide (DMST), expressed as tolylfluanid.

The chronic reference dose (RfD) is 0.026 mg/kg/d based on a NOAEL = 7.9 mg/kg/day, and a UF of 300 (USEPA 2002). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.026 mg/kg/d, and an ARfD of 0.17 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tolylfluanid is 1.7 mg/L.

An ADI for humans of 0 to 0.1 mg/kg bw has been developed (ICPS 1988), and adopted by the EC (2005), who also adopted an ARfD of 0.25 mg/kg/d. Reaffirmed in EFSA (2013).

The Acceptable Daily Intake (ADI) adopted in Australia for tolylfluanid is 0.1 mg/kg body weight, with a NOEL of 12.5 mg/kg.

On the basis of the results of the tests for genotoxicity and carcinogenicity in animals, the JMPR meeting concluded that tolylfluanid is unlikely to pose a carcinogenic risk to humans (INCHEM 2002).

The USEPA (2002) considered that tolylfluanid is “likely to be carcinogenic to humans” based on the following weight of the evidence considerations:

1 Tolylfluanid induced follicular cell thyroid tumours in high-dose male and female rats and were reproducible.

2 The weight of the evidence does not suggest that tolylfluanid is mutagenic. Although in vitro and in vivo mutagenicity assays found gene mutations and chromosomal aberrations in mammalian cells, the weight of them evidence does not support the mutagenic mode of action for the induction of thyroid tumours in rats.

3 Data are not adequate to support an alternative mode of action for the thyroid tumour induction.

### Derivation of Maximum Acceptable Value

No MAV.

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# Topramezone

CAS No. 210631-68-8. The IUPAC name for topramezone is [3-(4,5-dihydro-1,2-oxazol-3-yl)-4-mesyl-o-tolyl](5-hydroxy-1-methylpyrazol-4-yl)methanone. The CAS name is [3-(4,5-dihydro-3-isoxazolyl)-2-methyl-4-(methylsulfonyl)phenyl](5-hydroxy-1-methyl-1H-pyrazol-4-yl)methanone.

### Maximum Acceptable Value

Topramezone is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Topramezone is a [benzoylpyrazole](http://www.alanwood.net/pesticides/class_herbicides.html#benzoylpyrazole_herbicides) or [oxazole herbicide](http://www.alanwood.net/pesticides/class_herbicides.html#oxazole_herbicides) commonly used on cereals. Topramezone is a member of the class of herbicides known as HPPD inhibitors.

Topramezone appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at December 2013 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). EPA (2013) is an objection to the application to import into New Zealand a product containing topramezone.

### Forms and fate in the environment

In soil laboratory incubations under aerobic conditions in the dark, topramezone exhibited medium to very high persistence. Half-lifes in soil range from 11 to 69 days, and for metabolite M670H01, 25 to 75 days (EFSA 2014).

In two field leaching studies of up to four years duration at sites where topsoils were acidic (pH ca. 6) groundwater samples (depth 1.2 m or shallower and 1.9–3 m) had concentrations of topramezone and M670H01 at up to 0.061 μg/L and 0.016 μg/L respectively. Mobility of both substances was described as medium to very high, so represent a concern for groundwater in vulnerable aquifers.

In laboratory incubations in dark aerobic natural sediment water systems, topramezone exhibited moderate to very high persistence. In a water/sediment study carried out under outdoor conditions the metabolite M670H05 was a major transformation product accounting for 51 percent AR in the water of the system after 100 days.

Water solubility at pH 4 at 20°C is 510 mg/L, and at pH >9 it is >10 percent.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The Acceptable Daily Intake (ADI) adopted in EFSA (2014) for topramezone is 0.001 mg/kg body weight, based on a NOAEL of 0.5 mg/kg bw per day from the rabbit developmental studies, applying an increased uncertainty factor (UF) of 500. The acute reference dose (ARfD) is 0.001 mg/kg bw, based on the same NOAEL and UF as the ADI. The five times increased uncertainty factor was applied to account for the severe teratogenic effects observed at low dose levels in rabbits (1.5 mg/kg bw per day) giving a margin of safety of 500 to the overall developmental NOAEL and of 1,500 to the overall LOAEL for teratogenic effects in rabbits.

USEPA (2013) established a chronic RfD (and cPAD) of 0.004 mg/kg/d, and an acute RfD (and aPAD) of 0.008 mg/kg bw for infants and children and 0.005 for females  
13–49 years. The USEPA considered that topramezone is “not likely to be carcinogenic to humans at doses that do not alter rat thyroid hormone homeostasis”. They determined that the thyroid tumours arise through a non-linear mode of action, and the chronic reference dose (cRfD) is expected to be protective of alterations in hormone homeostasis that may result in thyroid tumour formation. Mutagenicity studies conducted on technical topramezone and its major metabolites did not demonstrate any mutagenic potential. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for topramezone is 0.165 mg/L.

APVMA adopted an ADI of 0.004 mg/kg/d for Australia. In June 2016 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

### Derivation of Maximum Acceptable Value

No MAV.

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# Toxaphene

CAS No. 8001-35-2. Toxaphene is also known as camphechlor, chlorocamphene, polychlorocamphene, and chlorinated camphene. Toxaphene is a reaction mixture of chlorinated camphenes containing 67–69 percent chlorine.

### Maximum Acceptable Value

There is no MAV for toxaphene in the DWSNZ. WHO (2004 and 2011) state that because toxaphene is unlikely to be found in drinking-water, the establishment of a guideline value is not deemed necessary.

The USEPA has set a drinking water standard (MCL) of 0.003 mg/L.

Toxaphene is a Priority Pollutant under the Clean Water Act (USA).

Toxaphene is one of the original 12 Persistent Organic Pollutants (POPs) under the Stockholm Convention; see <http://chm.pops.int/>. It also appears on the Rotterdam Convention (UNEP) list of chemicals in Appendix III (which effectively bans or severely restricts use of a chemical), see <http://www.pic.int/home.php?type=s&id=77>.

### Sources to water

Toxaphene is an insecticide which is currently banned for all uses in the United States (although in 1975 it was the most heavily used insecticide in the US). Toxaphene is a non-systemic contact and stomach insecticide, and piscicide (when added directly to water), containing over 670 polychlorinated bicyclic terpenes and chlorinated camphenes. It contains 67–69 percent chlorine by weight. It is usually found as a solid or gas, and in its original form it was a yellow to amber waxy solid that smelt like turpentine. It does not dissolve well in water, so it is more likely to be found in air, soil, or sediment at the bottom of lakes or streams, than in surface water. It s not registered for use in New Zealand as at 2008.

The median toxaphene concentration detected in ambient surface waters in the United States in 1980–1982, according to analyses of USEPA’s STORET water quality database, was 0.00005 mg/L.

### Forms and fate in the environment

Toxaphene is resistant to chemical and biological transformation in aerobic surface waters. It is not expected to undergo direct photolysis or photo-oxidation. Hydrolysis is also not an important fate process; a hydrolytic half-life of greater than 10 years for pH 5 to 8 at 25°C has been estimated. Toxaphene may be lost from the soil by evaporation, but, once it penetrates the soil, it is tightly bound to soil particles and very resistant to leaching. Detoxification of toxaphene in eight Wisconsin lakes was reported to be due to adsorption rather than biodegradation.

Water solubility has been reported from 0.4 to 3 mg/L.

NPIC (1994) quotes for toxaphene a soil half-life of 600 days, water solubility of 3 mg/L and a sorption coefficient (soil Koc) of 100,000. This resulted in a pesticide movement to groundwater rating of extremely low.

### Typical concentrations in drinking-water

Because neat technical toxaphene sorbs to particulates and is markedly hydrophobic, it has been argued that toxaphene would not be able to migrate more than about 10 cm down a soil profile, so would not be of concern as a groundwater contaminant. Such arguments tend to overlook the fact that technical toxaphene used as a pesticide was usually mixed with a hydrocarbon solvent (eg, xylene) as a carrier.

Toxaphene has been detected very rarely in drinking water supplies. Toxaphene concentrations ranged from 5 to 410 ppt (0.000005 to 0.0004 mg/L) in drinking-water samples collected in Flint Creek, Alabama, between 1959 and 1963.

Twenty-six water utilities in the US reported detecting toxaphene in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.0045 mg/L.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of toxaphene in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See section 6.2 in ATSDR (1996).

### Health considerations

Toxaphene is rapidly absorbed by the gastrointestinal tract. Toxaphene and its metabolites are excreted in the faeces and urine, and most of it is eliminated from the body within a few days.

As at July 2013 ATSDR (<http://www.atsdr.cdc.gov/mrls/index.html>) quotes a minimal risk level (MRL) of:

* 0.05 mg/kg/day for acute-duration oral exposure (1–14 days)
* 0.002 mg/kg/day for intermediate-duration oral exposure (15–364 days).

The reference dose or RfD (USEPA 2006/2009/2011) is 0.0004 mg/kg/d. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.01 mg/L.

IARC (1979) stated there is sufficient evidence that toxaphene is carcinogenic in mice and rats, and that in the absence of adequate data in humans, it is reasonable, for practical purposes, to regard toxaphene as if it presented a carcinogenic risk to humans. In 1987 IARC placed toxaphene in Group 2B – a probable human carcinogen.

No conclusive evidence is available to link cancer with toxaphene exposure in humans. However, a conclusive positive cancer bioassay was found for toxaphene administered to rodents in feed. A statistically-increased incidence of thyroid tumours was observed in rats and the incidence of hepatocellular tumours was significantly increased in mice. Based on these findings, USEPA has classified toxaphene as a B2, probable human carcinogen. The USEPA (2009/2011) quotes a health advisory of 0.003 mg/L for toxaphene, representing a 10-4 cancer risk.

Toxaphene appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

Toxaphene is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

No MAV.

The Minnesota Department of Health (MDH) has developed health-based rules and guidance to evaluate potential human health risks from exposures to chemicals in groundwater. The cancer health risk limit for toxaphene is 0.0003 mg/L.

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# Tralkoxydim

CAS No. 87820-88-0. The IUPAC name for tralkoxydim is (RS)-2-[(EZ)-1-(ethoxyimino)propyl]-3-hydroxy-5-mesitylcyclohex-2-en-1-one. The CAS name is 2‑[1‑(ethoxyimino)propyl]-3-hydroxy-5-(2,4,6-trimethylphenyl)-2-cyclohexen-1-one.

### Maximum Acceptable Value

Tralkoxydim does not have a MAV in the DWSNZ; and is mentioned in the WHO Guidelines.

### Sources to water

Tralkoxydim is a cyclohexene oxime or cyclohexanedione herbicide, applied in the US to actively growing weeds in wheat and barley to control wild oats, green foxtail, yellow foxtail, annual ryegrass (Italian) and persian darnel.

Tralkoxydim appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Contains 1,2-benzisothiazolin-3-one at 0.04 percent as a preservative.

### Forms and fate in the environment

Tralkoxydim hydrolysis is pH dependent with calculated half-lifes of 6.3 days at pH 5, 114 days at pH 7 and 1,594 days at pH 9. Volatilisation from moist soil surfaces and water is not expected to be an important fate based on an estimated Henry’s Law constant of 2.41 x 10-10 atm-cu m/mole. Tralkoxydim is not persistent to photodegradation in water, with calculated half-life was 19.3 days. A major degradate is tralkoxydim acid, reaching a maximum concentration of 12.5 percent of by 7–15 days post-treatment and declined to non-detectable concentrations by 30–65 days post-treatment. Soil adsorption/desorption data indicate that tralkoxydim and its degradates have low mobility at pH 5, but are very mobile in most of the tested soils at pH 9. The aerobic soil half life is five days. The dissociation constant (pKa) is 4.98 at 25°C.

Tralkoxydim shows rapid and extensive degradation in soil, producing a complex mixture of highly polar metabolites individually present at low level (EFSA 2015).

Tralkoxydim is not identified as a cause of impairment for any water bodies listed as impaired under section 303(d) of the Clean Water Act (USEPA 2011).

Solubility of tralkoxydim in water: 6 mg/L (pH 5.2), 7 mg/L (pH 6.5) and 8,850 mg/L (pH 9.0).

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The chronic Reference Dose (RfD) for tralkoxydim is 0.005 mg/kg/day. This value is based on the NOAEL of 0.5 mg/kg/day in the dog chronic feeding study with a 100‑fold safety factor to account for interspecies extrapolation (10x) and for intraspecies variability (10x). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.30 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tralkoxydim is 9.9 mg/L.

A DWLOC (drinking water level of concern) for cancer was calculated as 0.001 mg/L (USEPA 1998).

The following reference values have been finalised as part of the EC (2008) re‑evaluation: ADI 0.005 mg/kg bw/day, and ARfD 0.01 mg/kg bw. These values are quoted in EFSA (2015) too.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

In 1998 tralkoxydim is classified by the USEPA as “likely to be a human carcinogen” based on 1) the occurrence of rat benign Leydig cell tumours at all dose levels, 2) the lack of an acceptable carcinogenicity study in a second species, and 3) the relevance of the testicular tumours to human exposure cannot be discounted. The classification was changed in 2004 to “suggested evidence of carcinogenicity but not sufficient to assess human carcinogenic potential”. USEPA (2011) classified tralkoxydim as “suggestive evidence of carcinogenicity, but not sufficient to assess human potential”. There was no mutagenicity concern for tralkoxydim based on the available data.

Tralkoxydim was shown to be negative in assays for gene mutation in bacteria, forward gene mutation in mouse lymphoma cells in culture, chromosome damage in human lymphocyte cells, for DNA damage in rat hepatocytes, and for chromosome damage in vivo mouse micronuclei.

The USEPA (2005) concludes that there is a reasonable certainty that no harm will result from aggregate exposure to tralkoxydim residues from correct usage, and that there are no metabolites of toxicological concern associated with tralkoxydim.

### Derivation of Maximum Acceptable Value

No MAV.

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# Triadimefon and Triadimenol

Triadimefon: CAS No. 43121-43-3. The IUPAC name for triadimefon is (RS)-1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)butan-2-one. The CAS name is 1‑(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)-2-butanone.

Triadimenol: CAS No. 55219-65-3. The IUPAC name for triadimenol is (1RS,2RS;1RS,2SR)-1-(4-chlorophenoxy)-3,3-dimethyl-1-(1H-1,2,4-triazol-1-yl)butan-2-ol. The CAS name is β-(4-chlorophenoxy)-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol. Triadimenol appears as isomer A and isomer B, and the isomers comprise diastereomers SS, SR, RR. The manufacturing process is conducted to provide an A:B ratio around 80:20. See JMPR (2007 and 2011) for further information and CAS numbers.

Triadimefon is sometimes called tridimefon, and triadimenol is sometimes called tridimenol and triademenol (possibly in error). A trade name for triadimefon is bayleton.

### Maximum Acceptable Value

Triadimefon and triadimenol do not have a MAV in the DWSNZ; neither is mentioned in the WHO Guidelines.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.09 mg/L for triadimefon; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Triadimenol is often co-formulated with a wide range of other products.

Triadimefon and triadimenol contain an impurity, 4-chlorophenol (qv). Triadimefon should not contain more than 0.5 percent of 4-chlorophenol, and triadimenol should not contain more than 5 g/kg of 4-chlorophenol.

### Sources to water

Triadimefon and triadimenol are systemic conazole (N-substituted triazole) contact and systemic fungicides, inhibiting fungal sterol biosynthesis, and are often found in formulations with other fungicides. They are used to control powdery mildews, rusts and other fungal pests on cereals, fruits, vegetables, turf, shrubs and trees.

Triadimefon is reduced within plants to form triadimenol. While both forms are fungitoxic, the fungitoxicity of triadimefon depends on the rate at which it converts to triadimenol, which is the more active fungicide.

Triadimenol is mainly used as a seed treatment in the US. In Australia it is used to control ring spot on cabbage, cauliflower and broccoli. In Europe it is used on grapes.

Triadimefon and triadimenol appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Triadimenol has been found above the maximum residue limit in New Zealand fruits and vegetables, eg, tamarillos and spring onions (NZFSA).

### Forms and fate in the environment

In a sandy loam type of soil half of the initial amount of tridimefon was lost within 18 days. In loamy soil the half-life was about six days.

In water with a pH 3.0, 6.0, or 9.0, almost 95 percent of the tridimefon remained after 28 weeks. Triadimefon in sterile water solutions was found to be essentially stable at all temperature and pH conditions (pH 3 – pH 9), but under simulated natural sunlight in sterile aqueous solution triadimefon degraded rapidly with an experimental half-life of 7.6 hours; the experimental half-life corresponds to a calculated sidereal half-life of 1.4 days. The compound is very stable in water and does not readily undergo hydrolysis. Once it reaches groundwater, triadimenol is likely to degrade even more slowly than the parent compound.

Solubility of triadimefon in water: about 65 mg/L at 20ºC; triadimenol about 80 mg/L.

NPIC (1994) quotes for triadimefon a soil half-life of 26 days, water solubility of 71.5 mg/L and a sorption coefficient (soil Koc) of 300. This resulted in a pesticide movement to groundwater rating of moderate.

NPIC (1994) quotes for triadimenol a soil half-life of 300 days, water solubility of 47 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of moderate.

See JMPR (2007) for discussion on metabolites.

### Removal methods

Adsorption to certain soil types suggests that treatment processes that remove particulate matter may be effective at reducing the concentration of triadimefon in water, particularly in conjunction with activated carbon.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

A number of two-year studies have indicated that there are several toxic responses to low to moderate doses of triadimefon. Long-term studies of triadimefon in several species (rat, mouse, dog) over a range of doses indicated a reduction in body weight, changes in red blood cell counts, and an increase in blood cholesterol levels. Triadimefon has been associated with changes in the liver, decreased kidney weights, and altered urinary bladder structure in laboratory animals exposed to 18 to 60 mg/kg/day. Increased liver weights may be seen as an adaptation to toxic stress, rather than a toxic endpoint related to exposure. There is evidence that acute effects on the central nervous system may also occur.

The endpoint of concern for triadimefon and triadimenol is neurotoxicity, which was observed in rat, mice, and rabbit studies. Since no appropriate acute endpoint could be determined from the triadimenol database, the triadimefon subchronic neurotoxicity study in rats was chosen for the acute reference dose (ARfD) for triadimenol, as well.

EXTOXNET and IPCS quote an ADI for triadimefon in humans of 0–0.03 mg/kg bw. The USEPA chronic RfD for triadimefon and triadimenol is 0.034 mg/kg/day. The cPAD is 0.0034 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.034 mg/kg/d, and an ARfD of 0.034 mg/kg/d for triadimefon. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for triadimefon is 0.34 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.0034 mg/kg/d, and an ARfD of 0.0034 mg/kg/d for triadimenol. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for triadimenol is 0.034 mg/L.

Triadimenol and triadimefon are related substances and follow the same metabolic pathways in all matrices investigated. The ADI and ARfD apply to each product. In 2004 JMPR established an ADI of 0–0.03 mg/kg bw based on the NOAEL of 3.4 mg/kg bw per day for hyperactivity in a 13-week feeding study on neurotoxicity with triadimefon in rats and with a safety factor of 100. They established an ARfD of 0.08 mg/kg bw based on the NOAEL of 2 mg/kg bw for hyperactivity in a study of acute neurotoxicity in rats treated with triadimefon by gavage using a safety factor of 25 because the effects were Cmax-dependent and reversible.

IPCS and the EC quote an ADI for triadimenol in humans of 0–0.05 mg/kg bw; EC (2008) also adopted an ARfD of 0.05 mg/kg/d. EFSA (2016) reports the same ADI and ARfD.

The Acceptable Daily Intake (ADI) adopted in Australia for triadimefon is 0.03 mg/kg body weight, with a NOEL of 2.5 mg/kg bw from a long-term rat dietary study. The NOEL is based on haematological effects. The ADI incorporates a safety factor of 100.

The Acceptable Daily Intake (ADI) adopted in Australia for triadimenol is 0.06 mg/kg body weight, with a NOEL of 6.25 mg/kg bw.

The Acceptable Daily Intake (ADI) adopted in JMPR (2014) for triadimenol is 0.03 mg/kg body weight, and an ARfD of 0.08 mg/kg bw. Definition of the residue in plant and animal commodities (for the estimation of dietary intake and for compliance with MRLs): sum of triadimefon and triadimenol.

The Cancer Assessment Review Committee (CARC) assigned triadimefon and triadimenol a classification of Category C “possible human carcinogens”. As a result, a quantitative cancer risk assessment was not appropriate. Triadimefon appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

The triadimefon Category C (possible human carcinogen) classification is based on statistically significant increase in thyroid adenomas in male Wistar rats and statistically significant increases in hepatocellular adenomas in both sexes of the NMRI mouse.

The triadimenol Category C classification is based on increased incidence of hepatocellular adenomas in females.

The toxicity databases for triadimefon and triadimenol did not show any estrogen, androgen, or thyroid mediated toxicity.

The triazole fungicides, which include triadimefon, triadimenol, and propiconazole (see datasheet), and others, share the common metabolites 1,2,4-triazole, triazole alanine, and triazole acetic acid (also known as free triazoles). The risks associated with the free triazoles are all below the USEPA’s level of concern. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite.

The USEPA acute one-day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L. See datasheet for triazole metabolites for latest ADI and ARfD.

USEPA (2015) found that based on weight of evidence considerations, mammalian or wildlife EDSP Tier 2 testing is not recommended for triadimefon since there was no convincing evidence of potential interaction with the estrogen, androgen or thyroid pathways.

### Derivation of Maximum Acceptable Value

No MAV.

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# Tri-allate

CAS No. 2303-17-5. The IUPAC name for tri-allate is S-2,3,3-trichloroallyl diisopropyl(thiocarbamate). The CAS name is S-(2,3,3-trichloro-2-propenyl) bis(1‑methylethyl)carbamothioate.

Also called triallate.

### Maximum Acceptable Value

Tri-allate does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Tri-allate is a pre- or post-emergence selective thiocarbamate soil-incorporated herbicide used to control grass weeds in field and pulse crops. It is sometimes applied with other products, eg, trifluralin and isoproturon.

Tri-allate appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

The main impurities are bis-(2,3,3-trichloroallyl) sulfide (CAS No. 25647-79-4, <1.5 percent); 1,1,1,2,2,3-hexachloropropane (CAS No. 24425-97-6, <1 percent); bis-(2,3,3-tri-chloro-allyl) disulfide (CAS No. 82709-38-4, <1 percent); S-(3,3-dichloroallyl)-N,N-diisopropylthiocarbamate (<0.7 percent); and S-(2,3,3-trichloroallyl)-N-ethyl-N-isopropylthiocarbamate (<0.7 percent) – (IPCS 1994).

### Forms and fate in the environment

Tri-allate is relatively resistant to hydrolysis and photodegradation. Triallate adsorbs well to loam and clay soils (Koc = 2,400 g/mL) and is not readily dissolved in water. This information indicates that tri-allate is not likely to move through the soil, even though it has a lengthy soil half-life of 82 days. IPCS (1994) states that the soil half-life of tri-allate varies widely, depending on factors such as temperature, humidity, and organic matter content. Values from 3 to 195 days have been cited. Because of its strong tendency to be adsorbed on soil particles, tri-allate has a low leachability and partitioning to sediments represents a major sink in the environment.

However, if there is significant moisture and/or low levels of organic matter in the soil, triallate may become desorbed, from soil particles. Leaching and groundwater contamination is possible in such situations. The USEPA suggests that triallate does not pose a threat to the environment due to leaching because it is generally used where the water table is relatively low. In areas of heavy rainfall, or where the water table is near the surface, triallate could enter the groundwater.

The main removal processes would appear to be bacterial degradation and volatilisation. The metabolite TCPSA (2,3,3-trichloroprop-2-ene sulfonic acid), which is produced in significant quantities, is more mobile than the parent triallate (Koc = 35 mL/g) and is moderately persistent in soil (half-life = 66 days) (USEPA 2001).

Solubility in water: about 4 mg/L at 20ºC

NPIC (1994) quotes for triallate a soil half-life of 82 days, water solubility of 4 mg/L and a sorption coefficient (soil Koc) of 2,400. This resulted in a pesticide movement to groundwater rating of low.

### Removal methods

The strong soil adsorption suggests that treatment processes that remove particulate matter should be effective at reducing the concentration of tri-allate in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

In general, thiocarbamates, the chemical class in which triallate is included, are rapidly absorbed into the bloodstream from the gastrointestinal tract, readily broken down into polar metabolites and then excreted by treated animals. It is rarely possible to detect thiocarbamates in the blood. Although triallate is a carbamate, it does not inhibit cholinesterase activity.

In general, the RfD for chronic oral exposure is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime. The RfD is 0.013 mg/kg/d bw, based on a NOAEL of 1.275 mg/kg/day in a two-year dog feeding study (USEPA 1987).

USEPA (2001) revised this NOAEL to 2.5 mg/kg/d based on decreased survival in males and females, decreased mean body weights in males, and increased adrenal weights in males in the two-year chronic toxicity/carcinogenicity study in rats at the LOAEL of 12.5 mg/kg/day from which they derived a chronic (non-cancer) RfD of 0.025 mg/kg/day. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.025 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for triallate is 1.65 mg/L.

The metabolite TCPSA (2,3,3-trichloroprop-2-ene sulfonic acid) presents health concerns so is included with triallate in the US regulatory literature.

The EC (2009) derived an ADI for tri-allate of 0.025 mg/kg/d bw, and an ARfD of 0.6 mg/kg/d. The EC review established that for the active substance notified, the manufacturing impurity NDIPA (N-nitroso-diisopropylamine) is considered to be of toxicological concern and a maximum level of 0.02 mg/kg is established.

The Acceptable Daily Intake (ADI) adopted in Australia for triallate is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw.

Triallate is classified as a Group C chemical (possible human carcinogen), based on hepatocellular carcinomas in male mice, with a positive trend and borderline significance in female mice, and increased incidence of renal tubular cell adenomas in rats (USEPA 2001).

Reproductive, teratogenic, mutagenic and carcinogenic effects are unlikely at concentrations likely to be found in water.

### Derivation of Maximum Acceptable Value

No MAV.

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# Triazole metabolites

These are generally considered to include, with IUPAC names:

* 1,2,4‐triazole (1,2,4‐T) CAS 288-88-0 1H‐1,2,4‐triazole
* triazole alanine (TA) CAS 86362-20-1 3‐(1H‐1,2,4‐triazol‐1‐yl)‐D,L‐alanine
* triazole acetic acid (TAA) CAS 28711-29-7 1H‐1,2,4‐triazol‐1‐ylacetic acid
* triazole lactic acid (TLA) CAS 1450828-63-3 (2RS)‐2‐hydroxy‐3‐(1H‐1,2,4‐triazol‐1‐yl)propanoic acid

Triazole lactic acid is also called triazole hydroxypropionic acid. Triazolylypyruvic acid sometimes gets a mention.

### Maximum Acceptable Value

The triazole metabolites do not have a MAV in the DWSNZ, and are not mentioned in the WHO Guidelines.

### Sources to water

These are the common metabolites of 18 triazole active fungicides:

bromuconazole, cyproconazole, difenoconazole, epoxiconazole, fenbuconazole, fluquinconazole, flusilazole, flutriafol, ipconazole, metconazole, myclobutanil, paclobutrazol, penconazole, propiconazole, prothioconazole, tebuconazole, tetraconazole, triticonazole.

Others include azaconazole, hexaconazole, triadimefon, triadimenol and uniconazole.

The extent to which these common metabolites are formed in each crop or in environmental matrices is dependent on the particular triazole‐containing active substance and the way in which it is used.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

1,2,4-Triazole, triazole alanine, triazole acetic acid, triazole pyruvic acid and triazole lactic acid are the common metabolites derived from triazole-containing fungicides that act by inhibiting sterol synthesis. Triazole pyruvic acid doesn’t get much publicity in the literature.

EFSA( 2018) set an ADI for:

**1,2,4‐Triazole** at 0.023 mg/kg body weight (bw) per day based on the no‑observed‐adverse‐effect‐level (NOAEL) of 6.9 mg/kg bw per day, considering the decreased body weight gain in the newly submitted 12‐month rat study. At the same time an increased uncertainty factor (UF) of 300 was applied to cover the lack of a developmental neurotoxicity (DNT) study and carcinogenicity and dog studies. The RMS disagreed with such proposal, since they considered it to be more appropriate to set an ADI at 0.05 mg/kg bw per day based on the NOAEL of 15 mg/kg bw per day observed in the rat two‐generation study and by applying an UF of 300.

**Triazole alanine** was set at 0.3 mg/kg bw per day based on the NOAEL of 30 mg/kg bw per day, taking into account the increased incidence of hyoid angulated alae in fetuses observed in the newly submitted rabbit developmental study. An UF of 100 was applied.

**Triazole acetic acid** was set at 1 mg/kg bw per day, based on the NOAEL of 100 mg/kg bw per day in the newly submitted rat two‐generation (parental toxicity: decreased body weight gain and food consumption) and rabbit developmental studies (decreased body weight gain and food consumption for maternal and developmental toxicity, plus stomach mucosal erosions or ulceration for developmental toxicity), applying an UF of 100.

**Triazole lactic acid** was set at 0.3 mg/kg bw per day by bridging from the reference values for triazole alanine as a worst case approach for triazole lactic acid.

EFSA( 2018) set an ARfD for:

**1,2,4‐Triazole** at 0.1 mg/kg bw based on the NOAEL of 30 mg/kg bw per day from the rabbit developmental toxicity studies. An increased UF of 300 was applied to cover the lack of a DNT study and to ensure a sufficient margin of safety in relation to the lowest‐observed‐adverse‐effect level (LOAEL) for developmental effects.

**Triazole alanine** was set at 0.3 mg/kg body weight (bw).

**Triazole acetic acid** was set at 1 mg/kg bw.

**Triazole lactic acid** was set at 0.3 mg/kg bw

### Derivation of Maximum Acceptable Value

No MAVs.

### Bibliography

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# Triazophos

CAS No. 24017-47-8. The IUPAC and CAS name for triazophos is O,O-diethyl O-1-phenyl-1H-1,2,4-triazol-3-yl phosphorothioate. Sometimes called hostathion and methoxone – could be trade names.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because triazophos is unlikely to be found in drinking-water, the establishment of a guideline value is not deemed necessary.

### Sources to water

Triazophos is a broad spectrum organophosphorus insecticide and acaricide. It has strong contact poisoning and great permeability to plant tissues. It is usually used to control cutworms, noctuids, plant nematodes, pine moths and Lepidoptera pests in fruit trees and vegetables.

The technical grade is usually about 85 percent active ingredient. Triazophos does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register). This pesticide appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

Sixty-four days after application, 17 and 63 percent of parent triazophos remained in sand and sandy loam respectively. Triazophos tends to be held by soil particles so it is not expected to reach high concentrations in groundwater.

If released to soil, triazophos is expected to have moderate mobility based upon a Koc of 355. Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 3.1 x 10-8 atm-cu m/mole. Triazophos has measured biodegradation half-lifes of 2 to 87 days in various soils under different environmental conditions. If released into water, triazophos is expected to adsorb to suspended solids and sediment based upon the Koc. Triazophos had a half-life of 27 days in seawater and <35 to 47 days in surface water, however, no distinction was made between losses due to biodegradation, hydrolysis, adsorption, or photolysis. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. An estimated BCF of 74 suggests the potential for bioconcentration in aquatic organisms is moderate. Hydrolysis half-lifes of 30 to 250 days were measured for triazophos in water at 25°C and photodegradation half-lifes of 21 days and 67 days were measured for river water and sea water, respectively (EAWAG accessed February 2015).

Solubility of triazophos in water: about 40 mg/L at 20°C.

### Removal methods

Treatment processes that remove particulate matter should reduce the concentration of triazophos.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The 2002 JMPR established an ADI of 0–0.001 mg/kg bw and ARfD of 0.001 mg/kg bw. These values were reaffirmed in JMPR (2013).

The estimate of acceptable daily intake of triazophos for humans (NOAEL) 0.001 mg/kg body weight.

Long-term carcinogenicity studies in rats and mice at dietary concentrations of 0, 3, 27, or 243 mg/L and 0, 6, 30 or 150 mg/L demonstrated that triazophos has no carcinogenic potential in either species. The genotoxic potential of triazophos was assessed in an adequate range of tests in vitro and in a test for micronucleus formation in mice in vivo. The 2002 JMPR meeting concluded that triazophos is unlikely to pose a genotoxic hazard in vivo. On the basis of the absence of carcinogenic effects in mice and rats and the overall weight of evidence from the genotoxicity studies, the meeting concluded that triazophos is unlikely to pose a carcinogenic risk to humans.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Tribenuron

CAS No. 106040-48-6. The IUPAC name for tribenuron is 2-[4-methoxy-6-methyl-1,3,5-triazin-2-yl(methyl)carbamoylsulfamoyl]benzoic acid. The CAS name is 2-[[[[(4-methoxy-6-methyl-1,3,5-triazin-2-yl)methylamino]carbonyl]amino]sulfonyl]benzoic acid.

The commercial product is tribenuron-methyl (sometimes called Express), CAS No. 101200-48-0. Also called metometuron.

### Maximum Acceptable Value

Tribenuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Tribenuron-methyl is a triazinylsulfonylurea herbicide, which operates as an inhibitor of amino acid synthesis, used for post-emergence control of broad-leaved weeds in spring and winter cereals.

Tribenuron-methyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

The half-life of tribenuron-methyl in soil can be up to 14 days. Degradation in the soil occurs by hydrolysis and by direct microbial degradation. Hydrolysis is affected by soil pH, being faster in acidic than alkaline soils. Volatilisation is not expected to contribute significantly to the dissipation of tribenuron-methyl in the environment, as indicated by the low vapour pressure. A major metabolite is N-methyl triazine amine (4-methoxy-6-methyl-1,3,5-triazin-methylamine) which is more mobile and more persistent than the parent compound.

EFSA (2013) states that the DT90 values for some tribenuron-methyl metabolites were shown to exceed the DT90 trigger value of 100 days. Tribenuron-methyl shows very high to high mobility in soil. See EFSA (2017) for information about metabolites in soil and water.

Solubility in water is 50 mg/L (pH 5), 2,000 mg/L (pH 7) at 20ºC, and 18,000 at pH 9, which suggests it is fairly mobile and could enter groundwater.

NPIC (1994) quotes for tribenuron methyl a soil half-life of 12 days, water solubility of 280 mg/L and a sorption coefficient (soil Koc) of 46. This resulted in a pesticide movement to groundwater rating of moderate.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The oral Reference Dose (RfD) for Express is 0.008 mg/kg/d, based on observing elevated serum bilirubin and AST levels, increased urinary volume in a one-year dog feeding study (USEPA 1990). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.008 mg/kg/d for tribenuron-methyl. The USEPA chronic (lifetime) HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for tribenuron methyl is 0.056 mg/L (no acute one-day value available.)

The following reference values have been finalised as part of the EC (2005) re‑evaluation of tribenuron-methyl: ADI: 0.01 mg/kg-bw/day, and ARfD: 0.2 mg/kg-bw/day. Reaffirmed in EFSA (2013/2017).

The EC (2005) review established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. The Theoretical Maximum Daily Intake (TMDI; excluding water and products of animal origin) for a 60 kg adult is <0.4 percent of the Acceptable Daily Intake (ADI), based on the FAO/WHO European Diet (August 1994). Additional intake from water and products of animal origin are not expected to give rise to intake problems.

The Acceptable Daily Intake (ADI) adopted in Australia for tribenuron-methyl is 0.01 mg/kg body weight, with a NOEL of 0.95 mg/kg bw.

Tribenuron-methyl has not been evaluated by the FAO/WHO JMPR or the WHO IPCS. As at September 2008 the USEPA has classified tribenuron-methyl in Group C: a possible human carcinogen.

### Derivation of Maximum Acceptable Value

No MAV.

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# Trichlorfon

CAS No. 52-68-6. The IUPAC name for trichlorfon is dimethyl (RS)-2,2,2-trichloro-1-hydroxyethylphosphonate or (RS)-2,2,2-trichloro-1-(dimethoxyphosphinoyl)ethanol. The CAS name is dimethyl (2,2,2-trichloro-1-hydroxyethyl)phosphonate.

Trichlorfon is a racemic mixture of two isomers. Also called metrifonate, chlorofos or dimethyltrichlorohydroxyethyl phosphonate; occasionally spelt trichlorphon, or misspelt as trichlorofon. The butyrate ester has its own ISO common name, [butonate](http://www.alanwood.net/pesticides/butonate.html). Trichlorfon has many trade names.

### Maximum Acceptable Value

WHO (2004 and 2011) states that because trichlorfon is unlikely to be found in drinking-water, the establishment of a guideline value is not deemed necessary.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.007 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

### Sources to water

Trichlorfon is an broad spectrum systemic organophosphate insecticide used to control cockroaches, crickets, silverfish, bedbugs, fleas, cattle grubs, flies, ticks, leafminers and leaf-hoppers. It is applied to vegetable, fruit and field crops; livestock; ornamental and forestry plantings; in agricultural premises and domestic settings; in greenhouses, and for control of parasites of fish in designated aquatic environments. It is also used as an anthelminthic for treating domestic animals for control of internal parasites.

Formulations containing trichlorfon have been registered for use in New Zealand since 1968. The products containing trichlorfon that are currently (2009) registered for agricultural and veterinary medicine use in New Zealand are Neguvon 98 percent, Trifon and Partna. From 1 June 2011 trichlorfon for use on plants may no longer be imported into, or manufactured in, New Zealand. Trichlorfon can continue to be used as a veterinary medicine (an ectoparasiticide), but with stricter controls.

The main impurities are 2,2-dichlorovinyl dimethyl phosphate, ie, dichlorvos  
(0–0.2 percent), trichloroacetaldehyde (0–0.05 percent), dichloroacetaldehyde  
(0–0.03 percent), methyl hydrogen 2,2,2-trichloro-1-hydroxyethylphosphonate, demethyl trichlorfon (0–0.3 percent), and water (less than 0.3 percent). The technical product also contains phosphoric acid, 2,2,2-trichloro-1-hydroxyethylphosphonic acid, and dimethyl phosphate (IPCS 1991).

### Forms and fate in the environment

Trichlorfon appears to be stable under acid conditions; the half-life was 31 minutes at pH 9 and 34 hours at pH 7, but was 104 days at pH 5. Trichlorfon breaks down, or degrades, rapidly in aerobic soils, in which it has half-lifes between 3 and 27 days under nonsterile conditions. Dichlorvos (qv) and dichloroacetaldehyde are significant degradation products. Volatilisation from water and moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 1.7 x 10-11 atm-cu m/mole. If released into water, trichlorfon is not expected to adsorb to suspended solids and sediment based upon the Koc. Complete biodegradation of trichlorfon in river water occurred within five days at 10 mg/L, 13 days at 20 mg/L, and 20 days at 30 mg/L.

Solubility in water: at least 12 percent at 20°C. The half-life in water is 1–2 days.

NPIC (1994) quotes for trichlorfon a soil half-life of 10 days, water solubility of 12 percent and a sorption coefficient (soil Koc) of 10. This resulted in a pesticide movement to groundwater rating of high.

### Typical concentrations in drinking-water

Trichlorfon does not adsorb strongly to soil particles, and it is very mobile in soils of varying textures and organic contents. It is therefore likely to contaminate groundwater.

### Removal methods

Some newer advanced oxidation processes are expected to be effective at reducing the concentration of trichlorfon in water.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

### Health considerations

The reported trichlorfon intakes are far below the Acceptable Daily Intake (ADI) established by FAO/WHO and should not constitute a health hazard for the general population (IPCS 1992).

The absorption, distribution and excretion of trichlorfon is rapid. About 70–80 percent of a dose administered orally to mice was excreted during the first 12 hours following treatment. Dichlorvos (DDVP) is a breakdown product of trichlorfon. The preliminary human health risk assessment indicated the possibility of drinking water and inhalation exposures of concern from the degradation of trichlorfon into DDVP from trichlorfon turf use. However, since the preliminary risk assessment was written, the registrant for trichlorfon submitted soil dissipation data which indicated that, under predominant soil pH conditions, the actual rate at which trichlorfon degrades into DDVP is significantly lower than assumed in the preliminary risk assessment. As a result, the USEPA (2006) does not believe that there will be significant drinking water or inhalation exposures to DDVP from the use of trichlorfon on turf.

The chronic dietary RfD is quoted by USEPA (2006) to be 0.002 mg/kg/d based on a NOAEL of 0.2 mg/kg/d from chronic toxicity studies on the monkey. The population adjusted dose (PaD) is 0.0002 mg/kg/d (the most highly exposed population subgroup is children 1–6 years). The DWLOC (Drinking Water Level of Comparison) represents the maximum peak concentration of trichlorfon that may occur in water without a risk concern. The acute DWLOC is 0.312 mg/L for all populations and 0.082 mg/L for children 1–6 years old. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.002 mg/kg/d, and an ARfD of 0.10 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for trichlorfon is 1.0 mg/L.

Trichlorfon, like other organophosphates, causes neurotoxic effects at low concentrations following both acute and chronic exposure.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.002 mg/kg body weight, with a NOEL of 0.2 mg/kg bw from a long-term (10-year) dietary study in monkeys. The NOEL is based on inhibition of cholinesterase. The ADI incorporates a safety factor of 100.

IARC (1983) stated that the available data are insufficient to evaluate the carcinogenicity of trichlorfon to humans, ie, Group 3. The USEPA decided in 1999 that trichlorphon was likely to be carcinogenic to humans at high doses, but not likely to be carcinogenic at low doses; this is repeated in their September 2008 list.

### Derivation of Maximum Acceptable Value

No MAV.

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# Triclopyr

CAS No. 55335-06-3. The IUPAC name for triclopyr is 3,5,6-trichloro-2-pyridyloxyacetic acid. The CAS name is [(3,5,6-trichloro-2-pyridinyl)oxy]acetic acid. Triclopyr TEA is the triethylamine salt formulation of the herbicide triclopyr, CAS No. 60825-27-6. Sometimes spelt trichlopyr.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of triclopyr in drinking-water should not exceed 0.1 mg/L.

The WHO guidelines do not mention triclopyr.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.02 mg/L; excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

EPA established an environmental exposure limit of 0.059 mg/L (59 µg/L) for triclopyr in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Triclopyr, a substituted pyridine (a pyridinecarboxylic acid), may enter source waters as a result of its application as a broad spectrum systemic foliar herbicide, used as an ester (usually the butoxyethyl ester) or salt (usually the triethylamine salt), to control woody plants (eg, gorse, broom, blackberry, lupin and other brushweeds) and many broadleaved weeds in mainly non-crop areas. Unlike a similar product, 2,4,5-T, there is no possibility of dioxin impurities occurring in triclopyr.

Some trade names for herbicides containing this product are Garlon, Turflon, Access, Redeem, Crossbow, Grazon and ET. The herbicide may be mixed with picloram or with 2,4-D to extend its utility range. It is used in New Zealand to control Tradescantia (wandering willie).

Triclopyr appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The total annual usage of triclopyr in New Zealand in the late 1980s was 27,500 kg with the majority of use being in the South Island. ERMA notes that 44 tonnes of triclopyr were used in New Zealand in 2004, at an application rate of 6000 grams of active ingredient per hectare. It is sold as the triethylamine salt (solubility 23 percent) and the butoxyethyl ester (solubility 7 mg/L); both forms degrade quite rapidly to triclopyr acid.

Four herbicides (metsulfuron methyl, haloxyfop methyl, imazapyr isopropylamine and triclopyr triethylamine (TEA)) have been approved by the New Zealand Environmental Protection Agency (EPA) for restricted use over water, by authorised agencies, under a set of conditions (Auckland City 2013); EPA (2014).

#### 1 From treatment processes

No known sources.

#### 2 From the distribution system

No known sources.

### Forms and fate in the environment

If released to soil, triclopyr is expected to have high to very high mobility based on its Koc results ranging from 1.5 to 134. Volatilisation from moist soil surfaces is not expected to be an important fate process based on an estimated Henry’s Law constant of 9.8 x 10-5 Pa.m3/mole. Triclopyr undergoes fairly rapid biodegradation in soil with an average half-life of 46 days. In natural soil and in aquatic environments, two of the formulations convert rapidly to the acid which in turn is neutralised to a salt. Triclopyr is not adsorbed strongly to soil particles, and is degraded fairly rapidly by soil micro-organisms, with half-lifes of 8 and 18 days in silty clay loam and silt loam soils, respectively. Triclopyr is persistent under anaerobic conditions with a half-life of approximately 1,300 days. Concentrations of 500 mg/L had no apparent effects on the growth of common soil micro-organisms.

The half-life of triclopyr in soil is from 30 to 90 days, depending on soil type and environmental conditions, with an average of about 46 days. The half-life of one of the breakdown products (3,5,6-trichloro-2-pyridinol) in 15 soils ranged from 8–279 days with 12 of the tested soils having half-lifes of less than 90 days. Longer half-lifes occur in cold or arid conditions.

Water solubility is 440 mg/L and the sorption coefficient is 20 mL/g. If released into water, triclopyr is not expected to adsorb to suspended solids and sediment based on its range of Koc values. Triclopyr degraded slowly in a soil: water system incubated aerobically; the half-life is 142 days. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. Breakdown by the action of sunlight is the major means of triclopyr degradation in water. The half-life is 10 hours at 25°C (NPIC states 1 to 10 days). The major metabolites are trichloropyridinol (3,5,6-trichloro-2-pyridinol – comparable in toxicity to triclopyr), 5-chloro-3,6-dihydroxy-2-pyridinoloxyacetic acid, and oxamic acid. Details of degradation products can be downloaded from Ganapathy (1997), and AWWARF (2008).

Triclopyr is translocated readily throughout a plant after being taken up by either roots or the foliage. Cowberries with residues of 2.4 mg/L at six days had 0.7–1.1 mg/L at  
30–36 days, and 0.2–0.3 mg/L in 92–98 days. The estimated half-life in above ground drying foliage as in a forest over story is two to three months.

NPIC (1994) quotes for triclopyr amine salt a soil half-life of 46 days, water solubility of 210 percent and a sorption coefficient (soil Koc) of 20. This resulted in a pesticide movement to groundwater rating of very high. The triclopyr ester has a half-life of 46 days, water solubility of 23 mg/L and a sorption coefficient (soil Koc) of 780. This resulted in a pesticide movement to groundwater rating of low.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 296 zones, found triclopyr in two zones at concentrations of 0.0001 and 0.0006 mg/L (<1 percent of the MAV), with the median concentration being “nd” (limit of detection = 0.0001 mg/L). The P2 programme in 2001 found a sample with trichlopyr at 0.1 percent of its MAV (ESR 2001).

Triclopyr has been found four times in groundwaters, in Waikato, Nelson, Marlborough and Canterbury, ranging from 0.00002 to 0.2 mg/L (MAF 2006).

Triclopyr was tested but not found in a host of groundwater sites throughout the country (Williams et al 1998).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Triclopyr occurred at 0.02 µg/L, ie, 0.00002 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Triclopyr occurred at 0.14 to 0.3 µg/L, ie, up to 0.0003 mg/L.

### Removal methods

No information on methods of removing triclopyr from water is available; any triclopyr adsorbed to soil particles should be removed by treatment processes that remove particulate matter, particularly if assisted by activated carbon, otherwise trials with newer advanced oxidation processes may be needed. GAC should also be effective.

### Recommended analytical techniques

#### Referee method

No referee method has been given for triclopyr because no method meets the required criteria.

#### Some alternative methods

1. Liquid/Liquid Extraction and Gas Chromatography with Electron Capture Detector (APHA 6640B, although this is not listed in the 2005 edition).

### Health considerations

When rats were dosed intravenously at 5 mg/kg, most of the dose was excreted in urine. At 100 mg/kg urinary excretion still predominated. At higher doses, an increasing amount was in the faeces. In dogs, 0.5 mg/kg of triclopyr had a half-life of 14 hours for clearance from blood plasma, and a dose of 20 mg/kg had a half-life of 95 hours reflecting the unique capacity for excretion of organic acids by the dog. Excreted triclopyr is mostly the parent compound but small quantities of breakdown products are also present.

Triclopyr was found in greater quantities in the liver and fatty tissue of the rat when compared with the blood plasma. The dog had higher levels in the kidney than in the blood plasma, and in monkeys, residues in all tissues were the same as in blood plasma. The compound is not expected to concentrate to any significant degree in the tissues of animals.

#### Acute poisoning

The oral LD50 of triclopyr in rats ranges from 630 to 729 mg/kg and from 2,000 to 3,000 mg/kg for various formulated products. Similar differences were noted for skin toxicity in the rabbit. The LD50 for the technical material was greater than 2,000 mg/kg and greater than 4,000 mg/kg for the formulations. Inhalation of triclopyr (technical) did not affect rats but inhalation of some of the formulations did cause nasal irritations. A similar result was seen when rabbit eyes were exposed. The technical material had only a slight effect on rabbit eyes and the undiluted formulated material caused significant eye irritation. Other oral LD50 values for triclopyr are 550 mg/kg in the rabbit and 310 mg/kg in the guinea pig.

Triclopyr is slightly toxic to mallard ducks. When fed the compound, the LD50 was 1,698 mg/kg. Bobwhite quail and Japanese quail fed for eight days had LC50s of 2,935 ppm and 3,278 ppm, respectively.

The compound is practically non-toxic to fish. Triclopyr has a LC50 of 117 ppm for rainbow trout and a 96-hour LC50 of 148 ppm for bluegill sunfish. The compound is practically non-toxic to the aquatic invertebrate Daphnia magna, a water flea (LC50 for the triclopyr salt of 1,170 ppm). The compound is non-toxic to bees.

#### Chronic exposure

Rats fed diets containing between 3 and 30 mg/kg/day of triclopyr experienced no ill-effects. Males fed much higher doses (100 mg/kg) had decreased liver and body weight and increased kidney weight. The male mice were also sensitive at moderate doses. They had reduced liver weight at 60 mg/kg/day. Monkeys fed small amounts of triclopyr (30 mg/kg/day) had no adverse effects.

USEPA (1998) quotes a RfD of 0.05 mg/kg/d based upon the two-generation reproduction toxicity study in rats with a NOEL of 5.0 mg/kg/day; an uncertainty factor of 10 for interspecies differences in response and an uncertainty factor of 10 for intraspecies differences in response was applied. The acute NOEL was calculated at 30 mg/kg/day USEPA (1998) proposed that a provisional RfD of 0.03 mg/kg/day be used for 3,5,6-trichloro-2-pyridinol based on a one-year dog study with a NOEL of 3 mg/kg/day and an uncertainty factor of 100 for intra and interspecies variability.

USEPA (1998) reports an acute RfD (also = aPAD) of 1 mg/kg/d, and a chronic RfD (also = cPAD) of 0.05 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.05 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for triclopyr 1.65 mg/L.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.005 mg/kg body weight, with a NOEL of 0.5 mg/kg bw from a long-term dietary study in dogs. The NOEL is based on histopathological changes in the kidney. The ADI incorporates a safety factor of 100.

EC (2006) established an ADI of 0.03 mg/kg/d and an ARfD of 0.3 mg/kg/d.

Triclopyr fed to rabbits daily at low to moderate doses (25 to 100 mg/kg) caused some maternal toxicity and death but not foetal toxicity or birth defects. The maternal mortality was inconsistent with other studies. There is not enough data to draw any conclusion about the reproductive hazards of triclopyr due to chronic exposure in humans.

Pregnant rats given moderate doses (up to 200 mg/kg/day) on days 6–15 of gestation had offspring with mild fetotoxicity, but no birth defects. There were no teratogenic effects in rabbits treated in a similar manner at 10 or 20 mg/kg/day. The evidence suggests that the human risk of birth defects is fairly low due to chronic exposure to triclopyr.

Both bacteria and isolated cells did not mutate in response to the presence of triclopyr. Another mutagen study using rats was weakly positive, but negative in mice, the more sensitive species. There were no chromosome changes noted in rat bone marrow. Triclopyr is not considered to be mutagenic.

Rats and mice fed low levels (3 to 30 mg/kg/day) of triclopyr for two years showed no carcinogenic response. Even though the mice did have a high incidence of lymph cancer, this incidence was apparently characteristic of the particular strain of mice and did not represent a dose-related effect. As at September 2008 the USEPA has classified triclopyr in Group D: not classifiable as to human carcinogenicity.

### Derivation of Maximum Acceptable Value

The provisional MAV for triclopyr in drinking-water was derived by the MoH using a tolerable daily intake approach as follows:

3 mg/kg body weight/day x 70 kg x 0.1 = 0.105 mg/L (rounded to 0.1 mg/L)

2 L/day x 100

where:

* no observable adverse effect level = 3 mg/kg body weight per day from a two-year feeding study in rats
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for intra and inter-species variation)

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# Trifloxystrobin

CAS No. 141517-21-7. The IUPAC name for trifloxystrobin is methyl (E)-methoxyimino-{(E)-α-[1-(α,α,α-trifluoro-m-tolyl)ethylideneaminooxy]-o-tolyl}acetate.

The CAS name for trifloxystrobin is methyl (αE)-α-(methoxyimino)-2-[[[[(1E)-1-[3-(trifluoromethyl)phenyl]ethylidene]amino]oxy]methyl]benzeneacetate.

### Maximum Acceptable Value

Trifloxystrobin does not have a MAV in the DWSNZ, and WHO does not mention trifloxystrobin in the Guidelines.

### Sources to water

Trifloxystrobin is a strobilurin foliar fungicide used on cereals, vegetables and fruits. It often occurs with other pesticides (Bayer 2008). The mode of action of trifloxystrobin involves inhibition of mitochondrial respiration in fungi.

Trifloxystrobin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register), and was found above its default MRL in celery in an extensive study of New Zealand foods in 2007 (NZFSA Food Residues Surveillance Programme).

### Forms and fate in the environment

Soil half-lifes have been reported from 2–12 days. EFSA (2013) states that the DT90 value of trifloxystrobin based on the field and laboratory studies is less than 100 days. However, for the metabolite CGA 321113, the DT90 value is more than 500 days and for CGA 373466, a relevant soil metabolite, the DT90 value is up to 290 days.

The experimental photolytic half-lifes of trifloxystrobin in sterile aqueous buffered solutions (pH 5 and pH 7) under a xenon arc light (12 hours light followed by 12 hours dark intervals) were found to be 20.4 hours at pH 5 and 25°C and 31.5 hours at pH 7 and 25°C corresponding to predicted environmental half-lifes under natural summer sunlight at geographical latitude of 40°N of 1.1 and 1.7 days at pH 5 and pH 7 respectively. Dark controls at 25°C showed a half-life of 3.1 years at pH 5 and 27.4 days at pH 7.

Hydrolytic half-lifes at pH 5 can be measured in years; at pH 7 in weeks; at pH 9 in days. In the biologically active aquatic system of a paddy rice plot trifloxystrobin was rapidly degraded in both flooding water and soil, with a maximum half-life of about two to five days.

See JMPR (2004b) for discussion on metabolites. The major metabolite detected in all plants studied after one year was trifluoroacetic acid which accounted for up to 65.7 percent of the total residue (EFSA 2013).

Trifloxystrobin in water is relatively stable hydrolytically under sterile neutral and weakly acid conditions, whereas under alkaline conditions hydrolytic degradation increases with increasing pH. The free form of the acid metabolite, CGA-321113, appears to be a mobile and persistent metabolite that can be further degraded but at a slower rate than the parent compound. Trifloxystrobin has a low water solubility (about 0.6 mg/L), independent of pH.

In laboratory incubations in dark aerobic natural sediment water systems, trifloxystrobin exhibited low persistence, forming the major metabolite CGA 321113 (maximum 77 percent AR in water and 51 percent AR in sediment) exhibiting high to very high persistence (EFSA 2017).

EFSA (2017) reports that the potential for groundwater exposure as represented by 80th percentile annual average concentrations leaving the top 1 m soil layer above the parametric drinking water limit of 0.1 μg/L consequent to the uses assessed, was assessed as high for the relevant metabolites CGA 321113, NOA 413161 and NOA 413163 in geoclimatic situations represented by all nine FOCUS groundwater scenarios, leading to a critical area of concern.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

See JMPR (2004b).

### Health considerations

A chronic feeding study on the dog showed a NOAEL of 5 mg/kg/d because increased liver weight and hepatocellular hypertrophy were observed at the LOAEL of 50 mg/kg/day (USEPA 1999). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.038 mg/kg/d, and an ARfD of 2.5 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for trifloxtstrobin is 82.5 mg/L.

An ADI of 0.1 mg/kg body weight was derived (EC 2003) based on a two-year rat study, incorporating a safety factor of 100, adding that the setting of an ARfD was considered not necessary. EFSA (2012, 2013 and 2014) confirmed these values.

EFSA (2017) retained that ADI, and introduced an ARfD of 0.5 mg/kg bw based on skeletal anomalies in the rabbit developmental study.

The JMPR 2004 meeting adopted an ADI of 0–0.04 mg/kg/d, and decided that it was unnecessary to establish an ARfD for trifloxystrobin. These values were confirmed in FAO/WHO (2013) and JMPR (2015, 2017).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.05 mg/kg body weight, with a NOEL of 5 mg/kg bw. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

As at September 2008, trifloxystrobin has been classified by the USEPA as “not likely to be carcinogenic to humans”. The USEPA (1999) found that acute and chronic (non-cancer) aggregate risk and short- and intermediate-term occupational worker risk estimates for trifloxystrobin do not exceed the USEPA’s level of concern.

EFSA (2017) states that following a scientific assessment trifloxystrobin is considered unlikely to be an endocrine disruptor in mammals.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Trifloxysulfuron sodium

CAS No. 199119-58-9. The IUPAC name for trifloxysulfuron sodium is 1‑(4,6‑dimethoxypyrimidin-2-yl)-3-[3-(2,2,2-trifluoroethoxy)-2-pyridylsulfonyl]urea, sodium salt. The CAS name is N-[[(4,6-dimethoxy-2-pyrimidinyl)amino]carbonyl]-3-(2,2,2-trifluoroethoxy)-2-pyridinesulfonamide, sodium salt.

The CAS No. for trifloxysulfuron, the free acid form, is 145099-21-4.

### Maximum Acceptable Value

Trifloxysulfuron sodium does not have a MAV in the DWSNZ, and WHO does not mention trifloxysulfuron sodium in the Guidelines.

### Sources to water

Trifloxysulfuron sodium is a sulfonyl urea or [pyrimidinylsulfonylurea](http://www.alanwood.net/pesticides/class_herbicides.html#pyrimidinylsulfonylurea_herbicides) class of herbicide used to control sedges, grasses and broadleaf weeds. It is sold in New Zealand as Monument which contains 100 g/L (10 percent) trifloxysulfuron sodium and is applied at up to 0.3 L/ha. It is sold as Envoke in Australia.

As at late 2016, the New Zealand importer is applying for approval for the use of trifloxysulfuron sodium for use on turf.

### Forms and fate in the environment

The metabolism of trifloxysulfuron sodium when applied to an aerobic loam soil at 0.03 mg ai/kg soil was biphasic with an initial rapid disappearance with a 5.3–5.4 day half-life followed by a slower 96–108 day half-life. The overall DT50 and DT90 values were 30–50 and 250–300 days, respectively. Main metabolites were CGA 53052, CGA 382997, the amine CGA 368733 and CGA 368732 with the proposed pathway the same as for hydrolysis. When applied to four soils (two loams and two loamy sands) at 0.2 mg ai/kg soil, the DT50 and DT90 values were 66–78 and 220–260 days. A silt loam treated with 0.2 mg ai/kg soil and incubated aerobically had DT50 and DT90 values of 49 and 164 days, respectively, at 20°C and 40 percent maximum water holding capacity (MWC); when the MWC was reduced to 20 percent, these values increased to 123 and 408 days, respectively. The major metabolites were CGA 368732, CGA 368733, the sulfonyl guanidine NOA 440735, CGA 382997 and the guanidine NOA 443300. In adsorption/desorption studies in five soils, the mobility of trifloxysulfuron sodium was high to very high. The desorption KOC values were higher than the adsorption values, indicating that once adsorbed to soil, the compound does not desorb as easily. The metabolite CGA 382997 was also found in the leachate from soils. Therefore, it is reasonable to expect that heavy rainfall or irrigation shortly following trifloxysulfuron sodium application would result in residues in run-off from treated areas (APVMA 2002).

Photolysis was not an important removal process in aqueous solution as half-lifes of 14–17 and 18–19 days for irradiated and dark control treatments, respectively, showed that hydrolysis was more dominant in the pH 7 buffered solutions. Photolysis on soil surfaces was slower with irradiated and dark control half-lifes of 34–35 and 54–60 days, respectively (APVMA 2002).

Trifloxysulfuron sodium hydrolyses relatively quickly at acidic pH values with a half-life of 5.6–6.0 days at pH 4 and 20°C. At pH 5, the half-life was longer at 11.5–12 days while at environmentally relevant pH 7 it was slow at 37–41 days. The main degradation products at pH 4 and 5 were the urea CGA 368732, the pyrimidine amine CGA 53052 and the sulphonamide CGA 382997 (APVMA 2002).

Natural river and pond water-sediment systems dosed at 0.05 mg ai/L degraded trifloxysulfuron sodium with DT50 values of 5.2–10.6 days in the water only and 23–26 days in the whole systems. Major metabolites were CGA 368732 (with a DT50 of 29–67 days in the whole system) and NOA 436664 in both systems. A natural lake water-sediment system treated at 0.029 mg ai/L showed DT50 and DT90 values of 14 and 48 days in the whole water-sediment system, respectively, and 16 and 58 days in the water only. Metabolites were similar to other studies (APVMA 2002).

Trifloxysulfuron sodium water solubility is dependent on pH: 102 mg/L at pH 5.4 and 25,500 mg/L at pH 7.6. The vapour pressure at 25°C is <1 x 10-6 Pa. the octanol/water partition coefficient at pH 7 is log Pow = -0.42. Henry’s Law constant (mean) = 2.6 x 10‑5 m3/mol (APVMA 2002).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Trifloxysulfuron has low acute oral toxicity in both rats and mice (LD50 >5,000 mg/kg bw).

The ADI for trifloxysulfuron was established at 0.2 mg/kg bw/day based on a NOEL of 1.5 mg/kg bw/day in a 12-month dog dietary study, and using a 100-fold safety factor in recognition of the extensive toxicological database available for trifloxysulfuron. An ARfD of 6 mg/kg bw was established using the dose (600 mg/kg bw) at which no effects were observed in an acute oral neurotoxicity study in rats, and using a safety factor of 100 (APVMA 2002). In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

For chronic dietary exposure, the chronic RfD (cRfD) is from a combined chronic/ carcinogenicity study in rats and is based on increased tubular atrophy in the kidneys at the LOAEL of 99.3 mg/kg/day (NOAEL = 23.7 mg/kg/day); the cRfD = 0.237 mg/kg/d. For acute dietary exposure (general population), an acute neurotoxicity study in rats is being used to calculate the acute reference dose (aRfD) of 6.0 mg/kg/day; an aRfD of 0.5 mg/kg/d was derived for females aged 13–49 (USEPA 2008).

Trifloxysulfuron-sodium is classified as “not likely to be carcinogenic to humans”. Technical grade trifloxysulfuron-sodium did not demonstrate any mutagenic potential in a battery of 5 mutagenicity studies. There is not a concern for mutagenicity resulting from exposure to trifloxysulfuron-sodium (USEPA 2008).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

APVMA. 2002. *Evaluation of the New Active Trifloxysulfuron Sodium in the Product Envoke Herbicide*. National Registration Authority for Agricultural and Veterinary Chemicals [48 pp]. <http://apvma.gov.au/sites/default/files/publication/14086-prs-trifloxysulfuron.pdf>

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# Triflumuron

CAS No. 64628-44-0. The IUPAC name for triflumuron is 1-(2-chlorobenzoyl)-3-(4-trifluoromethoxyphenyl)urea. The CAS name is 2-chloro-N-[[[4-(trifluoromethoxy)phenyl]amino]carbonyl]benzamide. It has been misspelt as triflumoron.

### Maximum Acceptable Value

Triflumuron does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

N,N’-bis-[4-(trifluoromethoxy)phenyl]urea, 4-trifluoro-methoxyaniline, and toluene are relevant impurities. The maximum content in the technical material for N,N’-bis[4-(trifluoromethoxy)phenyl]urea should not be higher than 1 g/kg (FAO 2000) and for 4‑trifluoro-methoxyaniline it should not be higher than 5 g/kg. The maximum content for toluene has been agreed by mammalian toxicology to be 50 g/kg (EFSA 2011).

### Sources to water

The insecticide triflumuron is a benzoylurea or benzoylphenylurea product that inhibits chitin synthesis. It is used for the control of the house fly indoors for professional users. It is applied to locations in livestock and poultry houses where insects breed such as litter, the surface of manure, cesspools and bedding materials (ECHA 2015).

Triflumuron appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see [https://eatsafe.nzfsa.govt.nz/web/public/acvm-register and select entire register](http://www.nzfsa.govt.nz/acvm/registers-lists/acvm-register/index.htm)). One approved product is mixed with propoxur.

From September 2010, triflumuron will not be allowed to be used in the EU because it has not been possible to perform an acute risk assessment for the metabolite M07, because data was not sufficient to allocate an acute reference dose for this metabolite. Moreover, data were missing to determine an appropriate residue definition and to estimate the level of residues in processed fruit commodities. In addition, a high risk to aquatic organisms has been identified (EU 2009).

### Forms and fate in the environment

Triflumuron has a half-life in soils of about two to three weeks. It is not persistent in natural waters either, half-life less than a week. Significant metabolites are [(4‑trifluoromethoxy)phenylurea](http://sitem.herts.ac.uk/aeru/iupac/Reports/857.htm) (CAS No. 82971-90-2) and [2-chlorobenzoic acid](http://sitem.herts.ac.uk/aeru/iupac/Reports/1243.htm) (CAS No. 118-91-2). EFSA (2011) adds that triflumuron is low to moderately persistent in soil under dark aerobic conditions. Triflumuron was stable to hydrolysis at pH 5 and 7 and degrades with a half-life between 29 and 57 days at pH 9. In water sediment systems triflumuron partitioned to the sediment (DT50 = 4.1–7.1 days).

Following use of the formulated product in an animal house, potential exposure of the active substance to soil could arise via land applications of manure following storage. Subsequent leaching from affected areas could then result in loadings to surface water and groundwater (ECHA 2015).

Water solubility of triflumuron is about 0.04 mg/L, [(4-trifluoromethoxy)phenylurea](http://sitem.herts.ac.uk/aeru/iupac/Reports/857.htm) about 13,000 mg/L, and [2-chlorobenzoic acid](http://sitem.herts.ac.uk/aeru/iupac/Reports/1243.htm) about 3,700 mg/L.

### Recommended analytical techniques

#### Some alternative methods

See EFSA (2011) – LOQ = 0.03 μg/L.

### Health considerations

The Acceptable Daily Intake (ADI) adopted in Australia for triflumuron is 0.007 mg/kg body weight, with a NOEL of 0.7 mg/kg bw. IUPAC quotes an ADI of 0.014 mg/kg/d bw.

EC (in <http://ec.europa.eu/sanco_pesticides/public/index.cfm>) reports an ADI of 0.014 mg/kg/d bw, with the comment that an ARfD was not applicable, quoting an EFSA source. EFSA (2011, 2014, 2017) confirm these values, based on the overall NOAEL of the 90-day rat studies and applying a safety factor of 100. Plant metabolite and impurity M07 (4-trifluoro-methoxyaniline) was shown to be more acutely toxic than triflumuron and an ARfD of 0.005 mg/kg bw was proposed (a separate ADI not established as not necessary.

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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WHO. 2004. *Guidelines for Drinking-water Quality 2004* (3rd edition). Geneva: World Health Organization. Available at: [http://www.who.int/water\_sanitation\_health/dwq/guidelines/en/](http://www.who.int/water_sanitation_health/dwq/gdwq3/en/print.html). See also the addenda.

# Trifluralin

CAS No. 1582-09-8. The IUPAC name for trifluralin is α,α,α-trifluoro-2,6-dinitro-N,N-dipropyl-p-toluidine. The CAS name is 2,6-dinitro-N,N-dipropyl-4-(trifluoromethyl)benzenamine. Also called 4-(trifluoromethyl)-2,6-dinitro-N,N-dipropylaniline.

### Maximum Acceptable Value

Based on health considerations, the concentration of trifluralin in drinking-water should not exceed 0.03 mg/L.

WHO (2017) states that some impure technical grades of trifluralin could contain potent carcinogenic compounds and therefore these grades should not be used.

The maximum acceptable concentration for trifluralin in Canada is 0.045 mg/L.

The USEPA (2006/2009/2011) established a lifetime health advisory of 0.01 mg/L, where the lifetime health advisory is the concentration of a chemical in drinking water that is not expected to cause any adverse non-carcinogenic effects for a lifetime of exposure, and is based on exposure of a 70-kg adult consuming two litres of water per day. The Lifetime HA for Group C carcinogens includes an adjustment for possible carcinogenicity.

The *Australian Drinking Water Guidelines* (NHMRC, NRMMC 2011) include a guideline value of 0.09 mg/L; minor excursions above this level would need to occur over a significant period to be a health concern, as the health-based guideline is based on long-term effects.

Trifluralin should not contain more than 1 mg/kg of N-nitroso-di-n-propylamine (JMPR 1988).

### Sources to water

Trifluralin is a dinitroaniline pre-plant herbicide used for pre-emergence selective weed control in many crops including barley, peas, oilseed rape, and many others. It can be formulated in combination with many other pesticides. Technical-grade trifluralin may be contaminated with N-nitrosodi-n-propylamine (see datasheet in the organic chemicals section); many countries regulate the total nitrosamine content.

Trifluralin was found in 172 of 2,047 surface water samples and in one of 507 groundwater samples in the USA, with concentrations rarely exceeding 0.0005 mg/L. The 85th percentile of the levels in all non-zero surface water samples was 0.00054 mg/L.

Trifluralin appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). The total annual usage of trifluralin in New Zealand in the late 1980s was 7,800 kg with the majority of use being in the South Island. The highest usage was in the Ashburton County (3,300 kg). ERMA notes that 19 tonnes of trifluralin were used in New Zealand in 2004, at an application rate of 1,200 grams of active ingredient per hectare. It is no longer allowed to be used in the UK.

### Forms and fate in the environment

Trifluralin is somewhat volatile, with a vapour pressure of 0.006 Pa at 20°C and a Henry’s Law constant of 4.0 Pa m3/mol. In soil it undergoes photodecomposition, volatilisation, and biodegradation with soil half-lifes ranging from 20 to 132 days. The average soil half-life is six to eight months. The sorption coefficient is 8,000 mL/g. Trifluralin has a moderately high log octanol-water partition coefficient of 3 and a bioconcentration factor in aquatic organisms of up to 1,000 under conditions of constant exposure. Although it binds strongly to soils with high organic content, only up to 10 percent is adsorbed in sandy soils with low organic content. Because of trifluralin’s limited solubility and strong soil adsorption, the USEPA considered it unlikely to leach into groundwater.

Trifluralin has a very low water solubility (0.3 mg/L) with high soil affinity and is relatively immobile. Photodecomposition, volatilisation and microbial degradation are the principal processes responsible for the removal of trifluralin from surface water; each process has a half-life of a few days to a few weeks. Biodegradation and photodegradation processes may give rise to polar metabolites that may contaminate drinking-water sources.

NPIC (1994) quotes for trifluralin a soil half-life of 60 days, water solubility of 0.3 mg/L and a sorption coefficient (soil Koc) of 8,000. This resulted in a pesticide movement to groundwater rating of very low.

USGS (2006) give the following values: log Kow = 5.34; log Koc (where Koc is in mL/g) = 4.14; water solubility = 0.5 mg/L; Henry’s Law constant (KH in Pa.m3/mol) expressed as log KH = 1.00; half-life in aerobic soil = 169 days; half-life in water = >32 days.

See USEPA (1996) for discussion on the main degradation products.

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme, sampled from 343 zones, did not find any trifluralin at detectable concentrations (limit of detection = 0.0002 mg/L) (ESR 2001).

In 1987, trifluralin was detected in several municipal water supplies in Saskatchewan at trace (nanogram per litre) levels. It was not detected in drinking water supplies of 77 municipalities in Manitoba or Alberta (detection limits 0.05 to 0.5 µg/L). Trifluralin was detected in one of 91 wells at 0.041 mg/L in a 1984 survey in southern Ontario. Trifluralin has occasionally been detected at trace levels (below 0.001 mg/L) in surface waters in Manitoba. Trifluralin was not detected (detection limit 0.0001 mg/L) in an eight-week sampling of irrigation water in southern Saskatchewan (Health Canada 1989, edited 1992).

Trifluralin has been found twice in Otago groundwaters, ranging from 0.00002 to 0.0003 mg/L (MAF 2006).

In their second Pesticides in Groundwater Survey, ESR detected pesticides in 16 of the 118 wells tested; a few wells had more than one pesticide. No pesticides were above their MAV and 78 percent contained <1 µg/L. Nine herbicides and one fungicide were detected. The triazine group which includes atrazine, propazine, simazine and terbuthylazine were detected in 11 of the wells (Close 1996). Trifluralin occurred at 0.3 µg/L, ie, 0.0003 mg/L.

In their third Pesticides in Groundwater Survey, ESR detected pesticides in 33 of the 95 wells tested; 18 wells had more than one pesticide. Only three pesticides (cyanazine, MCPA and mecoprop) were found above their MAV, all in one well which was down-gradient of a known point source of contamination. Twenty pesticides and two triazine metabolites were detected; 76 percent of the detections were of pesticides in the triazine group (Close 2001). Trifluralin occurred at 0.02 µg/L, ie, 0.00002 mg/L.

Trifluralin was not detected in the small number of drinking-water samples analysed; it has been detected in surface water at concentrations above 0.0005 mg/L but rarely in groundwater (WHO 2004).

Five water utilities in the US reported detecting trifluralin in tap water since 2004, according to EWG’s analysis of water quality data supplied by state water agencies, with the highest concentration being 0.00008 mg/L.

### Removal methods

Granular activated carbon treatment down to 0.001 mg/L should be achievable (WHO 2004/2011/2017). Due to the strong soil adsorption and low water solubility conventional treatment (alum coagulation, sedimentation, filtration), and possibly air stripping, can also remove trifluralin from water effectively.

### Recommended analytical techniques

#### Referee method

Liquid/Liquid Extraction and Gas Chromatography with an Electron Capture Detector (EPA 508).

#### Some alternative methods

No alternative methods have been recommended for trifluralin because no methods meet the required criteria. See WHO (2003) for further information.

### Health considerations

Oral doses of trifluralin are not absorbed readily by the gastrointestinal tract of the rat. The absorbed fraction of trifluralin is metabolised extensively and trifluralin and its metabolites are excreted principally in faeces. Higher levels of trifluralin were found in fat than in the liver.

Toxic effects in animals associated with long-term exposure to trifluralin include slightly increased mean body weight gain, slight change in plasma lipids, and a statistically significant increase in liver weight.

The reference dose or chronic RfD (USEPA 2006/2009/2011) is 0.02 mg/kg/d as determined from a one-year feeding study in dogs; the NOEL was 2.4 mg/kg/day, using a safety factor of 100. The Drinking Water Equivalent Level or DWEL (USEPA 2006/2009/2011) is 0.7 mg/L. The oral RfD had earlier been 0.0075 mg/kg/d (USEPA 1989).

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2.5 mg/kg bw from a two-generation study in rats. The NOEL is based on decreased foetal and parental weights. The ADI incorporates a safety factor of 100.

The toxicological profile of trifluralin was evaluated in the framework of Directive 91/414/EEC, which resulted in an ADI being established at 0.015 mg/kg bw per day. An ARfD was not deemed necessary (EFSA 2013).

The International Agency for Research on Cancer has evaluated technical-grade trifluralin and classed it in Group 3 (not classifiable as to its carcinogenicity to humans). A number of long-term carcinogenicity/toxicity studies with pure (>99 percent) test material have not demonstrated evidence of carcinogenicity. Trifluralin of high purity does not possess mutagenic properties. Technical trifluralin of low purity may contain nitroso contaminants and has been found to be mutagenic.

In the USA, use of trifluralin was associated with an increased risk for non-Hodgkin’s lymphoma. A study of ovarian cancer in Italy did not suggest an association with trifluralin exposure. Both results were based on small numbers of exposed subjects. A larger US study (USEPA 1989) showed no association with occurrence of cancer. As at September 2008 the USEPA has classified trifluralin in Group C: a possible human carcinogen. The USEPA (2009/2011) quotes a health advisory of 0.4 mg/L for trifluralin, representing a 10-4 cancer risk.

USEPA (2015) concluded that based on weight of evidence considerations, mammalian EDSP Tier 2 testing is not recommended for trifluralin since additional testing is unlikely to impact the current EPA established regulatory endpoints for human risk assessments.

### Derivation of Maximum Acceptable Value

A tolerable daily intake approach has been used for the derivation of the MAV for trifluralin in drinking-water. The no-observable-adverse-effect level used in the derivation was established for mild hepatic effects from a one-year feeding study in dogs.

The MAV for trifluralin in drinking-water was derived as follows:

0.75 mg/kg body weight/day x 70 kg x 0.1 = 0.0263 mg/L (rounded to 0.03 mg/L)

2 L/day x 100

where:

* no observable adverse effect level = 0.75 mg/kg body weight per day for mild hepatic effects in a one-year feeding study in dogs
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of tolerable daily intake allocated to drinking-water = 0.1
* uncertainty factor = 100 (for inter and intra-species variation).

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# Triforine

CAS No. 26644-46-2. The IUPAC name for triforine is N,N′-{piperazine-1,4-diylbis[(trichloromethyl)methylene]}diformamide. The CAS name is N,N′‑[1,4‑piperazinediylbis(2,2,2-trichloroethylidene)]bis[formamide].

### Maximum Acceptable Value

Triforine does not have a MAV in the DWSNZ; triforine is not mentioned in the WHO Guidelines.

### Sources to water

Triforine is a systemic amide (piperazine derivative) fungicide, used for control of powdery mildew, rusts, black rot and scab. In the US, triforine was marketed for use on almonds, apples, asparagus, blueberries, cherries, hops, ornamentals, peaches and roses, and has a USEPA toxicity classification of I (highly toxic). Since 1996, triforine has not been used on food crops in the US. Triforine has been in formulations mixed with carbendazim, permethrin, mancozeb, and bupirimate. It is mainly used in products for domestic use, such as for the control of black spot, rust and powdery mildew on roses.

Triforine appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

Triforine appears in the EU “clear out” list (Directive 91/414/EEC) so should have come off the European market during 2008.

### Forms and fate in the environment

If released to soil, triforine is expected to have very moderate mobility based upon a Koc range of 200–527. Volatilisation from moist soil surfaces is not expected to be an important fate process based on an estimated Henry’s Law constant of 3.85 x 10-4 Pa.m3/mole. Triforine is moderately persistent in soil with a half-life of one to several months and it degrades rapidly in water through hydrolysis and photolysis with half-lifes of several days. A range of non-fungitoxic metabolic end-products are formed, presumably including piperazine. It is considered non-persistent in soil.

If released into water, triforine is not expected to adsorb to suspended solids and sediment based upon the Koc. Volatilisation from water surfaces is not expected to be an important fate process based on its estimated Henry’s Law constant. Triforine is hydrolysed in aqueous solution with a half-life of about two to three days at ambient temperature and the normal pH range for natural waters. Triforine decomposes in aqueous solution exposed to UV or daylight. Its water solubility is 6 to 12 mg/L at room temperature and pH 5 to 9.

NPIC (1994) quotes for triforine a soil half-life of 21 days, water solubility of 30 mg/L and a sorption coefficient (soil Koc) of 200. This resulted in a pesticide movement to groundwater rating of moderate.

JMPR (2014) reports: Octanol/water partition coefficient = log Pow = 2.2 at 20°C. Henry’s Law constant = 2.5 Pa x m3 x mol–1. Water solubility at 20°C: 11.3 mg/L (pH 5), 9.0 mg/L (pH 7) and 8.7 mg/L (pH 9). The calculated DT50 for hydrolysis = 2.5 to 3.5 (pH 5 to 9). Photolysis: initial DT50 under simulated sunlight (12 hours on / 12 hours off) = 1.5 days at pH 7 (25°C). Degradation half-lives of 4 to 706 days were determined for triforine in a variety of soils under aerobic conditions.

### Typical concentrations in drinking-water

Its mainly domestic use means triforine is not likely to be found in public water supplies.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

In a developmental study, rabbits were fed doses of 0, 5, 25 and 125 mg/kg/day of triforine. The maternal no-observable-effect-level (NOEL) was 5 mg/kg/day; the maternal lowest-effect-level (LEL) was 25 mg/kg/day. Rabbits exhibited reduced food intake and loss of body weight. The fetotoxic NOEL was 5 mg/kg/day; the fetotoxic LEL was 25 mg/kg/day, decreased average relative weight was observed.

Effects observed in subchronic and chronic toxicity studies were generally not severe. Liver effects included increased liver weights, increased cholesterol levels, and increased alkaline phosphatase levels. A mild anaemia was seen in several studies, apparently caused by damage to red blood cells because the bone marrow responded by increasing production of red blood cells.

Triforine was evaluated toxicologically by the 1977 JMPR, when no ADI was allocated, and again in 1978, when more toxicological data were made available and an ADI of  
0–0.02 mg/kg bw was established. The 1997 meeting confirmed this ADI on the basis of the NOAEL of 2.4 mg/kg bw per day in the two-year study of toxicity in dogs, with a safety factor of 100. The JMPR concluded that setting of the ARfD for triforine is not necessary (EFSA 2010).

JMPR (2014) calculated an ADI of 0–0.03 mg/kg bw for triforine, and an ARfD of 0.3 mg/kg bw.

EXTOXNET and IPCS quote an ADI for humans of 0.02 mg/kg bw.

USEPA (2008) states that based on the use pattern for triforine, acute and chronic dietary exposure is not anticipated.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.02 mg/kg body weight, with a NOEL of 2.7 mg/kg bw.

As at September 2008, triforine has been classified by USEPA as “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential”. This was based on tumours seen in both sexes of one species (mice) only at the limit dose (liver tumours in male mice and lung tumours in female mice). Therefore, there is no quantification of cancer risk for triforine (USEPA 2008). Triforine appears on the State of California EPA list of chemicals known to cause cancer or reproductive toxicity as at December 2008.

### Derivation of Maximum Acceptable Value

No MAV.

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# Trinexapac-ethyl

CAS No. 95266-40-3. The IUPAC name for trinexapac-ethyl is ethyl (RS)‑4‑cyclopropyl(hydroxy)methylene-3,5-dioxocyclohexanecarboxylate. The CAS name is ethyl 4-(cyclopropylhydroxymethylene)-3,5-dioxocyclohexanecarboxylate. Originally called cimectacarb and cimectacarb-ethyl; sometimes spelt (misspelt?) as cimetacarb.

This substance is a derivative of [trinexapac](http://www.alanwood.net/pesticides/trinexapac.html), CAS No. 104273-73-6.

### Maximum Acceptable Value

Trinexapac-ethyl does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Trinexapac-ethyl is a cyclohexadione plant growth regulator (retardant) that inhibits the biosynthesis of the phytohormone gibberellin (GA1), and is commonly used to control landscape weeds and grasses.

Trinexapac-ethyl appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Trinexapac-ethyl degrades rapidly in soil to trinexapac which displays low to moderate persistence. Trinexapac-ethyl and trinexapac exhibit low to high mobility in soil with adsorption decreasing (ie, mobility increasing) as the soil pH increases.

Biodegradation appears to be the major dissipation pathway for trinexapac-ethyl. In an aerobic metabolism study, half-lifes ranged from 2.8 hours in a loam soil to 4.3 days in a loamy sand soil. In an aerobic aquatic metabolism study, half-lifes ranged from 2.8 days in a river water-sand sediment system to 4.0 days in a pond water/sandy clay loam sediment system. In an anaerobic aquatic metabolism study, half-lives averaged 3.5 days in a pond water/lake water-sediment system. Biodegradation was slower under anaerobic soil conditions. The estimated half-life is about 25 days in a sandy loam soil (USEPA 2013).

Greater than 90 percent of the total residues after application of trinexapac-ethyl to bare ground remained in the top 10 cm of soil during the entire cultivation of the succeeding crops. In soil significant residues were only observed in the top soil layer (0–5cm) in the range of 0.065–0.076 mg/kg at planting or sowing and at  
0.028–0.080 mg/kg at harvest. In layers below, the total residues did not exceed 0.019 mg/kg and was in most cases <0.010 mg/kg (JMPR 2013).

In laboratory incubations in dark aerobic natural sediment water systems, trinexapac‐ethyl exhibited low persistence, forming the major metabolite CGA179500 (maximum 64 percent AR in water and 6.9 percent AR in sediment), exhibiting moderate persistence. In the sediment-water environment trinexapac-ethyl was converted by microbially mediated degradation to trinexapac which exhibits moderate persistence being microbially mineralised to CO2 (59 to 69 percent degraded after 111 days). The potential for groundwater exposure from the representative uses of trinexapac‐ethyl above the parametric drinking water limit of 0.1 μg/L was concluded to be low (EFSA 2018).

Water solubility of trinexapac-ethyl is about 10,200 mg/L at pH 5.5, ie, about 1 percent and 21,100 mg/L at pH 8.2 at 20°C. Henry’s Law constant at 25°C = 5.4 \_ 10–4 Pa \_ m3 \_ mol–1; a vapour pressure of 2.16 x\_ 10–3 Pa and a water solubility of 11,000 mg/L were used to calculate the Henry’s Law constant. The n-octanol/water partition coefficient = Kow = 1.5 at pH 5, -0.29 at pH 6.9 and -2.1 at pH 8.9. The hydrolysis half-life under sterile and dark conditions at pH 5 is 485 to 562 days, at pH 7 from 828 to 908 days, and at pH 9 about eight days. Trinexapac-ethyl is significantly degraded in irradiated samples equivalent to a half-life of 21.3 equivalent days of midday summer sunlight. JMPR (2013) also lists the major metabolites.

### Recommended analytical techniques

#### Referee method

No MAV.

#### Some alternative methods

The appropriate high‐pressure liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) method exists for monitoring trinexapac‐ethyl in soil with LOQ of 0.01 mg/kg. Trinexapac‐ethyl and trinexapac can be monitored in surface, ground and drinking water with a LOQ of 0.05 μg/L for each compound (EFSA 2018).

### Health considerations

The dog appears to be the most sensitive species. In adult animals, no adverse effects were seen in rats, rabbits, or mice below the limit dose (1,000 mg/kg/day) following subchronic or chronic oral exposure. In the dogs, however, decreased body weight gain and food consumption, diffuse thymic atrophy, and changes in the epithelial cells of the renal tubules were seen in the 90-day study at 516/582 mg/kg/day (males/females). Following chronic exposure, evidence of neurotoxicity was seen at 366/356 mg/kg/day in male and female dogs, respectively, including minimal, focal bilateral vacuolation of the dorsal medial hippocampus and/or lateral midbrain, which was associated with the astrocytes and oligodendrocytes. The lesions remained confined to the supporting cells in the central nervous system and did not progress to more advanced or more extensive damage of the nervous tissue. They were not associated with other neuropathological findings or overt neurological signs, so their biological significance is unknown.

The USEPA Office of Pesticide Programs developed an acute reference dose (aRfD) for trinexapac-ethyl of 0.6 mg/kg/day for females age 13 to 49 years based on a no observed effect level (NOEL) of 60 mg/kg/day in a developmental toxicity study in rabbits (effects at higher doses were: decreased number of fetuses per litter and increased post-implantation loss) and an uncertainty factor of 100. An aRfD was not developed for the general population (including infants and children) because there were no appropriate acute endpoints. Additionally, the USEPA established a chronic reference dose (cRfD) of 0.32 mg/kg/day based on a NOEL of 32 mg/kg/day from a chronic feeding study in dogs (effects at higher doses were: elevated serum cholesterol levels, mucoid feces, bloody feces, minimal focal vacuolation of the dorsal medial hippocampus and/or lateral midbrain) and an uncertainty factor of 100 (USEPA 2013).

The Acceptable Daily Intake (ADI) adopted in Australia for trinexapac-ethyl is 0.01 mg/kg body weight, with a NOEL of 1.4 mg/kg. In May 2017 APVMA decided that an ARfD was unnecessary due to its low oral toxicity or the absence of any developmental toxicity after a single dose (<https://apvma.gov.au/>).

IUPAC lists the ADI at 0.032 mg/kg/d. However, EFSA (2005) quotes 0.32 mg/kg-bw/d. EC (2006) established an ADI of 0.32 mg/kg/d, adding that an ARfD allocation was not considered necessary due to the low acute toxicity of trinexapac-ethyl.

The JMPR meeting (2013) established an acceptable daily intake (ADI) of 0–0.3 mg/kg bw per day, expressed as trinexapac acid equivalents, based on a NOAEL of 32 mg/kg bw per day for trinexapac-ethyl (equivalent to 29 mg/kg bw per day expressed as trinexapac acid equivalents) for cerebral vacuolation in male and female dogs following 52 weeks of dietary exposure, with the application of a 100-fold safety factor. In the absence of information to the contrary, including mechanistic data, the cerebral vacuolation observed in dogs was considered relevant to humans. The meeting concluded that it is not necessary to establish an acute reference dose (ARfD) for trinexapac-ethyl in view of its low acute oral toxicity and the absence of developmental toxicity or any other toxicological effects that would be likely to be elicited by a single dose.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.32 mg/kg/d, and an ARfD of 0.60 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for trinexapac-ethyl is 19.8 mg/L.

EFSA (2016/2018) states that data were sufficient to derive an acceptable daily intake (ADI) of 0.32 mg/kg bodyweight (bw) per day for trinexapac. No acute reference dose (ARfD) was deemed necessary.

The USEPA considers trinexapac-ethyl as not likely to be carcinogenic to humans, and EFSA (2005) states that there is no evidence of genotoxic potential.

### Derivation of Maximum Acceptable Value

No MAV.

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# Triticonazole

CAS No. 131983-72-7. The IUPAC name for triticonazole is (RS)-(E)-5-(4-chlorobenzylidene)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol. The CAS name is (5E)-5-[(4-chlorophenyl)methylene]-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol.

### Maximum Acceptable Value

Triticonazole is not mentioned in the WHO Guidelines, and there is no MAV in the DWSNZ.

### Sources to water

Triticonazole is a conazole fungicide which acts by inhibiting sterol demethylation. Triticonazole is mainly used for seed treatment in cereal crops.

Triticonazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2012 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Several triazole containing pesticides generate significant amounts of free triazole, triazole alanine or triazole acetic acid. For triticonazole, however, none of these metabolites were identified in significant amounts (EFSA 2009).

The estimated hydrolysis half-life of triticonazole is about 30 days; the soil half-life is about 230 days under aerobic and anaerobic conditions. It is not retained very strongly by soil particles so has the potential to enter groundwater.

Water solubility is about 8 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV, so not needed.

#### Some alternative methods

See EFSA (2009).

### Health considerations

The acute dietary RfD (females 13–50 years of age) is 0.5 mg/kg/d, whereas the acute dietary RfD (general population including infants and children) is 4 mg/kg/d. The chronic dietary RfD (all populations) is 0.17 mg/kg/d (USEPA 2002). As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> still quotes a RfD of 0.17 mg/kg/d, and an ARfD of 0.50 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for triticonazole is 16.5 mg/L.

An ADI of 0.025 mg/kg bw has been developed for triticonazole (EC 2010); an ARfD of 0.05 mg/kg bw was allocated. The review established that the residues arising from the proposed uses, consequent on application consistent with good plant protection practice, have no harmful effects on human or animal health. See datasheet for triazole metabolites for latest ADI and ARfD.

Triticonazole was negative for mutagenicity, and the cancer classification is “not likely to be carcinogenic to humans” based on a lack of evidence of carcinogenicity in the two guideline studies conducted on rats and mice (USEPA 2010).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Uniconazole

CAS No. 83657-22-1. The IUPAC name for uniconazole is (E)-(RS)-1-(4-chlorophenyl)-4,4-dimethyl-2-(1H-1,2,4-triazol-1-yl)pent-1-en-3-ol. The CAS name is (βE)-β-[(4-chlorophenyl)methylene]-α-(1,1-dimethylethyl)-1H-1,2,4-triazole-1-ethanol.

Four isomers are possible: two geometrical isomers, E and Z, each with two optical isomers, R and S because of the chiral centre. The major isomer is the ES isomer. The (S)-isomer of this substance has the common name [uniconazole-P](http://www.alanwood.net/pesticides/uniconazole-p.html), CAS No. 83657-17-4.

### Maximum Acceptable Value

Uniconazole does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

### Sources to water

Uniconazole is a conazole (or triazole derivative) fungicide and growth retardant, used for the improvement of fruit shape and reduction in vegetative growth in avocados by inhibiting the endogenous biosynthesis of gibberellin.

Uniconazole appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register).

### Forms and fate in the environment

Uniconazole-p is stable to hydrolysis and the principal degradation pathway appears to be by photolysis in solution. Microbial breakdown in aerobic soils in the dark is slow. Laboratory studies showed that uniconazole-p is not likely to leach from sandy-loam soils. However, when applied to sandy soils with low organic matter uniconazole-p is easily eluted with water. A field dissipation study showed some evidence for an initial rapid dissipation in one of the two soils, however, a significant amount of remained after the initial dissipation and dissipated with a half-life >100 days.

Water solubility of [uniconazole-P](http://www.alanwood.net/pesticides/uniconazole-p.html) is about 8.4 mg/L.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Uniconazole-p is rapidly absorbed after oral ingestion and extensively metabolised by the liver. There is no accumulation in the tissues and the metabolites are rapidly excreted in the faeces and urine. It has moderate acute oral toxicity.

The Acceptable Daily Intake (ADI) adopted in Australia for [uniconazole-P](http://www.alanwood.net/pesticides/uniconazole-p.html) is 0.02 mg/kg body weight, with a NOEL of 1.86 mg/kg.

The short-term NOEL in a rat feeding study was 30 ppm equal to 2.25 mg/kg bw/day in males and 2.42 mg/kg bw/day in females (APVMA 2000).

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.02 mg/kg/d, and an ARfD of 0.05 mg/kg/d for uniconazole-P. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for uniconazole-P is 1.65 mg/L.

As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.005 mg/kg/d, and an ARfD of 0.03 mg/kg/d for the 1,2,4-triazole metabolite. The USEPA acute one day HHBPs (Human Health Benchmarks for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for the 1,2,4-triazole, triazole acetic acid and triazole alanine metabolites are 0.30 mg/L. See datasheet for triazole metabolites for latest ADI and ARfD.

In repeat dose studies in mice, rats and dogs, the main adverse effect caused by oral ingestion of high doses of uniconazole-p was an increase in the size and weight of the liver. Fat accumulation in the liver was also consistently observed at high doses. Although observed less consistently, increases in the activity of some enzymes indicated altered liver function as a response to uniconazole-p exposure. In long-term studies, there was no evidence of an increase in cancer. This result is further supported by several studies which show that uniconazole-p does not damage genetic material. Uniconazole-p had no effects on reproductive behaviour or performance of rats and no effect on foetal development in rabbits. At doses that were not toxic to the mother, there were no effects on the rat foetus. In plants, uniconazole-p was shown to be extensively metabolised. The major component of the residue was unchanged parent compound (APVMA 2000).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Zinc pyrithione

CAS No. 13463-41-7. The IUPAC name for zinc pyrithione is bis [1-hydroxy-2(1 H)-pyridine-thionato] zinc. Zinc pyrithione is also known as zinc 2-mercaptopyridine N‑oxide, zinc 2-pyridinethiol-1-oxide, zinc omadine, ZPT and various trade names.

Copper pyrithione is also marketed, CAS No. 14915-37-8.

Has also been marketed overseas as sodium omadine (USEPA 1996). Sodium omadine exists as a mixture of two tautomeric forms: (I) 1-hydroxy-2(1H)-pyridinethione, sodium salt and (II) 2-pyridinethio-1-oxide, sodium salt. Their CAS Nos. are: (I) 15922-78-8 and (II) 3811-73-2.

### Maximum Acceptable Value

Zinc pyrithione does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

EPA established an environmental exposure limit of 0.008 mg/L for zinc pyrithione in fresh water (<http://www.epa.govt.nz/search-databases/Pages/substance-exposure-limit-register.aspx>).

### Sources to water

Zinc pyrithione is best known for its use in treating [dandruff](http://en.wikipedia.org/wiki/Dandruff) and [seborrhoeic dermatitis](http://en.wikipedia.org/wiki/Seborrhoeic_dermatitis). It also has antibacterial properties and is effective against many [pathogens](http://en.wikipedia.org/wiki/Pathogen) from the [streptococcus](http://en.wikipedia.org/wiki/Streptococcus) and [staphylococcus](http://en.wikipedia.org/wiki/Staphylococcus) class. It is a fungistat and bacteristat. Its other medical applications include treatments of [psoriasis](http://en.wikipedia.org/wiki/Psoriasis), [eczema](http://en.wikipedia.org/wiki/Eczema), [ringworm](http://en.wikipedia.org/wiki/Ringworm), [fungus](http://en.wikipedia.org/wiki/Fungus), [athletes foot](http://en.wikipedia.org/wiki/Athletes_foot), [dry skin](http://en.wikipedia.org/wiki/Dry_skin), [atypical dermatitis](http://en.wikipedia.org/w/index.php?title=Atypical_dermatitis&action=edit&redlink=1), [tinea](http://en.wikipedia.org/wiki/Tinea), and [vitiligo](http://en.wikipedia.org/wiki/Vitiligo). In medical uses, it is sometimes mixed with seleniun pyrithione. Zinc pyrithione should not be used in products for oral hygiene.

Zinc pyrithione is used to preserve a wide variety of food/drinking water contact, and non-food contact articles such as: adhesives; carpet fibres; carpet backings; rubber or rubber-backed bath mats; foam underlay for carpets; synthetic, non-leather materials; foam stuffing for cushions and mattresses; wire and cable insulation; vinyl, linoleum, tile and other synthetic floor coverings; wall coverings; plastic furniture; athletic flooring and mats; mattress liners, covers or ticking; moulding; mats; gaskets; weather stripping; coated fabrics for furniture cushions, boat covers, tents; tarpaulins and awnings; rubber gloves (non-surgical); garbage bags, cans, and other refuse containers; bathtub appliques; garden hose; pipe (non-potable water); ductwork; air filters; air filtration components and media for industrial, hospital, residential, and commercial heating and cooling; conveyor belts; shower curtains; sponge or fibre mops; household use sponges; toilet brush receptacles; toothbrush receptacles (non-bristle contact); scrub brushes (non-medical); sink mats and drain boards; storage containers; soap dish holders; towel bars; components of uppers in footwear.

Zinc pyrithione is also registered for incorporation into antifoulant boat paints to control the growth of slime, algae, and marine fouling organisms (eg, barnacles, tubeworms, etc) below the water line on recreational and commercial boat hulls (USEPA 2004).

Zinc pyrithione does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals). It (and the copper salt) also appears in the Timber Preservatives, Antisapstains and Antifouling Paints Transfer Notice 2004. See also EPA (2013).

Copper pyrithione acts as a booster biocide in the antifouling paint, by increasing the efficacy of the product in order to remove the most problematic soft fouling organisms, for example the common marine fouling species, algae eg, Enteromorpha spp. and Amphora spp which are tolerant of copper (ECHA 2014).

### Forms and fate in the environment

USEPA (2004) indicated that, in general, it appears that zinc omadine is not likely to persist and accumulate in the water phase. Since zinc omadine has a high adsorption coefficient to sediments and low desorption, it is likely to be adsorbed to sediments. Zinc omadine should degrade rapidly (half-life of 15 days) in sediments under aerobic conditions as demonstrated by the aerobic aquatic metabolism study.

An Australian review in 2001 of zinc pyrithione in the product International Intersmooth 360 Ecoloflex Antifouling Paint showed that hydrolysis was slight in sterile buffers with half-lifes of 96 to 123 days. Two degradates exceeded ten percent, pyrithione disulfide and pyrithione sulfinic acid. The aqueous photolysis half-life was very rapid at 13 to 18 minutes. Degradates greater than 10 percent included pyridine sulfinic acid, pyridine sulfonic acid, pyridine disulfide and pyridine/pyrithione mixed disulfide. It was concluded that much of the zinc pyrithione released to the environment was likely to degrade in the water column before reaching the sediment (from PMEP 2003).

Photolysis is probably an important route of for sodium omadine. Photolytic half-lifes of 40–126 minutes have been reported at a concentration of 100 mg/L, with irradiation by natural sunlight.

Water solubility of zinc pyrithione is about 15 mg/L. The solubility of sodium omadine in water is ~54.7 percent w/w at 25°C.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The RfD for sodium omadine was determined to be 0.005 mg/kg/day based on a NOEL of 0.5 mg/kg/day and an uncertainty factor of 100. The NOEL was obtained from a chronic rat study. The rat reproduction study with a parental NOEL of 0.5 mg/kg/day supports the RfD as a co-critical study (USEPA 1996).

In a two-year feeding study conducted on young Wistar rats, groups of 10 males and 10 females were fed diets containing approximately 0, 0.1, 0.25, 0.5, 1.25 and 2.5 mg/kg/day for adult animals. The highest level caused hind-limb paralysis in some animals. The no-effect level for males and females was 0.5 mg/kg/day. A dose level of 2.5 mg/kg/day given orally is a no-effect level for teratogenicity/embryotoxicity, and no mutagenic effect in any of the in vitro and in vivo studies conducted was observed (EC 2002).

The USEPA (1996) has classified sodium omadine as a Group D chemical (indicating insufficient weight of evidence of carcinogenicity for humans).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Zineb

CAS No. 12122-67-7. The IUPAC name for zineb is polymeric zinc ethylenebis(dithiocarbamate). The CAS name is [[2‑[(dithiocarboxy)amino]ethyl]carbamodithioato(2−)-κS,κS′]zinc. Also called dithane.

### Maximum Acceptable Value

Zineb does not have a MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

Zineb should not contain more than 0.5 percent of ethylenethiourea (ETU), and 200 mg/kg of arsenic.

### Sources to water

Zineb is a foliate [fungicide](http://en.wikipedia.org/wiki/Fungicide) and is a polymeric [complex](http://en.wikipedia.org/wiki/Complex_(chemistry)) of [zinc](http://en.wikipedia.org/wiki/Zinc) with the [ethylene bis(dithiocarbamate)](http://en.wikipedia.org/w/index.php?title=Ethylene_bis(dithiocarbamate)&action=edit&redlink=1) anion, commonly used to control downy mildew, blight and rusts in crops in the field and during transport and storage. All registrations for zineb have been voluntarily cancelled by the USA manufacturer (EXTOXNET 1996). Dithiocarbamates can act as a fumigant by rapidly breaking down into methylisothiocyanate (MITC).

Zineb does not appear on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). However, it is listed in Table 1 of ERMA’s Summary of Approvals of Substances Transferred under the Hazardous Substances (Chemicals) Transfer Notice 2006 (with amendments), as at 24 June 2008 (<http://www.ermanz.govt.nz/hs/transfer/summaryapprove.html>, then select Summary of Approvals: Chemicals (or pesticides)). It is approved as a component of anti-fouling paints (EPA 2013).

### Forms and fate in the environment

Zineb is subject to chemical breakdown (hydrolysis) and does not persist in soil. It adsorbs strongly to soil particles and usually does not move below the upper layer of soil. For this reason, zineb is unlikely to contaminate groundwater. Its bioactive half-life in the field is 16 days. Within four months after a field planted with alfalfa was sprayed, 99.7 percent of the applied zineb was lost.

If released to soil, zineb is expected to have low to moderate mobility based upon a Koc values of 308–1159. Volatilisation from moist soil surfaces is not expected to be an important fate process since zineb is a zinc salt. Zineb field half-lives range from  
23–43 days. If released into water, zineb is expected to adsorb to suspended solids and sediment based upon the Koc values. Hydrolysis may be an important environmental fate process as indicated by half-lives in relation to pH of 9 minutes at pH 3.8, 6.5 hours at pH 5.7, 96 hours at pH 7.0, and 405 hours at pH 8.0.

The EBDCs are generally unstable in the presence of moisture, oxygen, and in biological systems. They rapidly degrade to ethylenethiourea (ETU).

Water solubility of zineb is about 10 mg/L.

NPIC (1994) quotes for zineb a soil half-life of 30 days, water solubility of 10 mg/L and a sorption coefficient (soil Koc) of 1,000. This resulted in a pesticide movement to groundwater rating of low.

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

Ethylene bisdithiocarbamate pesticides (EBDCs), which include zineb, are generally considered to have low short-term mammalian toxicity. A major toxicological concern, however, is ethylenethiourea (ETU), an industrial contaminant and a breakdown product of zineb and other EBDC pesticides. In addition to having the potential to cause goitre, a condition in which the thyroid gland is enlarged, this metabolite has produced birth defects and cancer in experimental animals. ETU can be produced when EBDCs are used on stored produce, and also when fruit or vegetables with residues of these fungicides are cooked. ETU has been classified as a probable human carcinogen by the USEPA.

An estimate of temporary acceptable daily intake of zineb for man (IARC 1968) is  
0–0.025 mg/kg body-weight (alone or in combination with other ethylene bisdithiocarbamates). This value is based on experiments carried out with zineb and does not take account of chemical alterations after application.

JMPR (1993) states that zineb was previously evaluated by the Joint Meeting in 1963, 1965, 1967, 1970, 1974, 1977 and 1980. An ADI of 0–0.05 mg/kg bw, of which not more than 0.002 mg/kg bw may be present as ETU, was allocated at the 1980 meeting for zineb or the sum of maneb, mancozeb, and zineb. Little new information on zineb has become available since the previous evaluation. The 1993 meeting concluded that the toxicological data specifically generated for zineb were inadequate to estimate an ADI. However, because of the similarity of the chemical structure of zineb to that of the other ethylenebis(dithiocarbamate)s (EBDCs), the comparable toxicological profile of the EBDCs based on the toxic effects of ETU, and the fact that parent EBDC residues cannot be differentiated using presently-available regulatory analytical methods, zineb was included in the group ADI of 0–0.03 mg/kg bw for the EBDC group evaluated at this meeting (mancozeb, maneb, metiram). In 1993, the JMPR estimated a dithiocarbamate group ADI of 0–0.03 mg/kg bw for mancozeb, maneb, metiram and zineb based on thyroid toxicity. For their metabolite ethylenethiourea (ETU), an ADI of 0–0.004 mg/kg bw has been allocated (JMPR 2012). No ARfD value is quoted.

EXTOXNET (1996) lists the ADI at 0.03 mg/kg, and the RfD at 0.05 mg/kg/d. The oral RfD was calculated at 0.05 mg/kg/d (USEPA 1988), based on thyroid hyperplasia in chronic oral bioassay in rats.

The Acceptable Daily Intake (ADI) adopted in Australia for zineb is 0.005 mg/kg body weight, with a NOEL of 5 mg/kg.

IARC evaluated zineb as not classifiable as to its carcinogenicity to humans (Group 3) – IPCS (1976 – confirmed 1987).

Zineb is on the EC List of 66 Category 1 substances showing evidence of endocrine disrupting activity in at least one species using intact animals (EC 2015).

### Derivation of Maximum Acceptable Value

No MAV.

### Bibliography

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# Ziram

CAS No. 137-30-4. The IUPAC name for ziram is zinc bis(dimethyldithiocarbamate). The CAS name is (T-4)-bis(dimethylcarbamodithioato-κS,κS′)zinc. It has been in use since the 1930s, so has many trade names. It is also mixed with other products.

### Maximum Acceptable Value

Ziram does not have MAV in the DWSNZ, and is not mentioned in the WHO Guidelines.

The USEPA concluded on 22 September 2009 that ziram is known or anticipated to occur in PWSs and may require regulation. Therefore they added ziram to their CCL 3 (Drinking Water Contaminant Candidate List 3, USEPA 2009).

Any enforcement methods are based on the decomposition of dithiocarbamates with release of carbon disulphide (CS2). The ziram residues of concern are expected to contain the CS2 moiety.

EC (2004) states that the arsenic content must not exceed 250 mg/kg.

### Sources to water

Ziram is a dithiocarbamate fungicide used on a wide variety of plant fungi and diseases, and as a bird and mammal repellent. It may be applied to the foliage of plants, but it is also used as a soil and/or seed treatment. It has also been used as an accelerator in rubber manufacturing (a principal use) in the process of rubber vulcanisation, packaging materials, adhesives, and textiles.

Ziram appears on the NZFSA’s complete database of Agricultural Compounds and Veterinary Medicines (ACVM) as at 2009 (see <https://eatsafe.nzfsa.govt.nz/web/public/acvm-register> and select entire register). ERMA notes that 5.7 tonnes of ziram were used in New Zealand in 2004, at an application rate of 10,260 grams of active ingredient per hectare.

After 1 July 2017 antifouling paints containing ziram will no longer able to be manufactured in or imported into New Zealand (EPA 2013).

Dithiocarbamates were one of the commonest agricultural chemical residues found in an extensive study of New Zealand foods (NZFSA 2007). Dithiocarbamates can act as a fumigant by rapidly breaking down into methylisothiocyanate (MITC).

### Forms and fate in the environment

Ziram will be moderately bound to soils with a medium to high content of organic matter. A field half-life of 30 days has been estimated for ziram, indicating a low to moderate persistence. Thiram (qv) is a major metabolite and sometimes an impurity. Hydrolysis yields dithiocarbamic acid which breaks down to carbon disulphide and dimethylamine. In water, dimethyldithiocarbamic acid is also a major metabolite; N,N‑dimethylformamide and N,Ndimethylthioformamide have also been found.

Of the metallic dithiocarbamate fungicides, ziram is the most stable (cf. mancozeb). Because the compound is toxic to bacteria, biodegradation in sediment may be rather slow, or occur only at very low concentrations. If ziram gets to the bottom of bodies of water, it may persist for months. It is less stable in acid conditions.

Volatilisation from moist soil surfaces is not expected to be an important fate process based upon an estimated Henry’s Law constant of 6.2 x 10-10 atm-cu m/mole. If released into water, ziram is expected to adsorb to suspended solids and sediment based upon Rf values ranging from 0.33 to 0.62. Volatilisation from water surfaces is not expected based upon the estimated Henry’s Law constant.

Water solubility about 65 mg/L (also reported at as low as 3 mg/L).

NPIC (1994) quotes for ziram a soil half-life of 30 days, water solubility of 65 mg/L and a sorption coefficient (soil Koc) of 400. This resulted in a pesticide movement to groundwater rating of moderate.

### Typical concentrations in drinking-water

Ziram has not been detected in groundwater (EXTOXNET 1996).

### Recommended analytical techniques

#### Referee method

No MAV.

### Health considerations

The primary effects of short- and long-term treatment with ziram in mice, rats, and dogs were on the liver, thyroid gland, and testis. The hepatic effects were increased liver weight, degeneration, and focal-cell necrosis. Effects in the thyroid were C-cell hyperplasia and carcinomas, and that on the testes was sterility.

Ziram and other dithiocarbamates are metabolic poisons. Their acute toxic effects are similar to those of carbon disulfide which has led to the suggestion that this metabolite, common to all dithiocarbamates, is the cause of their effects. This is supported by the observation that most dithiocarbamates of very low acute toxicity are excreted unmetabolised in the faeces following oral dosing. Ziram is not a potent initiator of thyroid dysfunction among dithiocarbamates and the effects have not been shown to be dose dependent. The metabolically generated sulfur inhibits some intracellular enzyme systems (WHO 1987).

In 1967 IPCS derived a temporary acceptable daily intake (ADI) of 0–0.025 mg/kg bw for ziram or ziram in combination with other dimethyldithiocarbamates, on the basis of the NOAEL in a one-year study in dogs. This temporary ADI was lowered to  
0–0.005 mg/kg bw in 1974. A group ADI of 0–0.02 mg/kg bw for ferbam and ziram was allocated in 1977 and confirmed in 1980. A new estimate (1996) of ADI was derived for humans: 0–0.003 mg/kg bw (for ferbam and ziram) – see also JMPR (1996). Note that ferbam (ferric dimethyldithiocarbamate) does not appear on ERMA’s Full List of ACVM approved veterinary medicines and pesticides, as at 2009.

USEPA (2003)reports a RfD of 0.016 mg/kg/d, based on a NOAEL of 1.6 mg/kg/d from a 52-week oral study on dogs. The PaD was reported as 0.005 mg/kg/d. As at May 2014, <http://water.epa.gov/drink/standards/hascience.cfm> quotes a RfD of 0.016 mg/kg/d, and an ARfD of 0.05 mg/kg/d. The USEPA acute one-day HHBP (Human Health Benchmark for Pesticides) in drinking water – see Introductory Note 3c (page 2) – for ziram is 0.50 mg/L.

EC (2004) established an ADI of 0.006 mg/kg/d, and an ARfD of 0.08 mg/kg-bw/d.

The Acceptable Daily Intake (ADI) adopted in Australia is 0.01 mg/kg body weight, with a NOEL of 1 mg/kg bw.

In April 2000 the USEPA has classified ziram as “likely to be carcinogenic to humans”. In 2003 they reclassified ziram as “suggestive evidence of carcinogenicity but not sufficient to assess human carcinogenic potential”. In the early evaluation the carcinogenicity was due to a contaminant in the industrial formulation of ziram used in the cancer studies. Because there is limited evidence in experimental animals for the carcinogenicity of ziram, IARC evaluated ziram as not classifiable as to its carcinogenicity to humans (Group 3) (IPCS 1991).

### Derivation of Maximum Acceptable Value

No MAV.

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# 1080

CAS No. 62-74-8 for the sodium salt. The IUPAC and CAS name is sodium fluoroacetate. Also called fluoroacetic acid, sodium monofluoroacetate, sodium fluorethanoate and 2-fluoroacetic acid. The name of 1080 resulted from an invoice number at an early research station in the US!

CAS No. 144-49-0 refers to the fluoroacetate ion.

### Maximum Acceptable Value (provisional)

Based on health considerations, the concentration of 1080 in drinking-water should not exceed 0.0035 mg/L. The MAV in the 1995 DWSNZ had been 0.005 mg/L.

1080 is not mentioned in the WHO Guidelines.

### Sources to water

1080 is a highly toxic poison (rodenticide) used for the control of possums, deer, rats and rabbits. It was introduced increasingly during the 1940s and 1950s as a more effective and humane alternative to strychnine. It may enter source waters as a result of aerial application.

1080 occurs naturally in several plants, such as tea; recent studies at Lincoln University have detected natural traces of 1080 in puha. It has been found in more than 40 West Australian plants; possums in New Zealand come from the eastern seaboard of Australia and are more susceptible to the toxin, unlike their West Australian cousins who are more resilient. It has been used overseas in sewers and ships to control rats.

New Zealand uses approximately 80 percent of the world’s production of manufactured 1080 amounting to 3.2 tonnes of raw product in the period 1 July 2001 to 30 June 2002. Following a re-assessment by ERMA in August 2007, 1080 continues to be registered for use in New Zealand; it is a Class B, restricted use poison, and a license is required for its use.

The Parliamentary Commissioner for the Environment (PCE 2011) reviewed the use of 1080 in New Zealand.

To monitor 1080 operations, more than 500 water samples have been taken in the target area over the last five years. Less than 2 percent of them (10 samples) have contained detectable concentrations of 1080. All of these samples were well below the tolerable exposure limit (TEL) of 3.5 micrograms of 1080 per litre of water (0.0035 mg/L) set in the reassessment. The highest concentration detected was 0.3 micrograms per litre (0.0003 mg/L) of water. The TEL is set at a level that is protective of human health. None of the samples taken from areas in drinking water catchments have shown any measurable amounts of 1080, ie, <0.0001 mg/L (EPA 2013).

The Environmental Risk Management Authority, now called the Environmental Protection Agency (EPA), has delegated the function of granting permissions for the use of selected VTAs to Medical Officers of Health and Health Protection Officers who are also warranted HSNO enforcement officers and have completed relevant Ministry of Health courses. In addition to granting permission, the delegation also includes adding, deleting or otherwise varying any condition on a permission; and/or revoking a permission. See MoH (2013).

### Forms and fate in the environment

While 1080 is comparatively rapidly eliminated from living animals, it can persist in carcasses for many months in cool or dry conditions where it will break down more slowly and may pose a risk to scavenging dogs. Undigested baits in carcasses remain toxic for prolonged periods (Eason 2002).

Studies show that 1080 can be metabolised by soil micro-organisms. Sodium monofluoroacetate derived from baits will be dispersed by water since it is highly water soluble and mobile. If heavy rainfall follows the use of 1080 baits, leaching to unmeasurable concentrations (<0.0001 mg/L) may precede biodegradation. In comparison to cereal bait, 1080 is retained in carrot baits and will only slowly leach from carrots into the soil. In mild weather or warm conditions, such as 11 to 20ºC and 8 to 15 percent moisture, 1080 may be significantly defluorinated in one to two weeks. In less favourable conditions breakdown might take several weeks, and in extreme cold and drought 1080 residues might persist in baits or in the soil for several months (from Eason 2002).

1080 can be translocated from water or soil to plants and then defluorinated. It is absorbed by aquatic organisms but it is not bioaccumulated. NSW Government (2013) reports that fish and some crustaceans (eg, water fleas Daphnia sp.) are relatively tolerant to 1080, whereas some aquatic insects (eg, mosquito larvae) are susceptible. Some aquatic plants, such as duckweed (Spirodela oligorrhiza), have been found to be sensitive.

Water solubility is very high, about 100 percent.

A nationwide water testing programme carried out between 1990 and 2003 showed that only 5 percent of over 1,450 water samples tested had detectable traces of 1080. These levels were transient and associated with the visible presence of baits in small streams. The 1080 levels ranged from 0.0002 to 0.009 mg/L (Booth et al 1997; Eason 2002; ERMA 2007a).

If released to soil, fluoroacetic acid is expected to have very high mobility based upon an estimated Koc of 1.4. The pKa of fluoroacetic acid is 2.59, indicating that this compound will primarily exist in the dissociated form in the environment and anions generally do not adsorb more strongly to organic carbon and clay than their neutral counterparts. Fluoroacetic acid may volatilise from dry soil surfaces based upon its vapour pressure. Fluoracetic acid has been identified as one which could be removed by biological sewage treatment provided suitable acclimatisation can be achieved, suggesting that the compound may be subject to biodegradation in terrestrial or aquatic systems. If released into water, fluoroacetic acid is not expected to adsorb to suspended solids and sediment based upon the estimated Koc. The pKa value indicates fluoroacetic acid will exist almost entirely in the ionised form at pH values of 5 to 9 and therefore volatilisation from water surfaces is not expected to be an important fate process. An estimated BCF of 3 suggests the potential for bioconcentration in aquatic organisms is low. Hydrolysis is not expected to be an important environmental fate process since this compound lacks functional groups that hydrolyse under environmental conditions (EAWAG accessed February 2015).

### Typical concentrations in drinking-water

The P2 Chemical Determinand Identification Programme did not find 1080 at detectable concentrations (limit of detection = 0.0001 mg/L) (ESR 2001).

### Removal methods

No information is available about methods for removing 1080 from water.

### Recommended analytical techniques

#### Referee method

Derivatisation with dicyclohexylcarbodiimide and gas chromatography with electron capture detection (Ozawa and Tsukioka 1987, *Anal Chem* 59: 2914–17).

#### Some alternative methods

No alternative methods have been recommended for 1080 because no methods meet the required criteria.

### Health considerations

Animal studies have shown that 1080 is absorbed rapidly and excreted as unchanged fluoroacetate and a range of metabolites.

1080 poisoning results from the transformation of fluoroacetate into fluorocitrate within cell mitochondria. Acute poisoning is characterised by a symptom-free latent period of half to two hours or longer between ingestion and onset of symptoms (nausea, vomiting, diarrhoea and hyperactive behaviour leading to convulsions, coma and cyanosis). Ventricular fibrillation is noted commonly and is the primary cause of death. Early symptoms include alteration of heart sounds and premature, weak contractions.

The LD50 (dose required to kill half a sample human population) is 2.0 mg/kg bw. Therefore a 70 kg person would need to drink 70,000 litres of water containing 0.002 mg/L of 1080, in one sitting, to absorb a fatal dose. [Note: 0.002 mg/L is half the MAV, rounded up.] Even allowing a significant safety margin (typically applied to allow for sensitivity in the general population and uncertainty in the toxicological studies), a safety factor of 1,000 would still require a person to drink at least 70 litres of water containing 0.002 mg/L of 1080 before being considered at risk (DoC 2004).

The oral RfD was calculated at 0.00002 mg/kg/d (USEPA 1993) based on increased heart weight in females and males; decreased testis weight and altered spermatogenesis in males in a 13-week rat oral study (gavage); NOAEL = 0.05 mg/kg/d.

Eason and Turck (2002) found from animal toxicology studies commissioned by DoC and the AHB that 1080 was teratogenic, a male reproductive toxin and a myocardial toxin in rats.

The No Observable Effect Level (NOEL) for toxicity in rats (0.075 mg/kg-day) indicates that regular intake of 1080 contaminated water could cause sub-lethal effects. Based on this NOEL, a 70 kg person would need to drink 2,680 litres of water containing 0.002 mg/L of 1080 per day, for an extended period of time, for sub-lethal effects to occur. Allowing a safety margin of 1,000, a person would need to drink their entire daily intake of two litres a day of water from a contaminated source, for a period of weeks, to be considered potentially at risk. Similarly, a pregnant woman would need to drink at least three litres a day, all of her daily intake, during the first 90 days of pregnancy, to receive a daily intake one thousand times less than the NOEL (0.1 mg/kg-day) for developmental toxicity in rats (Eason and Turck 2002, and Tremblay et al 2002, in DoC 2004).

Work by Foronda et al (2007) found the BMD10 and BMDL10 for cardiomyopathy and testicular effects were 0.21 mg/kg bw and 0.10 mg/kg bw, respectively. These values are proposed for use in the eventual determination of the tolerable daily intake (TDI) for 1080. Based on the best fit of modelled dose–response data, a TDI of 0.03 µg/kg bw/day was proposed for human health risk assessment of 1080 (Foronda et al 2007a).

Assessment thresholds were established (ERMA 2007a) for acute, subchronic and chronic exposure to 1080. The acute threshold applied was the estimated minimum lethal dose (MLD) in humans 0.7 mg/kg bw. The subchronic exposure threshold established was the acceptable operator exposure (AOEL) of 0.2 μg/kg bw/day (appropriate only for workers). The Department of Labour’s biological exposure index for 1080 in urine was used for analysis of some data.

The chronic exposure threshold was the Acceptable Daily Exposure of 0.02 μg/kg bw/day. This was used to derive separate potential daily exposures (PDE) for different routes:

* PDEfood = 0.006 μg/kg bw/day
* PDEwater = 0.01 μg/kg bw/day
* PDEinhalation = 0.002 μg/kg bw/day
* PDEdermal = 0.002 μg/kg bw/day

### Derivation of Maximum Acceptable Value

The provisional MAV for 1080 was calculated by the New Zealand Ministry of Health using an NOAEL derived from a Department of Conservation teratology study of rats (Eason 1999) as follows:

0.1 mg/kg x 70 kg x 0.5 = 0.0035 mg/L

2 L x 500

where:

* no observable effect level = 0.1 mg/kg body weight per day
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of lowest lethal dose allocated to drinking-water = 0.5
* uncertainty factor = 500 (10 for intraspecies variation, 10 for interspecies variation, 5 for the inadequacy of the studies and database).

The MAV in the 1995 DWSNZ had been derived by the MoH as follows:

0.5 mg/kg x 70 kg x 0.2 x 2.5 = 0.005 mg/L

2 L x 2,000

where:

* lowest lethal dose in humans = 0.5 mg/kg body weight
* average weight of adult = 70 kg
* average quantity of water consumed by an adult = 2 L per day
* proportion of lowest lethal dose allocated to drinking-water = 0.2
* uncertainty factor = 2,000 (10 for intraspecies variation, 2 for interspecies variation, 10 for the inadequacy of the studies and database, 10 for nature and a severity of effect)
* arbitrary factor = 2.5 (the determination was done by a very conservative process which gave a result similar to that found in tea as it is normally consumed. Tea leaves are a natural source of 1080. Consequently, the 2.5 factor was applied for common sense reasons).

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