PHYSICAL AND CHEMICAL CHARACTERISTICS

Acephate

(endorsed 2011)

GUIDELINE

Based on human health concerns, acephate in drinking water should not exceed 0.008 mg/L.

RELATED CHEMICALS

Acephate (CAS 30560-19-1) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, including chlorpyrifos, diazinon, dichlorvos, ethion and temephos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, acephate would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Acephate (O,S-dimethyl acetylphosphoramidothionate) is used for the control insects on fruit, vegetable and nut crops. Acephate breaks down and is metabolised to methamidophos, another insecticide.

There are registered products containing acephate in Australia. These products are intended for professional use and are available as soluble concentrates intended to be diluted and applied by ground or aerial spray application. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to acephate and its metabolites is residues in food. Residue levels in crops grown according to good agricultural practice are generally low.

Agricultural use of acephate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

There are few data on concentrations of acephate in drinking water in Australia. Acephate has been detected in mains water in Poland with concentrations generally in the range of 0.0001 to 0.0015 mg/L (0.1 to 1.5 µg/L), and up to a maximum of 0.0106 mg/L (10.6 µg/L) (Badach *et al.* 2007). Acephate has also been reported in river water in Spain, with a mean concentration of 0.00047 mg/L (0.47 µg/L) and a maximum of 0.00217 mg/L (2.17 µg/L) over 20 sampling sites (Espigares *et al.* 1997).

TREATMENT OF DRINKING WATER

No reported instances of reliable removal of acephate from drinking water at typical activated carbon doses and contact times have been identified. Some case studies on activated carbon have been reported with very high carbon doses; for example, on the treatment of wastewater from a pesticide manufacturing plant (Banerjee 2002) or in benchscale tests (Suzuki 2002). Although acephate has a relatively short soil half-life of between 3 and 6 days, the hydolysis half life is much longer, at 169 days, rendering reservoir detention an unreliable treatment method for the removal of acephate from water.

MEASUREMENT

Residues of acephate and methamidophos are traditionally determined by gas chromatography–electrodialysis (Espigares *et al*. 1997, Badach *et al*. 2007). The detection limit by this method is 0.00005 mg/L (0.05 µg/L) (Badach *et al*. 2007). Analysis of highly polar, water-soluble organophosphates, including acephate and methamidophos, using hydrophilic interaction liquid chromatography with tandem mass spectrometry has produced much lower limits of detection (Hayama *et al*. 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for acephate is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.22 mg/kg bw/day from a 2-year dietary rat study. The NOEL was based on inhibition of cholinesterase. The ADI incorporates a safety factor of 100 and it was established in 1998.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Acephate is rapidly absorbed from the gastrointestinal tract and widely distributed in the body. It is rapidly eliminated, mainly in the urine, as unchanged acephate. It has a low potential for bioaccumulation. The primary metabolite is methamidophos.

Acute effects: Acephate has low to moderate oral acute toxicity, and low dermal toxicity. It is not a skin sensitiser. Clinical symptoms of toxicity were typical of cholinesterase inhibition and included tremors, prostration, coma, piloerection, ataxia, and salivation.

Short-term effects: Decreased erythrocyte cholinesterase activity was seen at the lowest dose tested of 0.5 mg/kg bw/day and above in a 21-day repeat-dose dermal study in rabbits. No other effects were seen.

Decreased plasma, erythrocyte, and brain cholinesterase activity was seen at a dose of 2.5 mg/kg bw/day (monkey) and 3.75 mg/kg bw/day (rat) in 1-month repeat dose dietary studies. Both studies used a single dose level and no other effects were seen. A NOEL was not established in either study.

Long-term effects: Long-term toxicity studies were performed in mice (2 years), rats (28 months), and dogs (2 years). Decreased brain, plasma and erythrocyte cholinesterase activity was seen at doses of 2 mg/kg bw/day (rats). The sole effect in dogs was decreased erythrocyte cholinesterase activity at the highest dose tested of 2.5 mg/kg bw/day. Histopathological changes in the liver (non-neoplastic lesions) at doses of 15 mg/kg bw/day and above were the only effect observed in mice. The lowest overall NOEL was 0.22 mg/kg bw/day in rats, and this is the basis for the current ADI.

NOTE: Important general information is contained in PART II, Chapter 6

Carcinogenicity: Based on a 2-year study in mice, there is no evidence of carcinogenicity for acephate.

Genotoxicity: Acephate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal developmental.

Poisons Schedule: Acephate is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF GUIDELINE

The health-based guideline value of 0.008 mg/L for acephate was determined as follows:

$$0.008 \text{ mg/L} = \frac{0.22 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.22 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Acrylamide

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of acrylamide in drinking water should not exceed 0.0002 mg/L.

GENERAL DESCRIPTION

Acrylamide occurs as a minor impurity in polyacrylamide. It may be present in drinking water through the use of polyacrylamides as flocculant aids in water treatment, and through the use of grouting agents containing polyacrylamide. Overseas studies have reported concentrations of up to a few micrograms per litre in drinking water.

When nonionic or anionic polyacrylamides are used in water treatment at a typical dose level of 1 mg/L, the maximum theoretical concentration of acrylamide has been estimated at 0.0005 mg/L, with practical concentrations 2–3 times lower. Residual levels of acrylamide from the use of cationic polyacrylamides may be higher.

Concern over the health effects of acrylamide has led some countries to introduce tight restrictions on its use for water treatment.

Polyacrylamide is used in food processing and exposure to acrylamide may also occur from this source.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Acrylamide has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

Acrylamide can be removed from drinking water by adsorption onto granular activated carbon. It is not removed effectively by conventional water treatment or with powdered activated carbon.

MEASUREMENT

Acrylamide can be analysed using high performance liquid chromatography with ultraviolet detection (Brown and Rhead 1979). The sample is brominated to form 2,3-dibromopropionamide, which is extracted with ethyl acetate and analysed. The limit of determination is 0.0002 mg/L.

HEALTH CONSIDERATIONS

Acrylamide is readily absorbed following ingestion or inhalation, or through the skin, and it forms a number of metabolites. It can accumulate in nervous system tissues and blood. The results of animal studies indicate that it is largely excreted as metabolites in urine and bile. It can cross the placenta.

An extensive review and summary of the human and animal toxicity data for acrylamide is available (IPCS 1985).

Humans exposed for a short time to well water contaminated with up to 400 mg/L of acrylamide showed

effects including confusion, disorientation, memory disturbances and hallucinations. They recovered fully within 4 months. Long-term occupational exposure has resulted in skin irritation, fatigue, foot weakness and sensory changes.

In animals, acrylamide is well established as a neurotoxicant. Short- and long-term effects are similar, with exposure causing paralysis in the hind limbs of cats, dogs and rats at doses from 5 mg/kg body weight per day. The animals recovered completely when short-term exposure stopped. Acrylamide can also impair reproductive organs in rats, cats and dogs at the same dose.

Animal studies indicate that acrylamide is a carcinogen. Male rats receiving low oral doses (0.5 mg/kg body weight per day) for 2 years had increased incidence of scrotal, thyroid and adrenal tumours. Female rats exposed for 18 months had increased tumours of the mammary glands, central nervous system, thyroid and uterus. Mice exposed to higher doses for 8 weeks showed an increased incidence of lung adenomas.

Several studies have reported that acrylamide is not mutagenic in bacteria, but induces gene mutations and chromosomal aberrations in mammalian cells both *in vitro* and *in vivo*.

The International Agency for Research on Cancer (IARC) has concluded that acrylamide is probably carcinogenic to humans (Group 2A, inadequate evidence in humans, sufficient evidence in experimental animals, and supporting mechanistic evidence) (IARC 1994).

DERIVATION OF GUIDELINE

The guideline value for acrylamide of 0.0002 mg/L is based on a consideration of health effects in relation to the limit of determination for analysis using commonly available techniques.

Health-based derivations can be determined as follows:

i) $$0.0007 \text{ mg/L} = \frac{0.2 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 0.2 mg/kg body weight per day is the no-effect level from a 93-day drinking water study using rats (Burek *et al.* 1980). Longer-term studies only identify lowest effect levels, which are significantly higher than the no-effect level used in the calculation.
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for a less than lifetime study). An additional factor of 10 for carcinogenicity was not applied as tumours occur at doses above those that cause neurotoxic effects. The use of this safety factor was recommended by the NHMRC Standing Committee on Toxicity.

ii) On the basis of a drinking water study using rats (Johnson *et al.* 1986), the excess cancer risk of lifetime consumption of water with an acrylamide concentration of 0.00005 mg/L (50 ng/L) was conservatively estimated by the World Health Organization (WHO), using a linear multistage model, at one additional cancer per million people.

NOTE: Important general information is contained in PART II, Chapter 6

The guideline value was set at the limit of determination because this is within the values derived from health considerations, and provides an adequate degree of protection. This is consistent with the general approach adopted for compounds that are known genotoxic carcinogens (see Section 6.4). The higher WHO guideline value of 0.0005 mg/L is based on an estimated lifetime risk of one additional cancer per 100,000 people.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Aldicarb

(endorsed 2011)

GUIDELINE

Based on human health concerns, aldicarb in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Aldicarb (CAS 116-06-3) belongs to the carbamate class of chemicals. There are many other pesticides in this class, including asulam, carbaryl, methomyl and pirimicarb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, aldicarb would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Aldicarb is an insecticide used in agriculture for the control of insects and nematodes in the soil. Aldicarb is taken up by plants, where it is metabolised into toxicologically active metabolites.

There is at least one registered product that contains aldicarb in Australia. Aldicarb products are intended for professional use and are available as a concentrated granular formulation to be incorporated by tractor equipment directly into the soil of citrus, cotton, and cane crops. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to aldicarb and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of aldicarb may potentially lead to contamination of source waters through processes such as leaching into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

There are few data on concentrations of aldicarb in Australian drinking waters. In Canada, aldicarb was reported in 111 of 1017 samples in surveys of private and municipal drinking-water supplies (detection limits 0.00001–0.003 mg/L [0.01–3.0 µg/L]); the maximum concentration was 0.028 mg/L (28 µg/L) (WHO 2003)

TREATMENT OF DRINKING WATER

Aldicarb removal in municipal water treatment has been investigated (Kruithof 1994). For the removal of pesticides, operational techniques such as air-stripping, GAC-filtration and ozonation are available and of these, GAC-filtration is considered moderately effective, although is very susceptible to competitive adsorption by natural organic matter.

Reverse osmosis and nanofiltration have been tested for effectiveness at removing Aldicarb degredates from environmental water samples and has been shown to be effective in some applications (Baier *et al*. 1987, Kiso *et al*, 2002).

The effectiveness of ultraviolet irradiation and peroxide, ozonation and chlorination for the removal of aldicarb from drinking water has been identified in laboratory studies (Mason *et al*. 1990, Huston and Pignatello 1999).

MEASUREMENT

Aldicarb and its sulfoxide and sulfone oxidation products can be determined simultaneously by capillary gas chromatography with a nitrogen-phosphorus detector (Health Canada 1995, WHO 2003). The detection limit is 1 µg/L for all three compounds.

High-performance liquid chromatography (HPLC) is often the method of choice and is the basis of United States Environmental Protection Agency (USEPA) Method 531 for carbamate pesticides. Aldicarb, its sulfoxide and its sulfone are separated by reversed-phase HPLC, and the analytes are then hydrolysed to methylamine followed by post-column derivatisation with ortho-phthalaldehyde and fluorescence detection. The detection limits are 0.0013, 0.0008 and 0.0005 mg/L (1.3, 0.8 and 0.5 µg/L) for aldicarb, the sulfoxide and the sulfone, respectively (Health Canada 1995, WHO 2003).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for aldicarb is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.01 mg/kg bw/day 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 and it was established in 1999.

The previous health value was 0.002 mg/L (NHMRC and NRMMC, 2004).

HEALTH CONSIDERATIONS

Metabolism: Aldicarb is readily absorbed from the gastrointestinal tract and widely distributed in the body. It is rapidly excreted, mainly via the urine. The primary metabolites are the sulfoxide and the sulfone.

Acute effects: Aldicarb has a high acute oral and dermal toxicity. Aldicarb is a skin sensitiser in guinea pigs. Significant plasma and erythrocyte cholinesterase inhibition was seen at doses of 0.025 mg/kg bw and above in a single dose study in human volunteers using drinking water as the dosing vehicle. Clinical symptoms of toxicity typical of cholinesterase inhibition, including tremors, prostration, coma, piloerection, ataxia, and salivation, were seen at the highest dose tested (0.06 mg/kg bw/day) in this study. The NOEL was 0.01 mg/kg bw/day and this is the basis for the ADI.

Short-term effects: Fourteen-day dietary studies in dogs reported reduced bodyweight and clinical signs of cholinesterase inhibition. Cholinesterase inhibition was observed at 0.02 mg/kg bw/day. In 3-month dietary studies in rats and dogs, effects included decreased body weight gain and food consumption in rats, and cholinesterase inhibition was reported at doses of 0.07 mg/kg bw/day and above.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: In medium-term (13-week) dietary studies in rats and dogs, effects were typical of cholinesterase inhibitors and included decreased cholinesterase activity in plasma (dogs and rats), erythrocytes and brain (rats only), at doses of 0.05 mg/kg bw/day and above (rats). Mortality was seen at doses of 0.1 mg/kg bw/day and above (rats). No other effects were seen (in both rats and dogs). The lowest overall NOEL was 0.02 mg/kg bw/day (rats).

In long-term dietary studies in rats and dogs, effects were typical of cholinesterase inhibitors and included plasma and erythrocyte cholinesterase inhibition at the lowest dose tested, 0.024 mg/kg bw/day (dogs), and above. Neuromuscular disturbances, hair loss, decreased bodyweight gain and associated decreases in food consumption, were seen at the highest dose tested in rats, 1.87 mg/kg bw/day. The NOEL in rats was 0.05 mg/kg bw/day. A NOEL was not found in the long-term dietary study in dogs.

Carcinogenicity: Based on long-term studies in rats, there is no evidence of carcinogenicity for aldicarb.

Genotoxicity: Aldicarb and its metabolites are not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A reproduction study in rats, and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or on foetal development.

Neurotoxicity: Reduced grip strength, inactivity, and delayed sensorimotor responses of offspring were seen in oral dosing studies in pregnant female rats given 0.3 mg/kg bw/day from gestation day 6 to lactation day 10 (23-26 days). The NOEL for effects on the developing nervous system was 0.1 mg/kg bw/day.

Poisons Schedule: Aldicarb is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.004 mg/L for aldicarb was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.01 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.01 mg/kg bw/day is the NOEL based on an acute human study.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated amount maximum of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from human studies to account for intraspecies variation.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Aldrin and Dieldrin

(endorsed 2011)

GUIDELINE

Based on human health concerns, aldrin and dieldrin when measured together in drinking water should not exceed 0.0003 mg/L.

RELATED CHEMICALS

Aldrin and dieldrin (CAS 309-00-2/CAS 60-57-1) belong to the organochlorine class of chemicals and are classified as persistent organic pollutants (POP). Other POPs that were previously used as pesticides include DDT and heptachlor (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present as contaminants in drinking water, aldrin and dieldrin when measured together would not be a health concern unless the concentration exceeded 0.0003 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Aldrin and dieldrin have been used previously as insecticides for the control of soil-dwelling pests and for the protection of wood structures against termites and wood borers.

There are no registered products that contain aldrin or dieldrin in Australia, but de-registered compounds may still be detected in water.

Exposure sources: Aldrin is largely converted to dieldrin, which persists in the environment. The general public may be exposed to low levels of dieldrin through residues in food and/or contaminated source waters from previous use of aldrin and dieldrin as insecticides. The residue definition of aldrin and dieldrin is defined as "sum of HHDN (aldrin) and HEOD (dieldrin)".

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data of aldrin or dieldrin in Australian drinking water could be found. The concentrations of aldrin and dieldrin in aquatic environments and drinking water in industrialised countries are normally less than 0.01 µg/L (WHO 2003).

TREATMENT OF DRINKING WATER

Aldrin is completely removed by either chlorination or activated carbon, while dieldrin is more recalcitrant, with removal efficacies of 30% for chlorination and 85% for activated carbon (Ormad *et al.* 2008).

MEASUREMENT

Aldrin and dieldrin are determined by extraction with pentane followed by gas chromatography with electron capture detection. The detection limits in tap water and river water are about 0.001 µg/L for aldrin and 0.002 µg/L for dieldrin (WHO 2003).

HISTORY OF THE HEALTH VALUES

The current tolerable daily intake (TDI) for both aldrin and dieldrin is 0.0001 mg per kg bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.025 mg/kg bw/day from 2-year dietary studies in rats and dogs. The NOEL is based on liver damage. The TDI incorporates a safety factor of 250 and was established in 2003

When aldrin and dieldrin were in use in Australia, the ADI was 0.0001 mg/kg bw, based on a NOEL of 0.025 mg/kg bw/day from the long-term dietary studies. As aldrin and dieldrin are no longer used in agricultural practice in Australia, the ADI was not maintained.

The previous health value for aldrin and dieldrin was 0.0003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Since aldrin is converted to dieldrin in the environment, the toxicity of dieldrin is the major consideration in relation to the health impact of aldrin and/or dieldrin in drinking water.

Metabolism: Aldrin and dieldrin are rapidly absorbed via the gastrointestinal tract in animals and humans. Aldrin is rapidly metabolised to dieldrin, and dieldrin is further metabolised, mainly in the liver. Aldrin and dieldrin accumulate in adipose tissue, from which they can be mobilised into blood. Some excretion of both compounds occurs, mainly as metabolites via urine and faeces. The major metabolite of dieldrin identified is the 9-hydroxy derivative.

Acute effects: Both aldrin and dieldrin have high acute oral and dermal toxicity. Skin sensitisation data are not available for aldrin or dieldrin.

Short-term effects: Short-term dietary studies in rats with both aldrin and dieldrin indicated an increase in relative liver weight and reversible hypertrophy of hepatocytes at dose levels above 5 mg/kg bw/day. In dogs, liver weight changes were observed at 0.05 mg/kg bw/day and muscular spasms and convulsions at high dose levels. In a two-year human volunteer study, no clinical signs of toxicity were reported up to doses of 0.2 mg/kg bw/day.

Long-term effects: Long-term dietary studies in mice, rats and dogs showed the liver to be the target organ of toxicity. In mice, there was liver enlargement and hyperplasia, and benign and malignant liver tumours at doses of 0.187 mg/kg bw/day and above. Clinical signs of toxicity, which included hair loss, diarrhoea, hyper-excitability, abdominal distention and tremors, were reported at doses of 0.5 mg/kg bw/day and above. Two-year dietary studies in rats and dogs reported by the Joint Meeting of Pesticide Residues (JMPR 1966, 1970, 1977) showed increased liver weights and microscopic liver lesions in rats at 0.1 mg/kg bw/day and above, and increased liver weight and liver damage at 0.075 mg/kg bw/day in dogs. The NOEL from these studies was 0.025 mg/kg bw/day, and this is the basis for the current Australian TDI.

Carcinogenicity: There was evidence of liver tumors in mice, but not rats, trout or hamsters. In epidemiological studies in workers, there was no evidence of an increased incidence of cancer related to exposure to aldrin and dieldrin.

Genotoxicity: Aldrin and dieldrin are not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: Reproductive studies in mice, rats and dogs up to 6 generations reported an increase in foetotoxicity and pre-weaning pup mortality at 0.125 mg/kg bw/day and above. Developmental toxicity studies in mice, rats and rabbits did not produce any evidence of effects on foetal development.

Immunotoxicity: There was no evidence of immunotoxicity based on studies in mice.

Poisons Schedule: Aldrin and dieldrin are included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.0003 mg/L for aldrin and dieldrin was determined as follows:

$$0.0003 \text{ mg/L} = \frac{0.025 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 250}$$

where:

- 0.025 mg/kg bw/day is the NOEL based on long-term (2-year) studies in rats and dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 250 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation and an additional safety factor of 2.5 based on concern about carcinogenicity observed in mice.

The World Health Organization established a health-based guideline value of 0.00003 mg/L for aldrin and dieldrin in 2003 (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Aluminium

(endorsed 2001)

GUIDELINE

Based on aesthetic problems caused by post-flocculation, the concentration of acid-soluble aluminium in drinking water should not exceed 0.2 mg/L. Water authorities are strongly encouraged to keep acid-soluble aluminium concentrations as low as possible, preferably below 0.1 mg/L.

No health-based guideline is set for aluminium at this time but this issue will be kept under review.

GENERAL DESCRIPTION

Aluminium may be present in water through natural leaching from soil and rock, or from the use of aluminium salts as coagulants in water treatment.

Aluminium is used in many industrial and domestic products including antacids, antiperspirants and food additives, and in vaccines. It is commonly used by the food industry for food containers and packaging, and many cooking utensils are made from aluminium.

Surveys in the United States and the United Kingdom have reported aluminium concentrations in natural water sources of 0.014–1.2 mg/L. Concentrations in some Australian water sources can be considerably higher due to the presence of clay minerals (aluminosilicates); for example, up to 18 mg/L in the Murray River. Residual aluminium concentrations in treated water depend on the concentration in the water source, the alum dose used, the pH, and the filtration efficiency.

Where alum is used as a coagulant in water treatment, post-flocculation effects can occur if the soluble aluminium concentration in the treated water exceeds 0.2 mg/L. Depending on pH, a whitish gelatinous precipitate of aluminium hydroxide can be formed in the distribution system which may result in customer complaints about 'milky coloured' water. Aluminosilicates in source water are very insoluble and do not cause post-flocculation problems.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, the concentration of aluminium varies from 0.01 mg/L to 0.9 mg/L, with typical concentrations of approximately 0.1 mg/L for fully treated supplies.

TREATMENT OF DRINKING WATER

Aluminium concentrations in drinking water can be reduced using the conventional water treatment practices of flocculation and filtration. A well-operated water filtration plant (even using aluminium as a flocculant) can achieve aluminium concentrations in the finished water of less than 0.1 mg/L.

MEASUREMENT

The term 'soluble' should be taken to mean truly soluble, not 'filterable through a 0.45 µm pore size filter'. Finely suspended aluminosilicate clay particles can pass through a 0.45 µm filter but are not truly soluble and will not cause post-flocculation problems.

Acid-soluble aluminium is determined after acidifying the sample to pH 1.5–2, followed by filtration through a 0.45 µm membrane filter. If analysis of the filtrate by the normal method (e.g. graphite furnace atomic absorption spectroscopy, APHA Method 3500-Al Part B 1992) gives a result above the guideline value, the filtrate should be re-analysed using the catechol violet colorimetric method (APHA Method 3500-Al Part E 1992), which provides a better estimate of the reactive aluminium component. The limit of determination for the latter method is approximately 0.01 mg/L.

Based on experience with their water supplies, authorities may choose to monitor total aluminium concentration and perform specific assays for acid-soluble aluminium only if total aluminium concentration exceeds 0.1 mg/L.

HEALTH CONSIDERATIONS

It has been estimated that for Australian adults, the intake of aluminium from food and beverages is approximately 5–7 mg/day. Drinking water contributes less than 2% of the total daily intake, and only 0.3–0.4% of the aluminium in water is absorbed by the body. Recent studies have shown that the bioavailability (i.e. uptake into the bloodstream) of aluminium in drinking water is similar to that of food (Stauber *et al*. 1999).

The metabolism of aluminium in humans is poorly understood. Studies indicate that less than 1% of dietary aluminium is absorbed by the gastrointestinal tract, with the remainder excreted in faeces. The small amount absorbed passes into the blood stream. Some aluminium accumulates in bone, liver and brain tissue but most is removed from the blood stream by the kidneys and excreted. In healthy adults, the total accumulated body load of aluminium has been estimated at about 35 mg. Whether this remains constant with age has not been determined.

There is considerable evidence that aluminium is neurotoxic. Kidney dialysis patients, in whom the gut barrier is bypassed, can accumulate aluminium in their blood resulting in an encephalopathy known as dialysis dementia. Investigations have established a correlation between the concentration of aluminium in water used to prepare dialysis fluid and the incidence of dialysis dementia. If this condition is not too far advanced it responds to chelation therapy. It appears that dialysis patients are much more susceptible to aluminium in dialysis fluid than from other sources such as food and antacids. Aluminium has also been linked to other conditions associated with the use of dialysis units including osteomalacia (a softening of the bones) and anaemia. Reverse osmosis or deionisation units are now used to treat dialysis water before use, and aluminium concentrations are kept below 0.01 mg/L.

Aluminium has been associated with two severe neurodegenerative diseases: Parkinsonism dementia (PD) and amyotrophic lateral sclerosis (ALS). Both conditions have a high incidence amongst the Chamorro people of Guam, an area where aluminium is naturally present in food and drinking water. ALS is common in the Pacific, Western New Guinea and the Kii peninsula of Japan. Both PD and ALS are characterised by loss of motor function and the presence of neurofibrillary tangles in the brain. One hypothesis suggests that chronic nutritional deficiencies of calcium and magnesium lead to increased absorption of aluminium, resulting in its deposition in neurons of the brain (Garruto and Yase 1986, Garruto *et al*. 1990). There was an appreciable decrease in the incidence of these conditions when the areas became westernised, with associated changes in dietary habits, importing of food and improvements to the water supply.

Elevated concentrations of aluminium have been found in the autopsied brains of people who had suffered Alzheimer's disease, in regions of the brain containing large numbers of the neurofibrillary tangles which are characteristic of the disease, and aluminium has been proposed as one of a number of causal agents (Perl and Brody 1980). There have been a number of epidemiological studies to determine if aluminium in drinking water plays a role in Alzheimer's disease. Although some studies indicated that a tentative link may exist, more recent evidence (Martyn *et al*. 1997) suggests that aluminium in drinking water is not associated with increased risk of Alzheimer's disease.

NOTE: Important general information is contained in PART II, Chapter 6

A number of animal studies of aluminium toxicity have been undertaken although there has been very little research done using aged animals. Most studies have used rats fed or injected with large amounts of aluminium and have reported only minor changes to bodyweight, with some behavioural changes and locomotor effects. Elevated concentrations of aluminium have been reported in the brain, liver and kidneys. The studies are not adequate to set a reliable no observable effect level (NOEL).

Aluminium is not generally thought to be mutagenic or genotoxic, although aluminium has been shown to bind to DNA of a number of animal species and has displayed mutagenic activity in some, but not all, tests using bacteria. Ingestion of aluminium is not known to cause cancer in humans or animals.

The NHMRC Standing Committee on Toxicity has reviewed the toxicological data for aluminium and concluded that there are insufficient data to set a NOEL.

DERIVATION OF GUIDELINE

Post-flocculation problems (described above) associated with the use of alum as a coagulant may occur if acid-soluble aluminium exceeds 0.2 mg/L. As the alum floc is soluble in dilute acid (pH 1.5–2), post-flocculation problems will generally be avoided if the acid-soluble concentration of aluminium is below 0.2 mg/L. Water authorities are strongly encouraged to keep acid-soluble aluminium concentrations as low as possible, preferably below 0.1 mg/L. Well operated water filtration plants, even those using aluminium salts as flocculants, should have little difficulty in achieving this.

A guideline value lower than 0.2 mg/L may need to be adopted by some water authorities, depending on the amount of naturally occurring organic material in the water.

Although data are insufficient to set a guideline value based on health considerations, there is public concern over the possible health effects of aluminium. This issue should be reviewed when further studies are undertaken.

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NOTE: Important general information is contained in PART II, Chapter 6

Ametryn

(endorsed 2011)

GUIDELINE

Based on human health concerns, ametryn in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Ametryn (CAS 834-12-8) belongs to the triazine class of chemicals. Other pesticides in this class include atrazine, propazine, symazine and cyanazine (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, ametryn would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Ametryn is a pre- and post-emergent herbicide for the control of summer grasses and broad-leaf weeds in sugarcane, pineapples and in industrial areas, such as roadsides and railway lines.

There are registered products containing ametryn in Australia. These products are intended for professional use and are formulated as a liquid concentrate or a water dispersible granule, either alone or with other active ingredients. These products are applied using ground boom, aerial and hand-held methods of spraying. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to ametryn is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of ametryn may potentially lead to contamination of sources waters through processes such as run-off, spray-drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Ametryn has been reported in Australian source waters at concentrations up to 0.3 µg/L in sugar cane growing areas (Mitchell *et al*, 2004). Similar results have been reported in drinking source waters of a sugar cane growing area of Brazil (Lanchote *et al*, 2000).

TREATMENT OF DRINKING WATER

Ametryn has been shown to be completely removed from water by chlorination when the chlorine dose is adjusted to match chlorine demand (Ormad *et al*. 2008).

Ozonation and activated carbon adsorption for ametryn removal has also been reported with moderate to low success (Ormad *et al*. 2008). Conventional coagulation/flocculation has been shown to be unreliable for removal, although complete removal can be obtained if activated carbon adsorption is practiced in conjunction with conventional clarification. Jar testing with different oxidants, adsorbents, coagulants, dose rates and contact times is recommended to optimise removal if ametryn is detected.

MEASUREMENT

Ametryn can be measured in drinking waters using solid phase extraction followed by high performance liquid chromatography with ultraviolet detection (Carabias-Martinez *et al*. 2006). The practical limit of detection for this method is 1 μg/L. Alternatively, ametryn can be monitored by direct aqueous injection liquid chromatography with electrospray ionisation–tandem mass spectrometry, with a reported detection limit of 0.05 μg/L (Huang *et al*. 2008).

HISTORY OF THE HEALTH VALUES

The acceptable daily intake (ADI) for ametryn is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2 mg/kg bw/day from a reproduction study in rats. The ADI incorporates a safety factor of 100 and was established in 2006.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Ametryn is absorbed readily from the gastrointestinal tract and is rapidly excreted (89% in urine and faeces over 7 days). Thirty-five metabolites were identified in the urine and faeces in the rat.

Acute effects: Ametryn has low acute oral and dermal toxicity. It is a skin sensitiser in guinea pigs. Symptoms associated with acute toxicity were dyspnoea, ruffled fur, diarrhoea, sedation, and curved body posture.

Short-term effects: Short-term dietary studies in rats and a 21-day dermal study in rabbits showed transient decreases in body weight and food consumption at dose levels of 1000 mg/kg bw/day.

Long-term effects: Long-term studies were conducted in rats and dogs. A 2-year dietary study in rats reported anaemia and evidence of liver damage at dose levels of 2.2 mg/kg bw/day. A one-year study in dogs reported anaemia and degenerative changes in a number of organs at dose levels above 8 mg/kg bw/day.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for ametryn.

Genotoxicity: Ametryn is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproduction and developmental effects: A reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development. There was a transient decrease in bodyweight gain at 2 mg/kg bw/day, which was the overall NOEL. This is the basis for the ADI.

Poisons Schedule: Ametryn is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons

Standard should be consulted for further information.

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for ametryn was determined as follows:

$$0.07 \text{ mg/L} = \frac{2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2 mg/kg bw/day is the NOEL based on a reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Amitraz

(endorsed 2011)

GUIDELINE

Based on human health concerns, amitraz in drinking water should not exceed 0.009 mg/L.

RELATED CHEMICALS

Amitraz (CAS 33089-61-1) is in the amidine class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, amitraz would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Amitraz is an acaricide (miticide) and insecticide used for the control of heliothis and aphids on cotton; for the control ticks on cattle, deer, sheep, goats, circus animals and dogs; and for the control of mange in pigs.

There are registered products containing amitraz in Australia. These are intended for both professional and home veterinary use. The products are applied by ground spray or aircraft when used on cotton. They are used as a spray or in a pour-on formulation when used on livestock. Amitraz is also incorporated into a collar or a shampoo for use on dogs. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure are use of the home veterinary products, and residues in the food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of amitraz may potentially lead to contamination of source waters through processes such as run-off, spray-drift or entry into groundwater. The veterinary use of amitraz provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of amitraz in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of amitraz in drinking water have been identified.

MEASUREMENT

No suitable analytical methods for amitraz in drinking water have been identified. If there is an identified need to monitor amitraz in drinking water, it is expected that gas-chromatography–mass spectrometry and high performance liquid chromatography–mass spectrometry would be suitable techniques. Both of these approaches have previously been used for monitoring amitraz in food products such as fruit and honey.

HISTORY OF THE HEALTH VALUES

The acceptable daily intake (ADI) for amitraz is 0.002 mg per kg of bodyweight (mg/kg bw) based on a no-observed-effect level (NOEL) of 0.25 mg/kg bw/day from a 2-year study in dogs. The ADI incorporates a safety factor of 100 and was established in 1986.

A health-based guideline value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Amitraz is absorbed rapidly from the gastrointestinal tract of humans, and is metabolised and excreted mainly in the urine within 72 hours. The main metabolites are 4-formamido-3-methyl benzoic acid and 4-acetamido-3-methyl benzoic acid. In dogs, peak blood levels were seen at 8 hours and 80% of the dose was excreted within 24 hours.

Acute effects: Amitraz has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: *S*hort-term dietary studies in mice indicated liver toxicity at 3 mg/kg bw/day and above.

Long-term effects: A 2-year dietary study in rats showed an increase in nervous and aggressive behaviour at 10 mg/kg bw/day. A 2-year study in dogs showed central nervous system depression on days 1 and 2 of treatment. There was also an increase in the blood glucose levels at doses above 0.25 mg/kg bw/day. The NOEL of 0.25 mg/kg bw/day is the basis for the ADI.

Carcinogenicity: An increase in hepatocellular adenomas and carcinomas was observed in female B6C3F1 mice at 60 mg/kg bw/day. This is considered to be a species-specific effect and not relevant to humans.

Genotoxicity: Amitraz is not considered genotoxic, based on *in vitro* or *in vivo* short-term studies.

Reproductive and developmental effects: A reproduction study in rats showed decreased bodyweight gain and reduced fertility in the dams together with decreased pup survival at 21 days in all generations treated at 50 mg/kg bw/day. A 28-week study in mice reported hormonal changes and effects on the oestrus cycle at 14.3 mg/kg bw/day. In developmental studies in rats and rabbits, there was evidence of foetal toxicity at dose levels of 12 and 25 mg/kg bw/day, respectively, but no evidence of teratogenicity.

Poisons Schedule: Amitraz is included in Schedule 6 of the of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.009 mg/L for amitraz was determined as follows:

$$0.009 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.25 mg/kg bw/day is the NOEL based on a long-term (2-year) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variations.

Amitraz is included in the World Health Organization guidelines for drinking water quality list of chemicals from agricultural activities excluded from guideline value derivation because it is "degrades rapidly in the environment and is not expected to occur at measurable concentrations in drinking-water supplies" (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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WHO (World Health Organization) (2004). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Amitrole

(endorsed 2011)

GUIDELINE

Based on human health concerns, amitrole in drinking water should not exceed 0.0009 mg/L.

RELATED CHEMICALS

Amitrole (CAS 61-82-5) belongs to the triazole class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, amitrole would not be a health concern unless the concentration exceeded 0.0009 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Amitrole is a herbicide used to kill weeds in public places and home gardens.

There are registered products containing amitrole in Australia. These are for professional and home garden use. Amitrole is used alone or in combination with other herbicides as concentrated solutions or as wettable powders, and these are generally applied as a spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to amitrole is direct exposure following home garden use. Amitrole is not currently registered for use on food crops and the maximum residue limits are set at the level of detection.

Use of amitole in public places and in the home garden may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATERS

Amitrole is a persistent herbicide that can easily pollute ground and surface waters used in drinking water production. No Australian data was found but concentrations in ground and surface water of up to 1.1 µg/L have been reported (Bobeldijk *et al.* 2001).

TREATMENT OF DRINKING WATER

Amitrole has been shown to be effectively removed by ozonation (Bozkaya-Schrotter *et al.* 2008). Moderate removal can also be achieved using powdered activated carbon adsorption (Lopez-Ramon *et al.* 2007).

MEASUREMENT

Numerous analytical methods have been described for the detection of amitrole. Gas chromatography can achieve a limit of detection of 0.1 µg/L in drinking water (Pachinger *et al.* 1992). High-performance liquid chromatographic (HPLC) methods are currently the analytical techniques of choice for amitrole and other polar compounds. Different HPLC methods for the determination of amitrole after derivatisation have been described. HPLC with electrochemical detection can achieve limits of detection of 0.1 µg/L. Solid-phase extraction followed by HPLC with atmospheric pressure chemical ionisation–tandem mass spectrometry can achieve a limit of detection of 0.025 µg/L in drinking water (Bobeldijk *et al.* 2001).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for amitrole is 0.0003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.025 mg/kg bw/day from a 1-year rat study. The ADI incorporates a safety factor of 100 and was established in 1984.

An acute reference dose has not been established for amitrole.

The previous health value was 0.01 mg/L (NHMRC and NRMMC, 2004).

HEALTH CONSIDERATIONS

Metabolism: Amitrole is readily absorbed through the gastrointestinal tract. It undergoes minimal metabolism and is excreted largely unchanged in the urine.

Acute effects: Amitrole has a low acute oral and dermal toxicity. Its potential for skin sensitisation is unknown.

Short-term effects: Short-term oral toxicity studies in rats reported histopathological changes in the thyroid and changes to the uptake of iodine by the thyroid at 20 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies were conducted in mice and rats. In mice, there were effects on thyroid weight and uptake of iodine at 15 mg/kg bw/day. In rats, there was a decrease in thyroid hormone levels, an increased incidence of thyroid hyperplasia and an increase in thyroid tumours at 2.5 mg/kg bw/day. The NOEL in the 1-year rat study was 0.025 mg/kg bw/day, and this is the basis of the ADI.

Carcinogenicity: In long-term studies in rats, amitole caused an increase in thyroid tumours, which is likely to be a consequence of an increased incidence of thyroid hyperplasia.

Genotoxcity: Amitole gave equivocal results in some *in vitro* studies, but negative results in *in vivo* studies. Based on the weight of evidence, amitole was not considered genotoxic.

Reproductive and developmental effects: In a reproduction study in rats and development studies in mice and rats, there was no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Amitrole is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.0009 mg/L for amitole was determined as follows:

$$0.0009 \text{ mg/L} = \frac{0.025 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.025 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Ammonia

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (corrosion of copper pipes and fittings), the concentration of ammonia (measured as ammonia) in drinking water should not exceed 0.5 mg/L.

No health-based guideline value is set for ammonia.

GENERAL DESCRIPTION

Ammonia dissolves rapidly in water to form an equilibrium mixture of free ammonia and the ammonium cation. It may be present in unchlorinated drinking water due to contamination of source water or through microbial metabolism. Ammonia is used in conjunction with chlorine to form chloramines to disinfect water supplies. Some residual will be present in the water, particularly if the chlorinator is not operating properly.

Ammonia is used commercially in animal feeds and fertilisers, and in the manufacture of fibres, plastics and explosives. Ammonia products are widely used as cleaning agents and food additives.

Most uncontaminated source waters have ammonia concentrations below 0.2 mg/L. High concentrations (greater than 10 mg/L) have been reported where water is contaminated with animal waste. Ammonia is unlikely to be detected in chlorinated supplies as it reacts quickly with free chlorine.

Ammonia in water can result in the corrosion of copper pipes and fittings, causing copper stains on sanitary ware. It is also a food source for some microorganisms, and can support nuisance growths of bacteria and algae, often with a resultant increase in the nitrite concentration.

The odour threshold of ammonia in water is 1.5 mg/L.

Ammonia can be an important indicator of pollution as it can be formed as an intermediate product in the breakdown of nitrogen-containing organic compounds, or of urea from human or animal excrement.

Food can contain substantial amounts of ammonia/ammonium and is the principal source of intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies concentrations of ammonia range up to 0.4 mg/L, but are generally less than 0.02 mg/L.

TREATMENT OF DRINKING WATER

Ammonia concentrations in drinking water supplies can be reduced by chemical or biological oxidation of ammonia to nitrate.

MEASUREMENT

The concentration of ammonia in water can be determined by a number of methods including colorimetric, titrimetric and potentiometric techniques. For determination of low concentrations, the phenate colorimetric method is commonly used (APHA 4500-NH_3 Parts D or H, 1992). The limit of determination for this method is 0.02 mg/L. Alternatively, the ammonia selective electrode method can be used (APHA 4500-NH_3 Part F, 1992) with a limit of determination of 0.03 mg/L.

Both of these methods determine the total free ammonia and ammonium ion measured as ammonia (NH_3).

HEALTH CONSIDERATIONS

Ammonia is an important metabolite in humans and animals. It is formed in the liver by the deamination of amino acids, and in the gastrointestinal tract by the breakdown of food by enzymes and bacterial flora.

Only an extremely small proportion of the ammonia absorbed in the intestinal tract originates directly from food or water. The major part is formed in the gut as a by-product of the breakdown of food. Almost all ammonia is absorbed. It is then transported to the liver and used mostly in the urea cycle.

An extensive review and summary of the human and animal toxicity data for ammonia is available (IPCS 1986).

Ammonia has a toxic effect on humans only if the intake becomes higher than the detoxification capacity of the body. At doses above 32 mg ammonium per kilogram body weight per day (over 1000 mg/L) ammonium chloride influences the metabolism by shifting acid-base equilibrium, affecting glucose tolerance and reducing tissue sensitivity to insulin.

In studies with animals, high doses of ammonia (over 100 mg/kg body weight per day) have generally not produced any significant toxic effects. Ammonium hydroxide did not result in an increase in the incidence of cancer when given to mice in their drinking water over a lifetime; however, there is some evidence that ammonia may act with cancer-causing compounds to increase the incidence of tumours.

Ammonia and ammonium chloride have shown mutagenicity in some tests with bacteria and animal cells.

DERIVATION OF GUIDELINE

Ammonia concentrations above 0.5 mg/L may attack copper pipes and fittings, or result in nuisance growths of microorganisms. Concentrations of ammonia that may cause health effects are unlikely to occur in drinking water supplies; accordingly, no health-based guideline is set.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Antimony

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of antimony in drinking water should not exceed the limit of determination of 0.003 mg/L.

GENERAL DESCRIPTION

Antimony, as the trivalent (Sb(III)) or pentavalent (Sb(V)) salts, has occasionally been detected in natural source waters. Occurrences are more common in areas near lead or copper smelting operations. Antimony–tin solder is beginning to replace lead solder and hence exposure to antimony in drinking water may increase in the future.

Antimony alloys and compounds are used in semiconductors, batteries, anti-friction compounds, ammunition, cable sheathing, and flame-proofing compounds. Antimony salts are used in glass, and in the manufacture of ceramics and pottery.

Studies overseas have generally found low concentrations in drinking water, typically less than 0.005 mg/L, but higher concentrations have been reported occasionally.

There are few data available on antimony concentrations in food. The United States Agency for Toxic Substances and Disease Registry has suggested that average daily consumption of antimony in food is about 0.018 mg.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for antimony.

TREATMENT OF DRINKING WATER

There are no published methods for removal of antimony from drinking water.

MEASUREMENT

The concentration of antimony in drinking water can be determined by hydride generation followed by analysis using atomic absorption spectroscopy. The limit of determination is approximately 0.001 mg/L. Alternatively, graphite furnace atomic absorption spectroscopy can be used with a limit of determination of 0.003 mg/L (APHA Method 3500-Sb Part B 1992).

HEALTH CONSIDERATIONS

Studies using rats have shown that about 15% of antimony is absorbed by the gastrointestinal tract. It is distributed mainly to the liver, spleen and heart, and to the thyroid and adrenal glands, and it is excreted in faeces and urine.

There have been a number of studies on the effects of long-term human exposure to antimony. One early study of adult male workers in an antimony smelter reported no adverse effects after persistent exposure over periods from 2 to 13 years. A more recent study where workers were exposed for 9 to 31 years to dust containing antimony trioxide and antimony pentoxide reported respiratory and eye problems as well as staining of the front tooth surface. A dermatitis condition was observed in more than half of the exposed workers. Other studies have reported heart irregularities, lung cancer, and spontaneous abortions

among female workers.

The toxicity of antimony to animals varies considerably depending on the compound used. No adverse effects have been associated with long-term exposure of rats to antimony trioxide. However, potassium antimony tartrate reduced the animals' lifespan, and antimony was found to accumulate in the heart, liver, kidney and spleen. It also affected blood glucose and cholesterol concentrations.

Animal studies have shown that antimony can cross the placenta. It may cause sterility, fewer offspring, and foetal damage.

Studies using male and/or female rats have reported that inhalation of concentrates of antimony trioxide and antimony ore increased the incidence of lung tumours in females. In ingestion studies on rats and mice, antimony did not appear to cause tumours.

Trivalent and pentavalent antimony salts have demonstrated mutagenic activity in tests with bacteria. They also induced chromosome aberrations in cultured mammalian cells.

The International Agency for Research on Cancer has concluded that antimony trioxide is possibly carcinogenic to humans by the inhalation route (Group 2B, inadequate evidence in humans, sufficient evidence in animals); and antimony trisulfide is not classifiable as to its carcinogenicity to humans (Group 3, inadequate evidence in humans and limited evidence in animals) (IARC 1989).

DERIVATION OF THE GUIDELINE

The guideline value of 0.003 mg/L for antimony in drinking water was derived as follows:

$$0.003 \text{ mg/L} = \frac{0.43 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 500}$$

where:

- 0.43 mg/kg body weight per day is the lowest effect level based on decreased lifespan and altered blood levels of glucose and cholesterol in a lifetime study using rats (Schroeder *et al*. 1970).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 500 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 5 because a lowest effect level was used instead of a no-effect level).

The WHO guideline value of 0.005 mg/L was derived from this calculation but rounded up.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Arsenic

(endorsed 2011)

GUIDELINE

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

GENERAL DESCRIPTION

Arsenic is a naturally occurring element which can be introduced into water through the dissolution of minerals and ores (where it exists mainly in the sulfide form), or from industrial effluent, atmospheric deposition (through the burning of fossil fuels and waste incineration), drainage from old gold mines, or the use of some types of sheep dip. Natural sources can make a significant contribution to the arsenic concentration in drinking water. Arsenate (i.e. pentavalent (As(V)) is generally the most common form in well oxygenated surface waters and drinking water, but under reducing conditions, such as those found in deep lake sediments or groundwaters, the trivalent form (As(III), arsenite) predominates.

Arsenic compounds have commercial and industrial uses as alloying agents in the manufacture of transistors, lasers and semiconductors, and in the processing of glass, pigments, textiles, paper, metal adhesives, ceramics, wood preservatives, ammunition and explosives. They are also used in the hide-tanning process, and to a limited extent as feed additives, pesticides and pharmaceuticals. Although inorganic forms of arsenic are the most common, organic arsenic compounds are also used.

In surface- and groundwater not affected by arsenic mineral deposits or pollution, the concentration of arsenic is generally less than 0.005 mg/L

Food may be an important source of arsenic intake. The average Australian adult dietary intake of arsenic is approximately 0.04 mg per day. Arsenic is concentrated by many species of fish and shellfish, and is present in poultry and livestock. Concentrations in vegetables are usually an order of magnitude less than those found in fish and meat. It is difficult to make direct comparisons between the arsenic intake from food and water because the form of arsenic and biological availability differ markedly. For example, a major portion of the arsenic in fish is present as highly complexed forms that are biologically unavailable, or as simple organic compounds (arsenobetaine and arsenocholine) that are essentially nontoxic.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In Australian drinking water supplies, typical concentrations of arsenic range from <0.001 mg/L to 0.03 mg/L.

TREATMENT OF DRINKING WATER

Arsenic can be removed from drinking water using conventional coagulation processes. It is desirable to convert trivalent arsenic to the pentavalent form before treatment by oxidation using chlorine or potassium permanganate. Lime softening can also be effective for removal from hard waters, but the efficiency is dependent on pH and valence state. The World Health Organization (WHO) (2003) states: "removal of arsenic to concentrations below 10 µg/litre is difficult in many circumstances," and Health Canada (2006) indicates that devices designed to remove arsenic from drinking water are certified to perform to 0.01 mg/L (10 µg/L) or less.

MEASUREMENT

The arsenic concentration in drinking water can be determined by hydride generation followed by atomic absorption spectroscopy. The limit of determination is approximately 0.001 mg/L. Alternatively, graphite furnace atomic absorption spectroscopy can be used, with a limit of determination of approximately 0.005 mg/L (APHA Method 3500-As Part B 1992).

HEALTH CONSIDERATIONS

The health considerations apply mainly to inorganic arsenic compounds, as they are more likely than the organic compounds to be present in drinking water supplies.

Soluble arsenic salts are readily absorbed by the gastrointestinal tract. After absorption, inorganic arsenic binds to haemoglobin, and is deposited in the liver, kidney, lungs, spleen, and skin. Inorganic arsenic does not appear to cross the blood-brain barrier but can cross the placenta. Very little ingested arsenic is excreted in faeces, but approximately 45-85% appears in the urine within 1 to 3 days.

Extensive reviews and summaries of the human and animal toxicity data for arsenic are available (IPCS 2001, WHO 2003, IARC 2004, Health Canada 2006, ATSDR 2007). Consumption of elevated levels of arsenic through drinking-water is causally related to the development of cancer at several sites, particularly skin, bladder kidney and lung. Cancer is considered to be the most sensitive toxicity end-point for setting a drinking water guideline for arsenic, however the mechanisms or modes of action by which arsenic causes cancer are yet to be definitively elucidated (WHO 2003).

Inorganic arsenic undergoes sequential reduction and methylation reactions leading to the formation of monomethylarsinic acid (MMA) and dimethylarsinic acid (DMA). This metabolism is regarded as bioactivating arsenic to more toxic forms. *In vitro* and *in vivo* chromosomal and DNA damage by arsenics are dose-dependent, with arsenite more potent than arsenate. Both MMA and DMA are directly genotoxic and are many times more potent than arsenite at inducing DNA damage (ATSDR 2007). Sub-populations that may be at greater risk from arsenic toxicity are those with gene variants of arsenic metabolism that lead to a higher percentage of MMA in the urine (Chen 2009, Smith and Steinmaus 2009).

The International Agency for Research on Cancer has concluded there is sufficient evidence in humans that arsenic in drinking-water causes cancers of the urinary bladder, lung and skin and has classified arsenic in drinking-water as carcinogenic to humans (Group 1) (IARC 2004).

DERIVATION OF GUIDELINE

The European Union (1998), WHO (2004), Health Canada (2008), USEPA (2008), and New Zealand (MoH NZ 2008) have drinking water guidelines for arsenic of 0.01 mg/L. Most of these were based on assessments conducted between 2003 and 2006; the previous Australian DWG was based on a 1988 evaluation. These overseas guidelines were based on considerations of the lowest concentration that is reasonably and economically achievable with water treatment technologies, measurability of arsenic at low concentrations, and lack of observed effects in humans at such low concentrations.

Epidemiological studies show that elevated cancer risks and other adverse health effects are not demonstrable at arsenic concentrations around 0.01 mg/L (e.g. Mazumder *et al.* 1998, Baastrap *et al.* 2008, Celik *et al.* 2008, Chen *et al.* 2009, Smith and Steinmaus 2009). On the other hand, there are many recent studies demonstrating a range of adverse health effects at higher concentrations (>0.05 or 0.1 mg/L) (e.g. Mazumder 2008, Majumdar *et al.* 2009, Mazumder *et al.* 2009, Smith and Steinmaus 2009). These health effects include skin, lung and bladder cancer; skin pigmentation and keratosis; diseases of the lung, liver, peripheral- and cardio-vascular systems; peripheral neuropathy; and diabetes. The majority of affected populations are from Indian, Bangladesh or Asian rural areas. Health Canada (2006) noted that recent epidemiological studies conducted in the United States had not found a clear association between cancer

risks and arsenic in drinking water at levels greater than 0.01 mg/L and below 0.05 mg/L. The study by Baastrap *et al*. (2008) is also informative as it was conducted in populations of similar socio-economic and nutritional status to those in Australia. This was a prospective Danish cohort of 57,053 people that was followed from 1970 to 2003; arsenic drinking water concentrations were up to 0.0253 mg/L (mean 0.0012 mg/L, 99th percentile 0.0057 mg/L), and no association with lung, bladder, liver, kidney, prostate, colorectum, or skin melanoma cancers was found.

After considering the above, a drinking water guideline of 0.01 mg/L was adopted for arsenic.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Asbestos

(endorsed 1996)

GUIDELINE

Data are insufficient to determine a guideline value for asbestos in drinking water.

GENERAL DESCRIPTION

Asbestos is a general term for certain fibrous silicate minerals. It can be present in drinking water from the dissolution of asbestos-containing minerals, industrial effluent, atmospheric deposition, and deterioration of asbestos cement pipes commonly used in water distribution systems.

The chemical and crystalline structure of asbestos results in products with a high tensile strength, durability, flexibility, and heat and chemical resistance. Asbestos has been used in construction materials such as asbestos cement pipes and sheets, electrical and thermal insulation, brake linings and clutch pads.

The extent of asbestos contamination of food has not been well studied because of the lack of a simple and reliable analytical method. Limited data indicate that the amount in food may be 10 times higher than that found in drinking water.

Studies in the United States and Canada have reported typical asbestos fibre numbers in drinking water of less than 1 MFL (million fibres per litre). Severe deterioration of asbestos cement pipes has been known to produce fibre numbers of up to 2000 MFL.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for asbestos; however, fibre numbers are probably similar to those reported overseas.

TREATMENT OF DRINKING WATER

Asbestos fibre numbers can be reduced by the standard water treatment processes of coagulation and filtration.

MEASUREMENT

Asbestos can be analysed using transmission electron microscopy with identification of the fibres by selected-area electron diffraction. This procedure is both costly and time consuming and is not suitable for routine analysis. The limit of determination is about 0.3 MFL.

HEALTH CONSIDERATIONS

The health hazards associated with inhalation of asbestos have been recognised for a long time. They include asbestosis, cancer of the bronchial tubes, malignant mesothelioma, and possibly cancers of the gastrointestinal tract and larynx (IPCS 1986).

In contrast, there has been little evidence that ingested asbestos causes cancer. A number of quite extensive epidemiological studies have been carried out on the effects of asbestos in the water supply. On the basis of these data there is no demonstrated excess risk of cancer even with high numbers of asbestos fibres in drinking water.

It is not clear whether asbestos fibres ingested in drinking water can pass through the walls of the

gastrointestinal tract in sufficient numbers to cause adverse effects. Experiments with laboratory animals indicate that penetration, if it occurs at all, is extremely limited.

Animal studies on the carcinogenic effects of ingested asbestos have been inconclusive.

Asbestos did not exhibit mutagenic activity in tests with bacteria but has induced chromosomal aberrations, malignant transformation of mammalian cells *in vitro*, and various biochemical alterations associated with tumour promoters.

The International Agency for Research on Cancer has concluded that asbestos is carcinogenic to humans by the inhalation route (Group 1, sufficient evidence of carcinogenicity in humans) (IARC 1987).

DERIVATION OF GUIDELINE

There are insufficient data to set a guideline value for asbestos in drinking water. It is unlikely, however, that the numbers of asbestos fibres present in most drinking water supplies would be a health concern. The weight of evidence indicates that ingested asbestos is not hazardous to health.

The guideline should be reviewed as soon as more toxicological data are available.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

IPCS (International Programme on Chemical Safety) (1986). Asbestos and other natural mineral fibres. Environmental Health Criteria, 53. World Health Organization, IPCS.

Asulam

(endorsed 2011)

GUIDELINE

Based on human health concerns, asulam in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Asulam (CAS 3337-71-1) belongs to the carbamate class of chemicals. Other pesticides in this class include aldicarb, methomyl, carbaryl and methiocarb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, asulam would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Users: Asulam (methyl sulfanilylcarbamate) is a selective, post-emergent systemic herbicide. It is used to control weeds in crops and pastures.

There are registered products containing asulam in Australia. These products are intended for professional use and all are aqueous concentrate liquids. Application methods include boom spray, aircraft and knapsack. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to asulam is residues in food. Residue levels in crops produced according to good agricultural practice are generally low.

Agricultural use of asulam may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Although asulam is considered to be amongst the most significant herbicides in use (Radcliffe 2002), it is not widely tested in drinking water. Where it has been tested, it has not generally been detected above guideline values.

TREATMENT OF DRINKING WATER

Asulam is a highly water soluble compound and therefore the effectiveness of its removal by activated carbon processes is limited (Matsui *et al.* 2003).

Partial removal of asulam may be achieved by ozonation (Abe and Tanaka 1996). However, advanced

oxidation techniques have been shown to remove asulam much more effectively than ozone treatment.

MEASUREMENT

Asulam may be detected in drinking waters by liquid chromatography–tandem mass spectrometry, with a practical limit of detection of 0.001 mg/L (1 µg/L) (Honing 2000).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for asulam is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 40 mg/kg bw/day from a 2-year rat study. The NOEL is based on effects on the thyroid and adrenal medulla. The ADI incorporates a safety factor of 2000 and was established in 1985.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: There is no information available on the absorption or metabolism of asulam.

Acute effects: Asulam has a low oral and dermal toxicity. Its skin sensitisation potential has not been determined, although it is structurally similarity to sulfonamide, which is a sensitiser. There was no evidence of neurotoxic symptoms normally associated with carbamates.

Short-term effects: A 6-month dietary study in dogs reported haematological changes at dose levels above 60 mg/kg bw/day and thyroid hypertrophy at 1500 mg/kg bw/day.

Long-term effects: Long-term studies were conducted in mice, rats and dogs. In all species, effects were noted on haematological parameters and on the thyroid gland. Thryoid hypertrophy was reported in mice at 180 mg/kg bw/day and reductions in white blood cells in dogs at 60 mg/kg bw/day. In rats, there were effects on the adrenals in both sexes and on the thyroid of males. The NOEL in the rat was 40 mg/kg/day, which was used as the basis for the ADI.

Carcinogenicity: Long-term studies in rats indicated an increased incidence of phaeochromocytomas in the adrenal medulla at the highest dose level only. This was not considered relevant at the dose levels to which humans are exposed.

Genotoxicity: Asulam is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Reproduction studies in rats and developmental toxicity studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Asulam is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.07 mg/L for asulam was determined as follows:

$$0.07 \text{ mg/L} = \frac{40 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 2000}$$

where:

- 40 mg/kg bodyweight/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 2000 is the safety factor applied to the NOEL from the long-term study in rats. It incorporates a safety factor of 10 for interspecies extrapolation, 10 for intraspecies variation, and an additional 20 for the failure of some studies to demonstrate NOELs.

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NOTE: Important general information is contained in PART II, Chapter 6

Atrazine

(endorsed 2011)

GUIDELINE

Based on human health concerns, atrazine in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Atrazine (CAS 1912-24-9) belongs to the triazine class of chemicals. There are a large number of herbicides in this class, including simazine, cyanazine, propazine, and ametryn (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, atrazine would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Atrazine is a herbicide for the control of weeds and grasses in agricultural crops.

There are registered products that contain atrazine in Australia. These products are intended for professional use. Atrazine is available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to atrazine and its metabolites is residues in food and drinking water. Residue levels in food produced according to good agricultural practice are generally low. Maximum residue limits (MRLs) are at the level of detection.

Agricultural use of atrazine may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATERS

Atrazine has been occasionally reported in Australian drinking waters, including in New South Wales, Queensland and Tasmania. It was detected at up to 0.0009 mg/L (0.9 µg/L) in surface waters in New South Wales (Tran *et al.* 2007) and 0.0013 mg/L (1.3 µg/L) in Queensland (Mitchell *et al.* 2005). In many countries, after application in agricultural areas, atrazine has been found in groundwater at levels of 0.00001–0.006 mg/L (0.01–6 µg/L) (WHO 2003). It has also been detected in drinking-water in several countries at levels of 0.00001–0.005 mg/L (0.01–5 µg/L) (WHO 2003) and as high as 0.0294 mg/L (29.4 µg/L) in Canada (Health Canada 1993). Regulation of atrazine use has become more stringent since the mid 1990s.

In cases where atrazine is present in drinking waters, there is a high likelihood that other closely related s-triazine metabolites with similar mammalian toxicity may also be present at similar concentrations.

TREATMENT OF DRINKING WATER

Atrazine can be a relatively difficult pesticide to treat in drinking water. Oxidation by chlorine or ozone is only partially effective at typical doses, and adsorption to activated carbon can be incomplete (Ormad *et al.* 2008). Conventional clarification/chlorination has been shown to be unreliable for the removal of atrazine from water (CARAT 2000). However, a combination of ozone, activated carbon and coagulation-flocculation can be effective (Ormad *et al.* 2008).

Atrazine has been shown to be near-completely removed when water undergoes advanced oxidation with iron-catalysed ultraviolet (UV) irradiation and peroxide, i.e. Fenton reaction (Huston *et al.* 1999), with only moderate removal reported for UV-peroxide in the absence of added iron (Kruithof *et al.* 2002), although much lower removal rates have been obtained at full-scale plants (CARAT 2000). Photodegredation of the pesticide has been investigated (Azenha *et al.* 2003). Relatively high removal rates through powdered activated carbon adsorption have been reported (Bozkaya-Schrotter *et al.* 2008).

MEASUREMENT

Atrazine can be measured by routine gas chromatrography–mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for atrazine is 0.005 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.5 mg/kg bw/day from a 2-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 (see 'Long-term effects').

The previous ADI for atrazine was set in 1985 at 0.0003 mg/kg bw/day, based on a NOEL of 0.6 mg/kg bw/day in a 2-year rat study and using a 2000-fold safety factor. This ADI was amended to its present level after submission of additional toxicity studies.

The previous health value was 0.04 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Atrazine is readily absorbed via the gastrointestinal tract in humans and rats. It is extensively metabolised, and is rapidly excreted in the urine and faeces, almost completely within 72 hours. Levels in tissues were low. The main metabolites were dealkylated forms that were of similar toxicity to atrazine.

Acute effects: Atrazine has low acute oral and dermal toxicity. It is not a skin sensitiser in humans, based on large-scale occupational studies, but is a sensitiser in guinea pigs.

Short-term effects: Four-week dietary studies in rats and dogs reported decreased food-use efficiency (rats only), and bodyweight gain at 21 mg/kg bw/day and above.

NOTE: Important general information is contained in PART II, Chapter 6

A 3-week oral study in female rats reported irregular ovarian cycles (but not persistent oestrus or diestrus) at 75 mg/kg bw/day.

Ninety-day dietary studies in rats and dogs reported reduced bodyweight gain and food consumption at 3.3 mg/kg bw/day in rats and at 5 mg/kg bw/day in dogs. Reduced testicular weights and anaemia were seen at 15 mg/kg bw/day in rats. In a 6-month dietary study in rats, there was suppression of the luteinising hormone surge (a process initiated in the pituitary that normally initiates ovulation), and disruption of the oestrous cycle at 3.6 mg/kg bw/day

Long-term effects: A 2-year dietary study in mice reported only decreased bodyweight gain at 36 mg/kg bw/day. One-year and 2-year dietary studies in rats reported decreased bodyweight gain, increased pituitary weight, pituitary adenomas, and mammary tumours (one strain only) at 4.2 mg/kg bw/day after 1-year. Behavioural effects, skeletal muscle degeneration, and mammary growths symptomatic of hormone perturbation were seen at 20 mg/kg bw/day and above in these studies. While the rat mammary tumours themselves are not considered relevant to humans, the increases in gonadotropin-releasing hormone and luteinising hormone from the pituitary, which are considered a precursor event to the development of rat mammary tumours, are considered relevant to humans. This is an area of ongoing research. In a long-term dog study, lethargy, increased heart rate, myocardial degeneration, and decreased heart weight were seen at 33 mg/kg bw/day. The lowest overall NOEL from these studies is 0.5 mg/kg bw/day, based on mammary tumours in rats. This NOEL is the basis for the current ADI.

Carcinogenicity: The weight of evidence from long-term studies in mice and rats indicates that atrazine is not carcinogenic in humans, since the rat mammary tumours are not considered relevant to humans.

Genotoxicity: Atrazine is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Two- and 3-generation reproductive studies in rats did not produce any evidence of effects on reproductive parameters. Developmental studies in rats produced some equivocal evidence of effects on foetal and post-natal development, but at doses much higher than those used in long-term studies.

Poisons Schedule: Atrazine is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for atrazine was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.5 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

NOTE: Important general information is contained in PART II, Chapter 6

The World Health Organization has established a health-based guideline value of 0.002 mg/L for atrazine in 1993 (WHO 2004). The WHO incorporated an additional 10-fold safety factor to reflect potential neoplasia; however, Australian authorities considered that the induction mechanism for the mammary tumours was not directly relevant to humans.

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NOTE: Important general information is contained in PART II, Chapter 6

Azinphos-methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, azinphos-methyl in drinking water should not exceed 0.03 mg/L.

RELATED CHEMICALS

Azinphos-methyl (CAS 86-50-0) belongs to the organophosphate class of chemicals and is structurally related to azinphos-ethyl. There are many pesticides in this chemical class, including acephate, chlorfenvinphos, diazinon, ethion, phorate, and terbufos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, azinphos-methyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Azinphos-methyl is an insecticide, acaricide (miticide), and molluscicide for the control of pests such as moths, grasshoppers, beetles, aphids, and slugs in agricultural crops.

There are registered products that contain azinphos-methyl in Australia. These products are intended for professional use on pome fruit, citrus fruit, macadamia nuts, grape, lychee, and blueberry crops. They are available as concentrated solutions to be applied in both concentrated and diluted forms by ground and aerial sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to azinphos-methyl and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of azinphos-methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on occurrence of azinphos-methyl in Australian waters. In the USA, the estimated environmental concentration in surface waters was 0.016 mg/L (USEPA 2006). Azinphos-methyl was not found in a survey of Canadian drinking water (Health Canada 1989).

TREATMENT OF DRINKING WATER

No specific data on the treatment of azinphos-methyl in drinking water have been identified.

MEASUREMENT

Azinphos-methyl can be measured by routine gas chromatrography–mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for azinphos-methyl is 0.025 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.25 mg/kg bw/day from 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, and was established in 2002.

The previous ADI was 0.001 mg/kg bw, based on a NOEL of 0.125 mg/kg bw/day for cholinesterase inhibition in a 2-year dog study, with a 100-fold safety factor. The ADI was amended following a review in 2002 of all available data on azinphos-methyl.

The acute reference dose (ARfD) of 0.075 mg/kg bw for azinphos-methyl was also 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.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Azinphos-methyl is readily absorbed via the gastrointestinal tract in rats. It is extensively metabolised, and is rapidly excreted in the urine and faeces, almost completely within 48 hours. The major metabolite was benzamide.

Acute effects: Azinphos-methyl has high acute oral toxicity in rats and mice, and high dermal toxicity in rats. It is a skin sensitiser in guinea-pig. Clinical signs of acute poisoning were typical of cholinesterase inhibition and included hyperexcitability, salivation, bronchoconstriction, headache, vomiting and other behavioural changes.

Short-term effects: A 28-day dietary studies in rats reported dose-dependent red blood cell and plasma cholinesterase inhibition at 0.8 mg/kg bw/day and above, and brain cholinesterase inhibition at 3.2 mg/kg bw/day. A 28-day oral dosing study with humans reported no toxic effects at 0.25 mg/kg bw/day. This NOEL is the basis for the current ADI.

In 12-16 week dietary studies in rats and dogs, cholinesterase in brain, erythrocytes, and plasma was inhibited at 1 mg/kg bw/day in rats. No changes were noted histologically. Deaths were reported at doses of 2.5 mg/kg bw/day and above. In dogs, red blood cell cholinesterase was inhibited at 0.25 mg/kg bw/day.

Long-term effects: In 2-year dietary studies in mice, rats, and dogs, erythrocyte and plasma cholinesterase were inhibited at doses of 0.5 mg/kg bw/day in dogs and brain cholinesterase was inhibited at 3 mg/kg bw/day and above. Clinical signs of toxicity were noted at 6.25 mg/kg bw/day and above.

Carcinogenicity: Based on a 2-year study in mice and rats, there is no evidence of carcinogenicity for azinphos-methyl.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: Azinphos-methyl was positive in some *in vitro* short-term studies, but not in *in vivo* studies. Overall, it was not considered to be genotoxic.

Reproductive and developmental effects: Three-generation reproduction studies in rats and mice, and developmental studies in rats, mice and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: Special neurotoxicity studies in rats by dietary administration found no evidence of delayed neurotoxicity.

Poisons Schedule: Azinphos-methyl is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.03 mg/L for azinphos-methyl was determined as follows:

$$0.03 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 30}$$

where:

- 0.25 mg/kg bw/day is the NOEL based on a short-term (28-day) oral dosing study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 30 is the safety factor applied to the NOEL derived from human studies. This safety factor incorporates a factor of 10 for intraspecies variation, with an additional safety factor of 3 to account for the use of short-term data.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Barium

(endorsed 2011)

GUIDELINE

Based on health considerations, the concentration of barium in drinking water should not exceed 2 mg/L.

GENERAL DESCRIPTION

Barium makes up approximately 0.04 per cent of the Earth's crust, and is the 16th most abundant non-gaseous element. Barium in drinking water is primarily from natural sources. Some barium salts such as the chloride and nitrate are soluble in water; others, including the carbonate, fluoride, phosphate and sulfate, are insoluble. Barium is not considered to be an essential nutrient for humans.

Barium compounds have a wide variety of industrial applications. They are used in the plastics, rubber, electronics, steel, optical, and textile industries. They are also used in ceramic glazes and enamels, in glass and paper making, as a lubricant additive, in pharmaceuticals and cosmetics, and as a rodenticide.

The concentration of barium in drinking water overseas is usually low, typically less than 0.02 mg/L.

Most foods contain small quantities of barium. The major dietary sources are milk, potatoes and flour. Some cereal products and nuts can contain large amounts. It has been estimated that average dietary intake is approximately 1 mg per day.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In Australian drinking water supplies, typical concentrations of barium range from <0.002 mg/L to 1.1 mg/L.

TREATMENT OF DRINKING WATER

Conventional water treatment using alum or ferric coagulation is not effective in removing barium from drinking water. Lime softening can remove more than 90%.

MEASUREMENT

The barium concentration in drinking water can be determined using inductively coupled plasma emission spectroscopy (APHA Method 3500-Ba Part C 1992), or atomic absorption spectroscopy (APHA Method 3500-Ba Part B 1992). For both methods the limit of determination is approximately 0.01 mg/L.

HEALTH CONSIDERATIONS

Reviews of the human and animal toxicity data for barium are available (IPCS 2001, OEHHA 2003, WHO 2004a, USEPA 2005, ATSDR 2007).

The degree of absorption from the gastrointestinal tract depends on the solubility of the barium compound, and on other factors including age, study duration, species, and fasting status of the animals. The presence of food in the gastrointestinal tract appears to decrease barium absorption, and absorption appears to be higher in young animals than in older ones. The range of reported oral absorption in animal studies was 0.7–85.0%; a default value of 20% gastrointestinal absorption of dissolved barium in drinking water is assumed by the Safe Drinking Water Committee of the National Research Council of the USA (IPCS 2001, OEHHA 2003). After absorption, barium is deposited in bone and teeth.

Barium toxicity is caused by the free cation, and highly soluble barium compounds are more toxic than insoluble compounds. In rodents, kidney toxicity appears to be the most sensitive effect, whereas in humans, cardiovascular (hypertension) effects have been of prime concern.

The identification of hypertension as a health end-point of concern for humans is supported by findings of hypertensive effects in humans who ingested acutely high doses of barium compounds, in workers who inhaled dusts of barium ores and barium carbonate, in experimental animals given barium intravenously, and in rats exposed to barium in drinking water while on calcium-restricted diets (IPCS 2001).

A number of epidemiological studies have been carried out on the effects of barium in drinking water on cardiovascular disease. Wones *et al*. (1990) exposed eleven normotensive volunteers to barium in drinking water for 10 weeks at concentrations up to 10 mg/L. No cardiovascular effects were observed at the maximum estimated dose of 0.21 mg per kg bodyweight per day (mg/kg bw/day). Between 1976 and 1977, Brenniman and Levy (1985) studied two populations (n = 1175 and 1203) in the United States where water softeners were not used and mean barium concentrations were 0.1 mg/L or 7.3 mg/L (range 2–10 mg/L for the latter). No differences were observed in blood pressure or incidence of kidney disease between the two communities. Assuming 70 kg body weight and 2 L/day drinking water consumption, the mean doses of barium were 0.003 mg/kg bw/day and 0.21 mg/kg bw/day. Thus, 0.21 mg/kg bw/day is a no-observed-adverse-effect level (NOAEL) in this study, however because no adverse effects were found, the NOAEL is likely to be higher than this value.

Chronic toxicity studies of barium chloride in drinking water of rats and mice caused kidney effects at the higher doses used. Relevant NOAELs in these studies were 45 mg/kg bw/day for female rats and 75 mg/kg bw/day in male mice (NTP 1994)

There is no evidence from chronic rodent studies that barium causes cancer. The weight of evidence indicates barium is not mutagenic in tests with bacteria and does not damage DNA.

DERIVATION OF GUIDELINE

A drinking water guideline of 2 mg/L has been set after considering the following.

Using animal data:

Based on the chronic male mouse-study data of the National Toxicology Program (NTP 1994), the United States Environmental Protection Agency (USEPA 2005) and Agency for Toxic Substances and Disease Registry (ATSDR 2007), the lower confidence limit for the benchmark dose at 5% incidence ($BMDL_{05}$) of renal effects was determined to be 63 and 61 mg/kg bw/day. A drinking-water guideline value of 6 mg/L (rounded) can be derived following the standard procedure:

$$5.6\ \text{mg/L} = \frac{60\ \text{mg/kg bw/day} \times 70\text{kg} \times 0.8}{300 \times 2\text{L/day}}$$

Where:

- 60 mg/kg bw/day is the $BMDL_{05}$ for kidney effects determined from a long-term drinking water study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.8 is a proportionality factor based on the assumption that 80% of daily intake attributable to drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 300 is the safety factor applied to the $BMDL_{05}$ derived from animal studies (10 for interspecies variations, 10 for intraspecies variations and 3 for database inadequacies).

NOTE: Important general information is contained in PART II, Chapter 6

The lowest NOAEL of 45 mg/kg bw/day from the chronic rat and mouse studies can also be used in the above equation to give a guideline value of 4 mg/L (rounded).

Using human data:

The NOAEL of 0.2 mg/kg bw/day from the Brenniman and Levy (1985) epidemiological study gives a drinking water guideline of 2 mg/L (rounded) as follows:

$$1.87 \text{ mg/L} = \frac{0.2 \text{ mg/kg bw/day} \times 70\text{kg} \times 0.8}{3 \times 2\text{L/day}}$$

Where:

- 0.2 mg/kg/day is the NOAEL in humans identified by Brenniman and Levy (1985).
- 3 is the safety factor applied to account for potential variability in response between humans. Justified on the grounds the study population was randomly selected from all people above the age of 18 years and therefore inherently included sensitive sub-populations. Furthermore, as the highest mean barium water concentrations in the study did not cause an adverse effect, the NOEL is likely to be higher than the one used to derive the drinking water guideline.

The World Health Organization (WHO 2004) established a guideline of 0.7 mg/L by dividing the mean barium water concentration of 7.3 mg/L in the Brenniman and Levy (1985) study by an uncertainty factor of 10 to account for human intraspecies variation. WHO (2006) acknowledges that this may be highly conservative.

The United States Environmental Protection Agency (USEPA 2006) indicates that 2 mg/L is the lowest level to which present technology and resources can reasonably be required to remove barium should it occur in drinking water.

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NOTE: Important general information is contained in PART II, Chapter 6

Benomyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, benomyl in drinking water should not exceed 0.09 mg/L.

RELATED CHEMICALS

Benomyl (CAS 17804-35-2) belongs to the benzimidazole class of carbamate compounds. Other pesticides in this class include carbendazim, dicamba and diflubenzuron (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, benomyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Benomyl is a systemic, broad-spectrum fungicide for use on fruit trees, nuts, vegetables, cereals, ornamentals and turf.

There are no registered products containing benomyl in Australia, as the active was suspended and subsequently withdrawn due to health concerns in December 2006. However, de-registered compounds may still be detected in water.

Exposure sources: The main source of public exposure to benomyl and its metabolites if used in the future would be residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of benomyl in the future may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of benomyl detected in Australian drinking water supplies have been identified.

TREATMENT OF DRINKING WATER

No definitive literature regarding the removal of benomyl from drinking water has been identified. Some field trials have been undertaken regarding the removal of benomyl from water using activated carbon and other adsorbents (Massey *et al.* 1992, Giry *et al.* 2001). Biodegredation (Matsumura *et al.* 1991) and ultraviolet irradiation (Grechko *et al.* 1982) in wastewater have been reported.

MEASUREMENT

No standard methods for the analysis of benomyl in drinking water have been identified. However, benomyl can be analysed by high–performance liquid chromatography with detection by ultraviolet absorbance (Marvin *et al*. 1991). The reported detection limit for this method is 0.009 $mg.L^{-1}$.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for benomyl is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.5 mg/kg bw/day from a 2-year dog study. The NOEL is based on an increase in testicular degeneration. The ADI incorporates a safety factor of 100 and was established in 2003.

The acute reference dose (ARfD) of 0.06 mg/kg bw/day for benomyl was established in 2003, 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.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Benomyl is rapidly and extensively absorbed via the gastrointestinal tract and distributed widely thoughout the body. It is metabolised to carbendazim (70% within 1 hour). Excretion is via the urine and, to lesser extent, faeces, and is essentially complete within 72 hours.

Acute effects: Benomyl has a very low acute oral toxicity; there are no data on acute dermal toxicity. There are reported cases of skin sensitisation in humans.

Short-term effects: In 70/90 day dietary studies in rats and dogs, there was reduced sperm count in rats at the highest dose tested of 20 mg/kg bw/day and increased liver weights at 125 mg/kg bw/day. In dogs, there were increased liver enzymes at 125 mg/kg bw/day.

Long-term effects: Long-term (2-year) dietary studies in mice and rats did not demonstrate any toxicity. In a 2-year study in dogs, there was testicular atrophy at doses of 12.5 mg/kg bw/day and above, and increased levels of liver enzymes in serum were seen at the highest dose tested of 62.5 mg/kg bw/day. The lowest overall NOEL was 2.5 mg/kg bw/day in dogs, which was used as the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there was evidence of carcinogenicity only in the mouse, where liver tumours were observed. These were considered to be species-specific, possibly as a result of liver toxicity. Based on the available data, benomyl was not considered to be a carcinogenic risk to humans.

Reproduction and developmental effects: Reproduction studies in rats and dogs reported decreased sperm production at 45 mg/kg bw/day. Testicular degeneration and atrophy was also reported at doses of 45 mg/kg bw/day (rats) and 12.5 mg/kg bw/day (dogs). Developmental studies in mice and rats (but not rabbits) reported teratogenic effects in the foetuses in the absence of any maternal toxicity at doses of 10 mg/kg bw/day.

Poisons Schedule: Benomyl is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.09 mg/L for benomyl was determined as follows:

$$0.09 \text{ mg/L} = \frac{2.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.5 mg/kg bw/day is the NOEL based on a long-term (2-year) study in dogs.
- 70 kg is taken as the average weight of an adult
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult
- 100 is the safety factor applied to the NOEL derived from the acute human study. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variations.

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NOTE: Important general information is contained in PART II, Chapter 6

Bentazone

(endorsed 2011)

GUIDELINE

Based on human health concerns, bentazone in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Bentazone (CAS 25057-89-0) belongs to the benzimidazole class of chemicals. Other pesticides in this class include benomyl, carbendazim and dicamba (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, bentazone would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Bentazone is a herbicide for the control of broad-leaf weeds in home garden lawns, turf and agricultural crops.

There are registered products containing bentazone or its sodium salt in Australia. These products are intended for professional and home garden use and are available as concentrated solutions to be applied using ground, aerial or hand-held spray methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to bentazone are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of bentazone may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No values for concentrations of bentazone in Australian waters were found. Bentazone has been used for a considerable period of time and has been detected in surface waters overseas at levels of 0.1 to 6 µg/L (WHO/SDE/WSH 2004).

TREATMENT OF DRINKING WATER

Bentazone has been shown to be completely removed by ozonation (Bozkaya-Schrotter *et al.* 2008). Moderate removal can be achieved using powdered activated carbon adsorption. Advanced oxidation using ultraviolet irradiation and peroxide has been demonstrated to achieve a moderate level of bentazone removal (Kruithof *et al.* 2002).

MEASUREMENT

Measurement of bentazone can readily be achieved to detection limits of 0.05 µg/L using dichloromethane extraction and gas chromatography with electron capture detection (FAO/WHO, 1991). Enhancement of sensitivity for analysis of bentazone in water can be achieved by use of solid phase extraction and gas-chromatography–mass spectrometry, achieving a detection limit of 0.02 µg/L (Thortensen *et al.* 2000).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for bentazone is 0.1 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 10 mg/kg bw/day. This NOEL is based on decreased bodyweight and significant changes in organ weights observed in a 2-year rat study. The ADI incorporates a safety factor of 100 and was established in 1988.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Bentazone is readily and extensively absorbed via the gastrointestinal tract. It is not extensively metabolised, and is rapidly excreted in the urine, almost completely within 24 hours.

Acute effects: Bentazone has low acute oral toxicity and moderate acute dermal toxicity.

Short-term effects: Three-month dietary studies in rats and dogs reported clinical signs of neurotoxicity, as well as changes in biochemical and haematological parameters and organ weight changes at 120 mg/kg bw/day.

Long-term effects: Long-term dietary studies in mice and rats reported decreased food consumption and bodyweight gain as well as significant changes in relative organ weights at 45.7 mg/kg bw/day.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for bentazone.

Genotoxicity: Based on *in vitro* and *in vivo* short-term studies, bentazone is not considered to be genotoxic.

Reproductive and developmental effects: A 3-generation reproduction study in rats and a developmental study in rabbits did not produce any evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Bentazone is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for bentazone was determined as follows:

$$0.4 \text{ mg/L} = \frac{10 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 10 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has established a health-based guideline value of 0.3 mg/L for bentazone in 1998 (WHO 2004).

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NOTE: Important general information is contained in PART II, Chapter 6

Benzene [CASRN 71-43-2]

(endorsed 2013)

GUIDELINE

Based on health considerations the concentration of benzene in drinking water should not exceed 0.001 mg/L.

GENERAL DESCRIPTION

Benzene is a clear, colourless-to-yellow liquid and highly flammable aromatic hydrocarbon. It is present in petroleum products such as motor fuels and solvents, and motor vehicle emissions constitute the main source of benzene in the environment. Benzene occurs naturally in crude oil and coal and is an additive and a by-product of oil-refining processes. It constitutes approximately 1-2% of unleaded gasoline by volume (US DHHS, 2011). Tobacco smoke is another significant source of exposure (WHO, 2010). It also occurs in natural gas and emissions from volcanoes and forest fires.

Human exposure to benzene occurs primarily through inhalation (WHO, 2010). When released to surface waters, benzene rapidly volatilises to the air (WHO, 2010). Benzene is not persistent in surface water or soil and either volatilises to air or is degraded by bacteria under aerobic conditions (WHO, 2010). For water contamination, benzene is therefore of most concern in groundwater. Benzene can also occur in foods and drinks as a product of the reaction between benzoate and ascorbic acid, and has been found in soft drinks in the UK at concentrations as high as 0.028 mg/L (FSA, 2006).

Benzene is also used widely as an industrial solvent by the chemical and pharmaceutical industries in the production of styrene/ethylbenzene, cumene/phenol and cyclohexane. The use of benzene as a solvent has been greatly reduced in recent years.

Unlike other petroleum hydrocarbons such as ethylbenzene, toluene and xylene the odour threshold for benzene is relatively high at 10 mg/L (WHO, 2003).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Benzene has only rarely been identified in Australian drinking waters. Natural concentrations in most water sources are usually very low. Benzene can occur naturally in groundwater as a result of proximity to, or contact with, coal seams, petroleum and gas deposits, and shales. It may be mobilised by extraction activities (Lesage *et al.*, 1997; Leusch and Bartkow, 2011; Volk *et al*, 2011). However, contamination can occur, usually via exposure to petrochemicals in surface waters or groundwater. Known sources of groundwater and surface water contamination include leakage from sub-surface fuel storage tanks (do Rego & Netto, 2007) and proximity to natural hydrocarbon deposits (IPCS, 1993). Emissions of fuel components from boating use is a known source of contamination of multiple-use lakes and reservoirs (Schmidt *et al.*, 2004). Benzene was reported in 9% of samples from an extensive groundwater survey undertaken in Denmark with the highest concentration being 0.034 mg/L (Juhler & Felding, 2003). Concentrations of up to 0.0027 mg/L were recorded in a NSW town water supply contaminated with petrol (Allen *et al.*, 2005). Groundwater from a contaminated well in the USA contained up to 0.3 mg/L of benzene (IPCS, 1993). Benzene has been reported at up to 0.004 mg/L in municipal drinking water in Taiwan (Kuo *et al.*, 1997), up to 0.01 mg/L in Germany (IPCS, 1993), and is occasionally detected in drinking waters in the USA (Williams *et al.*, 2004).

TREATMENT OF DRINKING WATER

Volatile organic chemicals such as benzene are most commonly treated in drinking water by aeration stripping and/or adsorption to granular activated carbon (GAC). A conventional biologically active sand filter has been shown to be highly effective for the removal of benzene from contaminated water, under suitable conditions (Arvin *et al.*, 2004). Effective bioremediation of highly contaminated groundwaters has also been demonstrated (Sedran *et al.*, 2004; Zein *et al.*, 2006).

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for the analysis of benzene (APHA, AWWA & WEF, 2012). An inert gas is bubbled through the sample and benzene is trapped on an adsorbent. The adsorbent is then heated and benzene analysed using gas chromatography with mass spectrometric (GC-MS) detection (Method 6200 B) or photoionisation (PI) detection (Method 6200 C) (APHA, AWWA & WEF, 2012). The method detection limit is 36 ng/L for GC-MS and 17 ng/L for GC-PI (APHA, AWWA & WEF, 2012).

HEALTH CONSIDERATIONS

Benzene is rapidly and efficiently absorbed (30-50%) following inhalation. Following ingestion, animal data indicate that nearly all is absorbed from the gastrointestinal tract. Less than 1% is absorbed through the skin. Following absorption it is widely distributed throughout the body. It is metabolised predominantly into phenol by the liver, and also by bone marrow (WHO, 2003).

Human health data are mainly from studies where benzene had been inhaled. Acute exposure to high concentrations affects the central nervous system causing dizziness, nausea, vomiting, headache and drowsiness. Inhalation of very high concentrations can cause death. Chronic and subchronic exposure to lower concentrations leads to a range of adverse effects on the blood system including pancytopenia, aplastic anaemia, thrombocytopenia, granulocytopenia and lymphocytopenia with white blood cells being the most sensitive (WHO, 2003; Health Canada, 2009). There is considerable evidence that occupational exposure to low benzene concentrations in air for periods as short as 1-5 years may result in leukaemia (ATSDR, 2007).

In animal studies, benzene caused leukaemia and other cancers when administered orally and by inhalation to rats and mice. It can also induce chromosome damage and gene mutation in mammalian cells. It was not found to be mutagenic in tests with bacteria.

The International Agency for Research on Cancer has concluded that benzene is carcinogenic to humans (Group 1, sufficient evidence of carcinogenicity in humans) (IARC, 1987).

DERIVATION OF GUIDELINE

The European Union (1998), WHO (2011), Health Canada (2006), USEPA (2008) and New Zealand (MoH NZ 2008) have set drinking water guidelines for benzene of 0.001-0.01 mg/L based on carcinogenic potential (leukaemia) of benzene in humans from inhalation associated with occupational exposures and/or a 2 year oral study in rats and mice (NTP 1986).

USEPA (2003) derived a cancer slope factor (CSF) of 0.015 to 0.055 per mg/kg/day based on linear extrapolation of leukaemia data from occupational exposure. This translated to a lifetime risk of one excess cancer case per 1 million people associated with a concentration of 0.001-0.01 mg/L of benzene (USEPA 2003).

NOTE: Important general information is contained in PART II, Chapter 6

Both USEPA (2003) and Health Canada (2006) identified that inhalation of volatilized benzene and dermal adsorption need to be added to ingestion of drinking water. Based on exposure from showering and bathing, Health Canada (2006) derived equivalent doses of 1.2L water per day to account for inhalation and 0.8L water per day to account from dermal adsorption. Using these equivalent doses and the USEPA (2003) cancer slope factor a guideline value can be calculated using the formula:

$$0.00032\text{-}0.0012 \text{ mg/L} = \frac{70 \text{ kg body weight} \times 10^{-6}}{4\text{L/day} \times 0.015\text{-}0.055 \text{ mg/kg/day (CSF)}}$$

where:

- 0.015 -0.055 mg/kg/day is the CSF range calculated by USEPA (2003) from occupational exposure to benzene
- 70 kg is the average weight of an adult
- 10-6 is the additional lifetime risk of one cancer from drinking water exposure
- 4L/day is the average dose including 2L/day for ingestion plus 1.2L equivalent dose/day for inhalation and 0.8L equivalent dose/day for dermal adsorption.

WHO (2003) also used the occupational leukaemia data to determine that a concentration of 0.001 mg/L in drinking water would entail a maximum lifetime risk of one additional case of cancer per 1 million people. Analysis of data from a 2 year gavage study in rats and mice (NTP 1986) using the robust linear extrapolation model produced similar results with an excess lifetime cancer risk of 1 per million people associated with 0.001-0.008 mg/L benzene based on leukaemia and lymphomas in female mice and oral cavity squamous cell carcinomas in male rats respectively (WHO, 2003). On the basis of these two calculations WHO (2003) identified that concentrations of 0.01 mg/L and 0.001mg/L were associated with excess cancer rates of 1 per 100,000 and 1 per 1,000,000 people respectively. WHO (2011) adopted a guideline value of 0.01 mg/L based on an estimated additional lifetime risk of one cancer per 100,000 people.

The concentration of 0.001mg/L associated with an excess cancer risk of 1 per 1,000,000 people calculated by WHO (2003) is within the range of 0.00032-0.0012mg/L. For consistency with WHO (2003, 2011), a health-based guideline of 0.001 mg/L has been adopted.

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NOTE: Important general information is contained in PART II, Chapter 6

Beryllium

(endorsed 2011)

GUIDELINE

Based on health considerations the concentration of beryllium in drinking water should not exceed 0.06 mg/L.

GENERAL DESCRIPTION

Beryllium can enter source water through the weathering of rocks, atmospheric deposition, and discharges. The primary source of beryllium in the environment is the burning of fossil fuels. Other less significant sources are slag and ash dumps.

Beryllium is used in a number of specialised applications including ceramic formulations, electrical and electronic components, and X-ray tubes. It is also used to stiffen the mantles of gas acetylene lamps.

Beryllium concentrations in drinking water overseas are generally very low, usually less than 0.001 mg/L. For example, the concentration of beryllium in drinking water was based on a survey of 1577 drinking-water samples throughout the United States, where beryllium was detected in 5.4% of samples with mean and maximum concentrations of 0.00019 and 0.00122 mg/L (0.19 and 1.22 µg/L), respectively. In Australian river waters the levels are reported to be < 0.00001 to 0.00012 mg/L (10–30 ng/L average) (WHO 2001).

If it is assumed the maximum concentration in drinking water in Australia is 0.0012 mg/L then 2 L/day will give a daily intake of 0.0024 mg beryllium. The World Health Organization (WHO 2001) reports an intake of 0.00012 mg/day from food as the mid point from an Australian survey. Thus the total intake of beryllium may be about 0.0025 mg/day. The proportion from water may approximately be as much as 95%.

Atmospheric exposure to beryllium is generally much less than from food or water, but constitutes a greater hazard. Cigarette smokers can be exposed to higher concentrations than nonsmokers.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for beryllium.

TREATMENT OF DRINKING WATER

There are no published methods for the removal of beryllium from drinking water supplies.

MEASUREMENT

The concentration of beryllium in drinking water can be determined by graphite furnace atomic absorption spectroscopy or inductively coupled plasma emission spectroscopy (APHA Method 3500-Be Parts B or C 1992). The limit of determination is approximately 0.002 mg/L.

HEALTH CONSIDERATIONS

Beryllium compounds are not readily absorbed by the gastrointestinal tract since they tend to be insoluble at pH values normally found in the gut. A significant proportion of the beryllium that is absorbed is incorporated into bone and has a biological half-life of more than one year.

The toxicology of beryllium has been reviewed by United States Environmental Protection Agency (USEPA 1998), the WHO (2001) and US Agency for Toxic Substances and Disease Registry (ATSDR 2002). Several chronic oral animal studies in dogs, rats and mice were reviewed. Dogs chronically exposed to soluble beryllium sulfate in the diet developed gastrointestinal lesions and bone marrow hypoplasia. Rickets were observed in rats exposed to sparingly soluble beryllium carbonate in the diet for 2–24 weeks, possibly due to decreased gastrointestinal absorption of phosphorus subsequent to formation of insoluble beryllium phosphate in the intestine.

WHO (2001) described the derivation of a tolerable daily intake (TDI) of 0.002 mg per kg bodyweight (mg/kg bw) by application of an uncertainty factor of 300 to a benchmark dose (BMD) of 0.46 mg/kg bw/day. The BMD was calculated at the lower 95% confidence interval for a 10% incidence of small intestinal lesions, assumed to be equal to a no-observed-adverse-effect level (NOAEL), in dogs chronically exposed to dietary beryllium sulfate tetrahydrate. The uncertainty factor of 300 included a factor of 10 intraspecies variation, 10 for interspecies variation, and a 3-fold factor for database deficiencies (no studies available on developmental effects and no mechanistic/mode of action data to suggest this may not be an issue). Although there are several chronic oral animal studies, there is a lack of human toxicity data by the oral route, reproductive/developmental end-points have not been adequately assessed, and oral studies examining immunological end-points are lacking. Since the principal study in dogs is of chronic duration and a benchmark dose was used, there are no uncertainty factors for duration or NOAEL/LOAEL (lowest observed adverse effect level) extrapolation. This derivation of the TDI uses the same logic, BMD_{10} and uncertainty factors as those described by the United States Environmental Protection Agency (USEPA 1998). The Agency for Toxic Substances and Disease Registry, using the same dog data but a different curving-fitting program to the USEPA (1998), determined a BMD_{10} of 0.56 mg/kg bw/day, to which they applied an uncertainty factor of 300 (same rationale as WHO 2001) to obtain a minimum risk level of 0.002 mg/kg bw/day (ATSDR 2002).

There are no reliable data on the human health effects of oral exposure to beryllium. Inhalation is known to cause serious health effects, with long-term exposure resulting in pulmonary granulomatosis (a type of lung tumour). The inhalation data led the International Agency for Research on Cancer to conclude that beryllium and beryllium compounds are carcinogenic to humans (Group 1, sufficient evidence of carcinogenicity in humans and sufficient evidence in animals) (IARC 1993).

There is no clear evidence that the compounds are carcinogenic when administered orally. Beryllium was not mutagenic in tests with different strains of bacteria, but caused chromosomal aberrations and gene mutations in cultured mammalian cells.

Experiments with laboratory mice have shown that beryllium can cross the placenta and is foetotoxic (toxic to the foetus).

DERIVATION OF GUIDELINE

Using the oral TDI of 0.002 mg/kg bw from WHO (2001), a drinking water guideline can be derived as follows:

$$0.06 \text{ mg/L} = \frac{0.002 \text{ mg/kg bw} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day}}$$

Where:

- 0.002 mg/kg bw is the tolerable daily intake and includes a 300 fold safety factor to allow for intraspecies and interspecies variation.
- 70 kg is taken as the average weight of an adult.
- 0.8 is a proportionality factor based on the assumption that 80% of total daily intake is attributable to the consumption of drinking water.

NOTE: Important general information is contained in PART II, Chapter 6

- 2 L/day is the estimated maximum amount of water consumed by an adult.

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NOTE: Important general information is contained in PART II, Chapter 6

Bioresmethrin

(endorsed 2011)

GUIDELINE

Based on human health concerns, bioresmethrin in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Bioresmethrin (CAS 28434-01-7) belongs to the pyrethroid class of chemicals. This is one of the largest groups of insecticides, and includes cyfluthrin, esfenvalerate, fenvalerate, permethrin, and flucythrinate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, bioresmethrin would not be a health concern unless the concentration exceeded 0.1 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Bioresmethrin is a household insecticide used for the control of flies, mosquitoes, spiders, ants, cockroaches, fleas, silverfish, and moths.

There are registered products that contain bioresmethrin in Australia. These products are intended for domestic use and are applied by spray directly onto insects or laid as baits in areas of infestation. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to bioresmethrin and its metabolites is the use of household insecticide products. Levels of exposure from these uses are low.

The domestic use of this chemical provides only limited potential for contamination of drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on occurrence of bioresmethrin in Australian waters could be found.

TREATMENT OF DRINKING WATER

No specific data on the treatment of bioresmethrin in drinking water have been identified.

MEASUREMENT

Bioresmethrin can be measured by routine gas chromatrography–mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for bioresmethrin is 0.03 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 3 mg/kg bw/day from a 2-year dietary rat study. The NOEL is based on evidence of mild liver toxicity in the form of increased relative liver weight, discolouration, hepatocellular hypertrophy, and fatty vacuolisation (steatosis) at doses of 15 mg/kg bw/day and above. The ADI incorporates a safety factor of 100 and was established in 1991.

The previous ADI for bioresmethrin was set in 1975 at 0.3 mg/kg bw, based on a NOEL of 30 mg/kg bw/day from a medium-term dietary study in rats, which showed evidence of mild liver toxicity. The ADI was amended after submission of a long-term dietary study in rats showing a lower NOEL for liver toxicity.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Bioresmethrin is rapidly absorbed via the gastrointestinal tract and extensively metabolised. It has wide, uniform distribution including the brain and testes in mammals. The primary metabolic pathway is hydrolysis and oxidation to 5-benzyl-3-furan carboxylic acid (BFCA). Bioresmethrin is slowly eliminated in the urine and to a lessor extent in faeces, almost completely within 6 days.

Acute effects: Bioresmethrin has low acute oral and acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: Two-week studies in rats and dogs did not demonstrate any toxicity at low dose levels. Effects in rats were confined to decreased liver and thymus weights, and decreased haemoglobin levels at doses of 1000 mg/kg bw/day. No toxicity was seen in dogs at this dose level. Three-month studies in rats and dogs reported increased liver weight, fatty deposits in the liver, increased liver enzyme activity, and decreased red blood cells at doses of 100 mg/kg bw/day in rats and at 250 mg/kg bw/day in dogs.

Long-term effects: A long-term dietary study in rats reported evidence of mild liver toxicity (increased weight, hepatocellular hypertrophy, fatty deposits, and increased serum enzyme activity) at doses of 15 mg/kg bw/day. The NOEL was 3 mg/kg bw/day and this is the basis for the current ADI.

Carcinogenicity: Based on a 2-year study in rats, there is no evidence of carcinogenicity for bioresmethrin.

Genotoxicity*:* Bioresmethrin is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: Short-term dietary studies in rats reported evidence suggestive of nervous system toxicity but only at extremely high dose levels, which are well in excess of the likely level of human exposure. The metabolite 5-benzyl-3-furancarboxylic acid (BFCA) is responsible for most of the nervous system toxicity from bioresmethrin in mammals.

Poisons Schedule: Bioresmethrin is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for bioresmethrin was determined as follows:

$$0.1 \text{ mg/L} = \frac{3.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 3.0 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization (WHO) has not established a health-based guideline value for bioresmethrin. This relates to the WHO's policy to exclude the use of pyrethroids for direct addition to drinking water as mosquito larvicides. This is based on concern over the developing of resistance to synthetic pyrethroids, which interferes with the global anti-malaria strategy (WHO 2006).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Boron

(endorsed 2011)

GUIDELINE

Based on human health considerations, the concentration of boron in drinking water should not exceed 4 mg/L.

GENERAL DESCRIPTION

Boron can be present in drinking water through the natural leaching of boron-containing minerals, or by contamination of water sources. The environmental chemistry of boron is not well understood. In water, the predominant form is probably boric acid, which does not dissociate readily.

Boron compounds are used in glass manufacture, cleaners, wood and leather preservatives, flame retardants, cosmetic products, antiseptics, and occasionally food preservatives; and as agricultural fertilisers, algicides, herbicides and insecticides.

In other countries, concentrations of boron in uncontaminated water sources are usually less than 1 mg/L. Concentrations up to 6.5 mg/L have been reported in ground water supplies, but these higher concentrations are associated with seawater intrusion.

Boron is present naturally in many food products, with high amounts found in foods of plant origin, especially fruits, leafy vegetables, nuts and legumes. It has been estimated that intake of boron from food is about 10 times that from water. The daily consumption of boron is 10-25 mg. This value, however, will vary from country to country depending on population dietary habits, geographical area and soil geochemistry. In the United States, average intake values for adults range from 0.87 to 1.34 mg/day and 90 percentile intakes are about 1.5 to 2 mg/day (IOM 2001, USEPA 2008a). In Australia, the estimated dietary intake for boron is 2.2 mg/day (Samman *et al*. 1998).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Boron is not often monitored in Australian drinking water supplies, but the limited information available indicates that boron concentrations are less than 0.1 mg/L.

TREATMENT OF DRINKING WATER

The concentration of boron in drinking water can be reduced by the use of granular activated carbon, or by lime softening.

MEASUREMENT

The boron concentration in drinking water can be determined using inductively coupled plasma emission spectroscopy (APHA Method 4500-B Part D 1992). The limit of determination is approximately 0.05 mg/L.

HEALTH CONSIDERATIONS

Boron, as soluble borate (borax) or boric acid, is rapidly and completely absorbed after ingestion. It is widely distributed throughout the body and up to 90% is excreted in urine as unchanged compound.

There have been a number of reported cases of poisoning following the ingestion of high doses of boron. Symptoms include gastrointestinal disturbances, skin eruptions, and central nervous system stimulation and depression. Long-term occupational exposure to boron can lead to similar symptoms.

Short-term studies with rats and dogs reported testicular atrophy at high doses (5000 mg/kg bodyweight) of boric acid and borate. This condition was also observed in longer-term studies with rats, mice and dogs over 2 years. Reproductive studies reported that rats became sterile at the highest doses. No increase in the incidence of tumours was observed in long-term studies using mice.

A tolerable daily intake (TDI) of 0.16 mg/kg bodyweight (mg/kg bw) has been derived by the the World Health Organization (WHO 2004a). This TDI is based on the no-observed-adverse-effects level (NOAEL) of 9.6 mg/kg bw/day for foetal bodyweight effects in a rat developmental study (Price *et al.* 1996), with an uncertainty factor of 60 (10 for interspecies and 6 for human intraspecies variation).

Tests for mutagenicity using bacteria and mammalian cells have been mostly negative. Neither boric acid nor borate induced chromosomal aberrations in mammalian cells.

Boron is suspected of being a trace nutrient in mammals and some authors argue for such a role in humans (Nielson 1996), however recent reviews concluded that a clear biological function for boron in humans has yet to be established (IOM 2001, USEPA 2008b).

Although boron is an essential trace element for plants, certain plants (e.g. citrus fruit, stone fruit, some nut trees) are sensitive to the toxic effects of boron if irrigation water has concentrations higher than about 0.5 mg/L (Lazarova and Bahri 2005). WHO (2004) indicates that this concentration is below the level that can be achieved by practical treatment methods. Application of waste water containing 0.8–1.3 mg/L to young orange trees for three years was well tolerated (Reboll *et al.* 2000).

DERIVATION OF GUIDELINE

The background intake from diet is given as 2.2 mg/day (Samman *et al.* 1998) and from consumer products, 0.1 mg/day (WHO 2003). Assuming a bodyweight of 70 kg for an average adult, this is equivalent to a background intake of 0.03 mg/kg bw/day. When subtracted from the TDI of 0.16 mg/kg bw, the remaining 0.13 mg/kg bw/day can be allocated to intake from water.

When the above considerations are applied in the standard equation for deriving a drinking water guideline in Australia, a value of 4 mg/L (rounded down from 4.55 mg/L) is attained.

$$4\ \text{mg/L} = \frac{0.13\ \text{mg/kg bw/day} \times 70\ \text{kg}}{(2\ \text{L/d})}$$

Where:

- 0.13 mg/kg bw/day is the tolerable intake allocated to water.
- 70 kg is taken as the average weight of an adult.
- 2 L/day is the estimated maximum amount of water consumed by an adult.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Bromacil

(endorsed 2011)

GUIDELINE

Based on human health concerns, bromacil in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Bromacil (CAS 314-40-9) belongs to the urea group of chemicals. There are no other pesticides in this group of chemicals (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, bromacil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Bromacil is a herbicide for the control of weeds and grasses in fruit orchards and plantations, commercial and industrial areas, rights of way and around agricultural buildings.

There are currently products registered in Australia that contain bromacil or its sodium salts. Bromacil products are intended for professional use. The products are available as powdered or granulated formulations and applied in diluted form using ground or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to bromacil and its metabolites are residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of bromacil may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of bromacil in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Advanced oxidation using ultraviolet irradiation and peroxide has been demonstrated to achieve a moderate level of bromacil removal (Kruithof *et al*. 2002).

MEASUREMENT

Bromacil can be measured in drinking waters by solid phase extraction followed by liquid chromatography–mass spectrometry.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for bromacil is 0.1 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 10 mg/kg bw/day from a long-term (2-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 and was established in 1988.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Following gastrointestinal absorption, bromacil is excreted via the urine in rats and humans mainly as the metabolite 5-bromo-3-sec-butyl-6-hydroxymethyluracil. Urine samples from the formulation workers indicated that both bromacil and the major metabolite occur in a hydrolysed form. Five other metabolites have been identified.

Acute effects: Bromacil has low acute oral and dermal toxicity. Bromacil is a skin sensitiser in a guinea-pig test.

Short-term effects: In repeat-dose (90-day) dietary studies in rats, the target organs of toxicity were the liver, kidney and thyroid. At dose levels above 2.5 mg/kg bw/day, food consumption and relative organ weights were decreased. Toxic effects were seen in the liver and thyroid at the higher dose levels.

Long-term effects: In an 18-month dietary study, mice were fed at doses up to 714 mg/kg bw/day of bromacil. The reported effects were in the liver and testicle at high doses.

Two-year studies were conducted in rats and dogs. In rats, the reported effects were decreased bodyweight and increased relative thyroid weight at doses above 10 mg/kg bw/day. There were no effects reported in dogs up to the dose level of 30 mg/kg/day. The NOEL of 10 mg/kg/day found in the rat study was used to establish an ADI of 0.1 mg/kg bw/day for bromacil.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for bromacil.

Genotoxicity: Bromacil is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Three-generation reproduction and developmental studies in rats and rabbits showed no adverse effects on reproduction in either species. Evidence of delayed development occurred in rats and rabbits but only at maternally toxic doses which were at levels well in excess of the likely level of human exposure.

Poisons Schedule: Bromacil is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for bromacil was determined as follows:

$$0.4 \text{ mg/L} = \frac{10 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 10 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Bromate

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of bromate in drinking water should not exceed 0.02 mg/L.

GENERAL DESCRIPTION

Bromate is not a normal component of water but may be formed from bromide during ozonation. Concentrations up to 0.09 mg/L have been reported in ozonated drinking water. Bromate is a strong oxidant and will probably react with organic matter in water, forming bromide as a by-product.

Bromate is used in home hair permanent-wave neutralising solutions. Although it is used in some foods overseas, Australian Food Standards do not allow bromate to be used in food in Australia.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

It is unlikely that bromate would be present in Australian reticulated drinking water supplies unless ozonation is used for disinfection.

TREATMENT OF DRINKING WATER

There are no published methods for the removal of bromate from drinking water supplies.

MEASUREMENT

The concentration of bromate in drinking water can be determined using ion chromatography with conductivity detection. The limit of determination is about 0.005 mg/L.

HEALTH CONSIDERATIONS

Bromate is rapidly absorbed from the gastrointestinal tract of rats. Although bromate was not subsequently detected in tissue, bromide concentrations were significantly increased in plasma, red blood cells, pancreas, kidney, stomach and small intestine.

Most cases of human poisoning from bromate are due to accidental or intentional ingestion of home permanent-wave solutions, which can contain 2–10% bromate. Toxic effects include nausea, abdominal pain and diarrhoea, central nervous system depression and pulmonary oedema, most of which are reversible. Irreversible effects include kidney failure and deafness.

In rats exposed to bromate in drinking water for 15 months, adverse effects included inhibited body-weight gain, marked kidney damage, and renal adenocarcinoma. Kidney tumours have been reported in other long-term studies using male and female rats, but not with female mice; male rats also exhibited peritoneal mesotheliomas. There is evidence that tumours occur only after a minimum total cumulative dose has been exceeded.

Bromate exhibited mutagenic activity in tests using bacteria, and caused chromosomal aberrations in cultured mammalian cells. Some evidence of DNA damage has also been reported in rats given potassium bromate.

The International Agency for Research on Cancer has concluded that bromate is possibly carcinogenic to humans (Group 2B, no data in humans but sufficient evidence in animals) (IARC 1986).

DERIVATION OF GUIDELINE

The guideline value for bromate in drinking water was derived as follows:

$$0.02 \text{ mg/L} = \frac{30 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.2}{2 \text{ L/day} \times 10{,}000}$$

where:

- 30 mg/kg body weight per day is a lowest effect level from a 15-month drinking water study using rats (Nakano *et al*. 1989).
- 70 kg is the average weight of an adult.
- 0.2 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 10,000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations, 10 because a lowest effect level was used instead of a no-effect level and 10 for carcinogenic and mutagenic effects).

The World Health Organization (WHO) guideline value of 0.025 mg/L was based on a calculation that estimated an additional lifetime risk of seven fatal cancers per 100,000 people. It was recognised that this approach may not be appropriate if, as reported, tumours only occur above a dose threshold. The two different approaches, however, result in essentially the same guideline value.

This guideline should be reviewed when new data are available.

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NOTE: Important general information is contained in PART II, Chapter 6

Bromoxynil

(endorsed 2011)

GUIDELINE

Based on human health concerns, bromoxynil in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Bromoxynil (CAS 1689-84-5) is in the hydroxybenzonitrile class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, bromoxynil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Bromoxynil is a post-emergent herbicide used to control broad-leaf weeds.

There are registered products containing bromoxynil in Australia. These products are intended for professional and home garden use and are applied by aircraft or boom spray by professional use, and by hand-held spray in the home garden. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to bromoxynil are use in the home garden and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of bromoxynil may potentially lead to the contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of bromoxynil in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Current literature suggests that bromoxynil can be effectively removed by oxidation with ultraviolet (UV) radiation, UV and ultraviolet peroxide, chlorine and UV, ozonation, and by chlorination, with various levels of success depending on the water quality conditions (Guittonneau *et al.* 2005). Ozonation is considered the most effective, with chlorination the least effective (Guittonneau *et al.* 2005). Jar testing to identify the effectiveness of various oxidants in specific waters is recommended if bromoxynil is detected. Oxidation of any kind will result in the formation of by-products and therefore a by-product management

plan is also recommended.

Photodegradation has shown to provide some removal of bromoxynil (Texier *et al.* 1998); however more research is required to determine the optimal conditions. Activated carbon has also been shown to remove bromoxynil effectively from water, but is dependant on the water quality and the application methods of the carbon (Yang *et al.* 2004).

MEASUREMENT

The practical limit of quantification for bromoxynil in water is 0.001 mg/L, using liquid chromatography–tandem mass spectrometry (Alder *et al.* 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for bromoxynil is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.3 mg/kg bw/day from a 12-month dietary study in dogs. The ADI incorporates a safety factor of 100 and was established in 1993.

The previous health value was 0.03mg/L (NHMRC and NRMMC 2004)

HEALTH CONSIDERATIONS

Metabolism: Bromoxynil is readily absorbed via the gastrointestinal tract and widely distributed in the body in mammals. Virtually all absorbed bromoxynil is eliminated unchanged. It is slowly excreted mainly via the faeces, with some excretion in urine. Bromoxynil has a low potential for bioaccumulation.

Acute effects: Bromoxynil has a moderate acute oral toxicity and low dermal toxicity. There is no evidence of skin sensitisation.

Short-term effects: In medium-term dietary studies in dogs, there was decreased bodyweight gain, increased blood urea nitrogen, and kidney and liver weight changes at a dose of 12 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in rats and dogs. A 2-year rat study reported decreased bodyweight gain at 8.2 mg/kg bw/day and evidence of adverse effects in the liver, kidney and stomach at 26 mg/kg bw/day. A 1-year dog study reported reduced bodyweight gain at 1.5 mg/kg bw/day and evidence of anaemia at 7.5 mg/kg bw/day. The NOEL of 0.3 mg/kg bw/day in dogs is the basis of the ADI.

Carcinogenicity: Benign liver tumours were slightly increased in mice at 1.5 mg/kg bw/day and above, but these tumours were considered to be specific to mice and not of human relevance. Based on this and a 2-year study in rats, bromoxynil is not considered to have carcinogenic potential in humans.

Genotoxicity: Bromoxynil is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Bromoxynil is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for bromoxynil was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.3 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.3 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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Cadmium

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of cadmium in drinking water should not exceed 0.002 mg/L.

GENERAL DESCRIPTION

Contamination of drinking water by cadmium may occur as a result of impurities in the zinc of galvanised pipes or in solders used in fittings, water heaters, water coolers and taps. Cadmium can also be released to the environment in waste water, through contamination of fertilisers, and by metallurgical industries.

Cadmium metal is used as an anticorrosive coating on steel but its use is being phased out. Cadmium compounds are commonly used as pigments in plastics, in batteries and in some electrical components.

Cadmium concentrations in nonpolluted natural waters overseas are usually lower than 0.001 mg/L.

Food is the main source of cadmium intake. The estimated average Australian adult dietary intake of cadmium is approximately 0.03 mg per day. Smoking is a significant additional source of cadmium.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies concentrations of cadmium are usually less than 0.002 mg/L.

TREATMENT OF DRINKING WATER

Cadmium can be effectively removed from drinking water by lime softening (98% removal in the pH range 8.5 to 11.3) and coagulation with ferric chloride (90% removal above pH 8 but less effective at lower pH).

MEASUREMENT

The cadmium concentration in drinking water can be determined using graphite furnace atomic absorption spectroscopy (APHA Method 3500-Cd Part B 1992). The limit of determination is approximately 0.0002 mg/L.

HEALTH CONSIDERATIONS

Absorption of cadmium in the gastrointestinal tract depends on a number of factors including the solubility of the compounds ingested, but a healthy person typically absorbs 3–7% of ingested cadmium. This figure may be higher in people with iron, calcium and protein deficiency. Cadmium accumulates in the kidney and is only released very slowly, with a biological half-life in humans of 10 to 15 years.

An extensive review and summary of the human and animal toxicity data for cadmium is available (IPCS 1992).

In humans, long-term exposure can cause kidney dysfunction leading to the excretion of protein in the urine. This may occur, in a certain proportion of people, if the amount of cadmium exceeds 200 mg/kg renal cortex tissue; about 10% of the population is estimated to possess this sensitivity. Other effects can include osteomalacia (softening of the bones). Cases of Itai-Itai disease have been reported in Japan among elderly women exposed to highly contaminated food and water. Symptoms are similar to osteomalacia accompanied by kidney dysfunction characteristic of cadmium poisoning.

Epidemiological studies have looked for a connection between lung cancer and workplace cadmium inhalation, but the results have been inconclusive.

Long-term inhalation studies with rats have reported an increase in the incidence of tumours of the lung. No increase in the incidence of tumours was found when cadmium salts were administered orally.

There is no clear evidence that cadmium is mutagenic. Many tests have reported negative results but there have been some reports of gene mutation and chromosome abnormalities in mammalian cells. The positive results are reported as being weak and only present at high concentrations.

The International Agency for Research on Cancer has concluded that cadmium is probably carcinogenic to humans (Group 2A, limited evidence of carcinogenicity in humans and sufficient evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline value for cadmium in drinking water was derived as follows:

$$0.002 \text{ mg/L} = \frac{0.0007 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day}}$$

where:

- an intake of less than 0.0007 mg/kg body weight per day will ensure that over a 70 year lifetime, cadmium in the body will be kept below the critical amount of 200 mg/kg renal cortex tissue (JECFA 2000). This figure was based on calculations that take into account an absorption rate of 5%, a daily excretion rate of 0.005% of body burden, and an adequate safety factor.
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.

No additional safety factors are necessary as they have been included in the intake value.

The guideline value takes into account the higher cadmium intake, per kilogram of body weight, by infants and children.

The World Health Organization guideline value of 0.003 mg/L is slightly different due to rounding in the calculation. The difference is not significant.

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NOTE: Important general information is contained in PART II, Chapter 6

Captan

(endorsed 2011)

GUIDELINE

Based on human health concerns, captan in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Captan (CAS 133-06-2) belongs to the phthalimide class of chemicals. There are currently no other pesticides in this class in use (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, captan would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Captan is a fungicide for the control of fungal diseases in turf, ornamentals, agricultural crops and seedlings.

There are registered products that contain captan in Australia. These products are intended for professional use and are available as water-dispersible granules or as a dust. Captan is applied to turf, ornamentals, and agricultural crops as a dilute or concentrated spray using ground or hand-held equipment. Captan is applied as a powder to seedlings. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to captan is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of captan may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on captan occurrence in Australian drinking water supplies were found. In the Nile river, captan has been found at 0.0003 mg/L (0.3 µg/L) (Abbassy *et al.* 1999).

TREATMENT OF DRINKING WATER

Captan can be degraded by ozone, ultraviolet (UV) irradiation and chlorine. Destruction of captan in water using short wavelength UV light has been reported (Peterson *et al*. 1990). Captan is also rapidly degraded in 50 and 500 mg/L chlorine solutions at pH 7 and 10.7 (Ong *et al*. 1996). Ozonation is effective in degrading captan and degradation rates increased at higher pH and temperature (Ong *et al*. 1996).

MEASUREMENT

Captan can be extracted by liquid/liquid extraction with dichloromethane. The extract is dried with sodium sulfate, concentrated, and analysed by gas chromatography–mass spectrometry in selected ion monitoring mode. The method can achieve a limit of detection (LOD) of 0.0005 mg/L (0.5 µg/L). Captan can also be extracted using solid-phase extraction (SPE) and measured using high performance liquid chromatography (HPLC) (Marvin *et al*. 1990, Wang *et al*. 2007) or gas chromatography/negative chemical ionization-mass spectrometry (Barreda *et al*. 2006). A fully automated system for on-line SPE followed by HPLC with tandem detection with a photodiode array detector and a fluorescence detector (after post-column derivatisation) can achieve a LOD of 0.001 mg/L (1 µg/L) (Patsias and Papadopoulou-Mourkidou 1999).

Trace-level determination of captan can be achieved by solid-phase micro-extraction and gas chromatography coupled with electron-capture detection (LOD=0.000015 mg/L [0.015 µg/L]) or with mass spectrometric detection (LOD=0.00004 mg/L [0.04 µg/L]) (Lambropoulou *et al*. 2000). Captan can be analysed by EPA Method 617 (Determination of organohalide pesticides and PCBs in industrial wastewater) using electron capture gas chromatography or EPA Method 8081A (Organochlorine pesticides, by gas chromatography: capillary column technique) using electron capture detector or an electrolytic conductivity detector.

An optical biosensor consisting of a glutathione-S-transferase-immobilized gel film can detect captan in contaminated water at 0.002 mg/L (2 µg/L) (Choi *et al*. 2003). A spectrophotometric method for the determination of captan based on its reaction with thiosemicarbazide can achieve a LOD of 0.0005 mg/L (0.5 µg/L) at an absorbance of 315 nm (Galeano *et al*. 2002).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for captan is 0.1 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 10 mg/kg bw/day 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, and was established in 1997.

The acute reference dose (ARfD) of 0.1 mg/kg bw/day for captan was established in 1997, based on a NOEL of 10 mg/kg bw/day from a developmental study in rabbits. The ARfD incorporates a safety factor of 100.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Captan is well absorbed via the gastrointestinal tract in mice and rats. In rats, the highest levels were found in kidneys, liver, blood or gastrointestinal tract, particularly in the distal small intestine. In mice, higher levels were found in the duodenum and large intestine. In mice and rats, captan is rapidly and extensively excreted. In mice, captan is excreted in the urine as metabolites (44%), in the faeces mostly unchanged (22%), and in expired air as CO_2 (19%). In rats, captan is extensively metabolised and rapidly excreted mostly in the urine (80-90%) and the remainder in the faeces. The major urinary metabolites in both mice and rats were thiazolidine-2-thione-4-carboxylic acid (TTCA) and dithiobis-methanesulfonic acid derivatives.

NOTE: Important general information is contained in PART II, Chapter 6

In human volunteers captan was rapidly excreted in urine as TTCA (4-9%) and tetrahydrophthalimide (THPI) (1-3%).

Acute effects: Captan has low acute oral and dermal toxicity. It is a skin sensitiser in both laboratory animals and humans.

Short-term effects: Short-term dietary studies in mice reported dose-related hyperplasia in the duodenum and associated inflammatory cell response at doses of 120 mg/kg bw/day and above. Decreased bodyweight gain, and hyperplasia and hypertrophy in the glandular forestomach were reported at higher doses.

Long-term effects: Long-term dietary studies in mice reported a dose-related increase in the incidence of hyperplastic lesions and benign and malignant tumours in the duodenum at 122 mg/kg bw/day. At higher doses, there was also an increase in benign and malignant tumours in the jejunum/ileum. In long-term dietary studies in rats, decreased bodyweight gain was observed at 96 mg/kg bw/day. Long-term dietary studies in dogs reported no treatment-related effects up to doses of 300 mg/kg bw/day.

Carcinogenicity: Long-term studies in rats provide no evidence of carcinogenicity for captan. In long-term studies in mice, tumours in the duodenum were observed but were considered to occur via an inflammatory mechanism specific to mice, and were reported at dose levels well in excess of the likely level of human exposure.

Genotoxicity: Captan was positive in some *in vitro* short-term assays, but overall it was not considered to be genotoxic.

Reproductive and developmental effects: One and three-generation reproduction studies in rats did not produce evidence of reproductive toxicity. In developmental toxicity studies in rabbits, there was no effect on the foetus at doses that were not maternotoxic. These doses are well in excess of the likely level of human exposure in drinking water. The most sensitive effects reported were decreased bodyweight and food consumption in dams, and in the foetus there was an associated increased incidence of cysts on the liver and increased number of skeletal variations at doses of 30 mg/kg bw/day and above. The NOEL for these effects was 10 mg/kg bw/day, and this is the basis for the current ADI.

Poisons Schedule: Captan is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for captan was determined as follows:

$$0.4 \text{ mg/L} = \frac{10 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 10 mg/kg bw/day is the NOEL based on a short-term (developmental toxicity) study in rabbits.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Carbaryl

(endorsed 2011)

GUIDELINE

Based on human health concerns, carbaryl in drinking water should not exceed 0.03 mg/L.

RELATED CHEMICALS

Carbaryl (CAS 63-25-2) is in the carbamate class of chemicals. Other pesticides in this class include aldicarb, methomyl, oxamyl and pirimicarb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, carbaryl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Carbaryl is an insecticide effective against a broad range of insects, mites, lice, millipedes and other pests.

There are registered products containing carbaryl in Australia. These products are for professional and home garden use on lawns and turf; on horses, ponies and dogs; and other agricultural uses. They are applied as a wettable formulation spray domestically or by aerial spraying or boom spray in agriculture. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to carbaryl are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of carbaryl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Monitoring studies for carbaryl in raw and tap water are limited. No specific data from Australia were found. Carbaryl has been detected in water at µg/L concentrations but degradation is relatively rapid, with 1-naphthol identified as the major degradation product. Indirect and direct photolysis of carbaryl produces different naphthoquinones as well as some hydroxyl substituted naphthoquinones (Gunasekara *et al*. 2008).

Carbaryl is one of the three most frequently detected insecticides in surface water, according to US Geological Survey reports from 1991-2001. It is estimated that higher levels of carbaryl occur in surface water than in groundwater, based on available monitoring data and modeling. A 3-year monitoring study undertaken in the USA revealed that carbaryl was present in drinking water sources in the majority of the monitored sites (13 of 16 sites). The concentrations measured at these sites were low (0.002 to 0.031 µg/L) in raw water and generally lower in treated drinking water (USEPA 2004).

TREATMENT OF DRINKING WATER

It is estimated that conventional drinking water treatment (i.e. coagulation, flocculation and settling) can reduce carbaryl concentration by 43% of the concentration prior to treatment. (USEPA 2004). Therefore, it is estimated that a carbaryl concentration below 0.05 mg/L should be achievable by conventional drinking-water treatment (WHO 2008). Ozone has been shown to be 99% effective in removing carbaryl from water. Similarly, granular activated carbon adsorption can effectively remove carbaryl during treatment. However, chlorine and hypochlorite may be ineffective at removing or degrading carbaryl. Softening of hard waters will reduce carbaryl concentrations (via alkaline hydrolysis), as softening raises the pH of the water (USEPA 2004).

High and stable removal efficiency of carbaryl can also be achieved using an anion exchange membrane anodic fenton treatment. This treatment oxidises carbaryl to 1-naphthol and 1,4-naphthoquinone (Wang *et al*. 2002, Kong *et al*. 2007).

MEASUREMENT

There are several methods for analysing carbaryl in drinking water. Its concentration in drinking-water may be determined by extraction, hydrolysis, derivatisation and separation by gas-liquid chromatography with electron capture detection or mass spectrometry. Detection limits vary according to the method, but typical limits of detection (LODs) of 0.2 µg/L are reported, and high-performance liquid chromatography (HPLC) with mass spectrometry is considered the conventional method of analysis.

HPLC using pre-concentration, elution, separation and ultraviolet determination can achieve a LOD in tap water between 0.03-0.2 µg/L (Driss *et al*. 1993). Another study using HPLC with fluorometric detection reported a LOD of 1.4 mg/mL for carbaryl (Massey *et al*. 1995). However, HPLC with fluorometric detection does not always provide the required specificity for determining carbaryl residues (Makihata *et al*. 2003). Solid-phase extraction followed by reversed-phase liquid chromatography can achieve LODs in the range 3-15 ng/L for the determination of nine N-methylcarbamate pesticides, including carbaryl, from drinking water (Morrica *et al*. 2005). Liquid chromatography electrospay ionisation tandem mass spectrometry, without a concentration procedure, has also been used for the measurement of carbaryl (LOD 2 µg/L) (Makihata *et al*. 2003).

Carbaryl can be analysed using the United States Environmental Protection Agency (USEPA) method 8270: Semivolatile Organic Compounds by Gas Chromatography/Mass Spectrometry (GC/MS): Capillary Column Technique, or the USEPA method 531: Direct Aqueous Injection high performance liquid chromatography (HPLC) with Post Column Derivatisation.

Other methods include immunoassay techniques, which achieve a LOD of 1.38 µg/L (Mauriz *et al*. 2006), or direct analysis by laser-induced fluorescence, which achieves a LOD in tap water of 20 ng/L (Burel-Deschamps *et al*. 2006).

NOTE: Important general information is contained in PART II, Chapter 6

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for carbaryl is 0.008 mg per kg of bodyweight (mg/kg bw) based on a lowest-observed-effect level (LOEL) of 16 mg/kg bw/day observed in a 2-year dietary study in mice. The ADI incorporates a safety factor of 2000 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 acute reference dose (ARfD) of 0.01 mg/kg bw/day for carbaryl was established in 2002, based on a no-observed-effec leve (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.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Carbaryl is rapidly absorbed via the gastrointestinal tract in rodents and humans and is extensively metabolised. Excretion is predominantly via the urine, where ten metabolites have been identified. The potential for bioaccumulation is low.

Acute effects: Carbaryl has moderate oral toxicity and low dermal toxicity. Symptoms of acute poisoning include hyperexcitability, salivation, bronchoconstriction, headache, and vomiting. Carbaryl does not cause skin sensitisation.

Short-term: In a short-term dietary study in dogs, the major effect was depression of plasma cholinesterase at dose levels greater than 1.4 mg/kg bw/day.

Long-term effects: Long-term studies were conducted in rats and dogs. In a 2-year dietary study in rats, there was decreased bodyweight gain and cholinesterase inhibition at 70 mg/kg bw/day. A 1-year dietary study in dogs showed cholinesterase inhibition at 3.8 mg/kg bw/day and above,

Carcinogenicity: Studies in rodents reported renal and urinary bladder tumours in rats and liver tumours in mice at high dose levels only. These tumours are considered to develop via a non-genotoxic mechanism at dose levels greatly exceeding the likely human exposure level. In mice, vascular tumours were also observed at the lowest dose of 16 mg/kg bw/day. This LOEL is the basis for the ADI.

Genotoxicity: Carbaryl caused chromosome breakage in some *in vitro* studies, but overall, it was not considered to be genotoxic.

Reproductive and developmental effects: A 2-generation reproduction toxicity study in rats reported maternotoxicity and reduced pup survival at 4.7 mg/kg bw/day. Developmental studies in rats and rabbits reported maternotoxicity and foetotoxicity at 30 mg/kg bw/day and 150 mg/kg bw/day respectively. There was no evidence of teratogenicity.

Neurotoxicity: A 13-week oral neurotoxicity study in rats reported blood and brain cholinesterase depression and behavioural effects at 1 mg/kg bw/day and above. No pathological changes were noted.

Poisons Schedule: Carbaryl is included in Schedule 4, 5 or 6 in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No.1 (2010), depending on the concentration and use of the product. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.03 mg/L for carbaryl was determined as follows:

$$0.03 \text{ mg/L} = \frac{16.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 2000}$$

where:

- 16.0 mg/kg body weight per day is the LOEL for the formation of vascular tumours observed in a long-term (2-year) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the average maximum amount of water consumed by an adult.
- 2000 is the safety factor applied to the LOEL derived from animal studies. This safety factor incorporated a factor of 10 for interspecies extrapolation and 10 for intraspecies variation. There is an additional factor of 10 for the use of a LOEL and an additional factor of 2 for the uncertainty as to the mode/mechanism of vascular tumour formation and for the inability to dismiss the relevance of vascular tumours to humans.

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NOTE: Important general information is contained in PART II, Chapter 6

Carbendazim/Thiophanate-methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, carbendazim in drinking water should not exceed 0.09 mg/L.

RELATED CHEMICALS

Carbendazim (CAS 10605-21-7/ CAS 23564-06-9) belongs to the benzimidazole class of chemicals. Thiophanate methyl belongs to the thiophanate class of chemicals, although it is often regarded as a benzimidazole. Thiophanate-methyl is converted to carbendazim in the environment (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse of thiophanate-methyl or carbendazim, it would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Carbendazim is a broad-spectrum systemic fungicide used for the control of a wide range of fungal diseases such as mould, spot, mildew, scorch, rot and blight in a variety of crops, including cereals, fruit (pome, stone, citrus, cucurbits, strawberries, bananas, mangoes, etc), vines, ornamentals, pasture, and turf.

Thiophanate-methyl is a fungicide used for the control of soil-borne diseases of ornamental plants.

There are registered products containing carbendazim and registered products containing thiophanate-methyl in Australia. Carbendazim-containing products are intended for professional use and are generally available as suspension concentrates, to be mixed with water for application as a spray or dip. Some products are also used as timber preservatives. Thiophanate-methyl containing products are intended for professional use and are available as concentrated powders or granules, to be mixed into soil/potting mix before sowing or applied as a diluted drench directly to plant beds. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: Carbendazim is the major environmental degradant of thiophanate-methyl and is therefore the relevant environmental contaminant for both chemicals. The main source of public exposure to carbendazim is residues in food. Residue levels in crops grown according to good agricultural practice are generally low.

Agricultural use of carbendazim and/or thiophanate-methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of carbendazim in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of carbendazim in drinking water have been identified.

MEASUREMENT

Carbendazim may be measured in drinking water using high performance liquid chromatography coupled with a variety of spectrometric detection techniques (JunkerBuchheit and Witzenbacher 1995, Crescenzi *et al*. 1997, Di Corcia *et al*. 2000, Hogendoorn *et al*. 2000, Van Hoof *et al*. 2002, Deng *et al*. 2007). Limits of detection below 1 µg/L can be achieved by most of these techniques.

HISTORY OF THE HEALTH VALUES

The current acceptable dietary intake (ADI) for carbendazim is 0.03 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.5 mg/kg bw/day from a 2-year dog study. The NOEL is based on evidence of adverse effects on the liver. The ADI incorporates a safety factor of 100, and was established in 1979.

The current ADI for thiophanate-methyl is 0.02 mg/kg bw, based on a NOEL of 2 mg/kg bw/day 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 and was established in 1991.

The previous health value for carbendazim was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Since thiophanate-methyl is converted to carbendazim in the environment, the toxicity of carbendazim is the major consideration in relation to the health impact of thiophanate-methyl in drinking water.

Metabolism: Carbendazim is readily absorbed via the gastrointestinal tract, extensively metabolized, and excreted in the urine (86%) and faeces. The main metabolite is 5-hydroxy carbendazim (5-HBC-S). Approximately 98% of carbendazim and its metabolites are excreted within three days.

Acute effects: Carbendazim has low acute oral and dermal toxicity in rats. It is not a skin sensitiser.

Short-term effects: In short-term studies in rats, there were decreased sperm counts and testicular degeneration at 200 mg/kg bw/day. Liver toxicity was also observed at dose levels above 7.5 mg/kg bw/day.

Long-term effects: Long-term studies were conducted in mice, rats and dogs. In rats, there was evidence of diffuse testicular atrophy at 250 mg/kg/bw/day. In dogs, there were histopathological changes in the liver, increases in cholesterol, and changes in liver enzyme levels at 15 mg/kg bw/day. In both rats and dogs, there were testicular effects at 250 and 125 mg/kg bw/day, respectively. The NOEL of 2.5 mg/kg bw/day in the dog study is the basis for the ADI.

Carcinogenicity: There was an increase in hepatocellular adenomas and carcinomas in some strains of mice, but these were considered species-specific and not relevant to humans.

Genotoxicity: Carbendazim can cause aneuploidy as a result of interference with the formation of the mitotic spindle. It is negative for genotoxicity in other *in vitro* and *in vivo* studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: In a reproduction study in rats, carbendazim produced testicular degeneration and reduced fertility at 50 mg/kg bw/d. Developmental studies conducted via gavage in rats (but not dietary studies) demonstrated skeletal malformations at 30-90 mg/kg bw/day in the absence of any maternal toxicity. In rabbits, gavage studies produced embryotoxicity at doses at and above 20 mg/kg bw/day and teratogenicity at 125 mg/kg bw/day.

Neurotoxicity: There was no evidence of delayed neurotoxicity.

Poison Schedule: Carbendazim is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Thiophanate-methyl is included in Schedule 5 or 6 depending on the concentration. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.09 mg/L for carbendazim/thiophanate-methyl was determined as follows:

$$0.09 \text{ mg/L} = \frac{2.5 \text{ mg/kg bodyweight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.5 mg/kg bw/day is a NOEL based on a long-term (2-year) dog study with carbendazim.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: Important general information is contained in PART II, Chapter 6

Carbofuran

(endorsed 2011)

GUIDELINE

Based on human health concerns, carbofuran in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Carbofuran (CAS 1563-66-2) belongs to the carbamate class of chemicals. Other pesticides in this class include aldicarb, bendiocarb, carbaryl, methiocarb, methomyl, pirimicarb and propoxur (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, carbofuran would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Carbofuran is a broad-spectrum insecticide and nematicide used to control worms and other pests in a variety of crops.

There are registered products containing carbofuran in Australia. These are intended for professional use and are available in concentrated solutions or as granular formulations that are applied directly to crops and soil. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to carbofuran is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of carbofuran may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of this compound in Australian drinking water could be found and, given its physicochemical properties and rapid degradation, it is unlikely to persist in waters. Carbofuran was only detected in one sample of 678 samples in a survey of Canadian municipal and private water supplies (Health and Welfare Canada 1991). It has also been detected in streams in the USA (Kimbrough and Litke 1996).

TREATMENT OF DRINKING WATER

Carbofuran has been shown to be nearly completely (99.9%) removed when water undergoes advanced oxidation with iron-catalysed ultraviolet irradiation and peroxide (Fenton reaction) (Huston and Pignatello 1999). Conventional clarification/chlorination has been demonstrated to be unreliable for the removal of carbofuran from water, although softening clarification improves removal through conventional plants substantially (CARAT 2000).

MEASUREMENT

Carbofuran in water is commonly analysed in Australian laboratories using high-performance liquid chromatography with pre-column derivitisation with orthophthalaldehyde and fluorescence detection of the derivative. The detection limit is usually around 1 µg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for carbofuran is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.33 mg/kg bw/day from a 1-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 and was established in 1987.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Carbofuran is rapidly absorbed via the gastrointestinal tract and undergoes rapid metabolism. The metabolites are formed by oxidative and hydrolytic pathways and are rapidly excreted, mainly in the urine.

Acute effects: Carbofuran has high acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: A 6-week intraperitoneal study in mice reported reduced cholinesterase activity.

Long-term effects: In long-term dietary studies in mice, rats and dogs, the most sensitive effect observed was inhibition of brain cholinesterase levels. The lowest dose at which this was observed was 0.66 mg/kg bw/day in dogs. Histopathological alterations in testicular tissue, lungs, liver and thyroid were also observed at this dose in dogs.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for carbofuran.

Genotoxicity: Carbofuran is not considered genotoxic, based on *in vitro* and *in vivo* short-term tests.

Reproductive and developmental effects: Two multigeneration reproduction studies in rats and developmental toxicity studies in mice, rats and rabbits reported no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Carbofuran is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for carbofuran was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.33 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.33 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization established a health-based guideline value of 0.007 mg/L for carbofuran in 1998 (WHO 2006).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Carbon tetrachloride

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of carbon tetrachloride in drinking water should not exceed 0.003 mg/L.

GENERAL DESCRIPTION

Carbon tetrachloride is not produced in drinking water as a by-product of chlorination, but it may be present in chlorine used for disinfection. It has occasionally been found overseas as a contaminant in drinking water supplies at concentrations less than 0.003 mg/L.

The major use of carbon tetrachloride is in the commercial production of chlorofluorocarbons which are used as refrigerants, foam-blowing agents and solvents. It is also used in the manufacture of paint and plastics.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Preliminary data indicate that concentrations of carbon tetrachloride in major Australian reticulated supplies are significantly less than 0.001 mg/L.

TREATMENT OF DRINKING WATER

Carbon tetrachloride can be removed from drinking water by adsorption onto granular activated carbon.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of carbon tetrachloride (USEPA Draft Method 551 1990). Sodium chloride is added to the sample and carbon tetrachloride extracted using methyl tert-butyl ether. The extract is then analysed using gas chromatography with an electron capture detector. The limit of determination is approximately 0.000004 mg/L (4 ng/L).

HEALTH CONSIDERATIONS

Carbon tetrachloride is absorbed readily from the gastrointestinal tract, the respiratory tract and the skin. It is distributed to all major organs, with highest concentrations in fatty tissues. It is metabolised in the liver to chloroform and other products, and excreted in breath, urine and faeces.

In humans, acute inhalation can result in central nervous system depression, and kidney and liver toxicity. Occupational exposure to carbon tetrachloride by inhalation has been associated with cancer of several organs but the evidence is inconclusive. No data are available on the effects of long-term ingestion of carbon tetrachloride. In animals, the effects of long-term exposure include toxicity to the liver and kidney. Liver tumours have been reported in studies with mice, rats and hamsters, but at doses higher than those that cause liver toxicity.

Carbon tetrachloride does not exhibit any evidence of mutagenic activity in tests with bacteria or cultured liver cells.

The International Agency for Research on Cancer has concluded that carbon tetrachloride is possibly carcinogenic to humans (Group 2B, inadequate evidence in humans but sufficient evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline value of 0.003 mg/L for carbon tetrachloride was determined as follows:

$$0.003 \text{ mg/L} = \frac{1.2 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000} \times \frac{5}{7}$$

where:

- 1.2 mg/kg body weight per day is the no-effect level based on a 90-day gavage study using mice (Condie *et al*. 1986).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for less than lifetime study). An additional factor of 10 for carcinogenicity was not applied as tumours occur at doses that have already resulted in liver toxicity.
- 5/7 is used to convert data based on a 5 day per week gavage study to a 7-day week equivalent.

The World Health Organization guideline value of 0.002 mg/L was based on an adult body weight of 60 kg. The difference in the guideline values is not significant.

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NOTE: Important general information is contained in PART II, Chapter 6

Carboxin

(endorsed 2011)

GUIDELINE

Based on human health concerns, carboxin in drinking water should not exceed 0.3 mg/L.

RELATED CHEMICALS

Carboxin (CAS 5234-68-4) belongs to the carboxamide class of chemicals. Other pesticides in this class include oxycarboxin (a metabolite of carboxin) (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population to carboxin is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, carboxin would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Carboxin is a systemic fungicide for the control of smut and bunt in seeds (wheat, barley, oats and maize) prior to planting.

There are currently products registered in Australia that contain carboxin. These products are intended for professional use and are available as concentrated solutions to be applied directly or in diluted form as a seed dressing. A dust formulation is also available. The seed dressing is applied prior to sowing. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to carboxin and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of carboxin may potentially lead to contamination of source waters through processes such as run-off or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on carboxin in Australian waters. In the USA, modelling by the United States Environmental Protection Agency suggests maximum concentrations of 0.63 µg/L and 0.095 µg/L in surface water and groundwater, respectively (USEPA 2004).

TREATMENT OF DRINKING WATER

No specific data on the treatment of carboxin in drinking water have been identified.

MEASUREMENT

Carboxin in water can be measured by gas chromatography–mass spectrometry, with a method detection limit of 1.4 µg/L (USEPA 1995).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for carboxin is 0.08 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 8.5 mg/kg bw/day from a long-term (2-year) dietary study. The NOEL is based on liver effects in mice. The ADI incorporates a safety factor of 100 and was established in 1987.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Carboxin is readily absorbed via the gastrointestinal tract. It is extensively metabolised, and is excreted in the urine and faeces almost completely within 96 hours. A major metabolite is oxycarboxin, which also has fungicidal activity.

Acute effects: Carboxin has low to very low acute oral and dermal toxicity. Carboxin is not a skin sensitiser.

Short-term effects: A four-week dietary study in rats reported liver effects at dose levels above 90 mg/kg bw/day. These effects were still present (although not as severe) 3 weeks after cessation of treatment.

Two 90-day dietary studies in rats reported effects on both the liver and kidney at dose levels above 10 mg/kg bw/day.

Long-term effects: Long-term dietary studies in mice reported decreased survival in females and effects on the lung at 750 mg/kg bw/day, and effects on the liver at 375 mg/kg bw/day and above. The NOEL based on changes in the liver was 8.5 mg/kg bw/day.

Long-term dietary studies have also been performed on rats and dogs. Effects reported in rats include decreased bodyweight, decreased food consumption and decreased survival (males only) at 30 mg/kg bw/day. There was no evidence of toxicity in dogs at 15 mg/kg bw/day.

Genotoxicity: Carboxin is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproduction and developmental effects: A 3-generation reproduction study and a developmental study in rats did not produce any evidence of reproductive or teratogenic effects. A developmental study in rabbits reported effects only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Carboxin is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.3 mg/L for carboxin was determined as follows:

$$0.3 \text{ mg/L} = \frac{8.5 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 8.5 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies variation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Carfentrazone-ethyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, carfentrazone-ethyl in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Carfentrazone-ethyl (CAS 128639-02-1) belongs to the triazolinone class of chemicals. Another pesticide in this class is amicarbazone (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, carfentrazone-ethyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Carfentrazone-ethyl is a herbicide used alone, or in combination with other herbicides, for the control of certain broad-leaf weeds prior to establishment of a variety of crops including winter cereals, pyrethrum, fruit trees, nuts, cotton and grapevines. It is also used to control weeds in commercial and industrial settings, in public areas, and around agricultural buildings and yards. In addition, carfentrazone-ethyl is used to control aquatic weeds in rice and for desuckering grapevines.

There are registered products that contain carfentrazone-ethyl in Australia. These products are dry flowables, emulsifiable concentrates or micro-encapsulated formulations, and are intended for professional use. They are most commonly applied by broadcast methods (boom spray). Back-pack hand spray is also used, with aerial application recommended for some products for cotton desiccation only. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to carfentrazone-ethyl is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of carfentrazone-ethyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater. In addition, carfentrazone-ethyl can also be applied directly into water bays of rice crops.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of carfentrazone-ethyl in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No reports of the treatment of carfentrazone-ethyl in drinking water have been identified. However, it has been reported that carfentrazone-ethyl is rapidly converted to carfentrazone-chloropropionic acid and then gradually degraded under aerobic aquatic conditions (Elmarakby *et al.* 2001).

MEASUREMENT

Solid-phase extraction (SPE) and gas chromatography with electron-capture detection has been used for sensitive, simple, and reliable analysis of carfentrazone-ethyl residues in water. Recent research has demonstrated that the use of multiwalled carbon nanotubes as a SPE adsorbent for analysis of carfentrazone-ethyl can achieve a limit of quantitation of 0.03 μg/L (Dong *et al.* 2009).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for carfentrazone-ethyl is 0.03 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 3 mg/kg bw/day from a long-term (2-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 and was established in 1998.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Carfentrazone-ethyl is readily absorbed via the gastrointestinal tract in mice and rats. It is extensively metabolised, the main metabolites being carfentrazone-ethyl-chloropropionic acid and 3-hydroxymethyl-carfentrazone-ethyl-chloropropionic acid. Most of the administered dose is excreted as metabolites in the urine within 24 hours.

Acute effects: Carfentrazone-ethyl has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea pigs.

Short-term effects: Repeat-dose studies indicate that the primary targets for carfentrazone-ethyl toxicity are the red blood cells (RBC) and the liver. In 28-day and 90-day dietary studies in mice, rats and dogs, effects were noted on blood parameters at very high dose levels only (in excess of 500 mg/kg bw/day).

Long-term effects: An 80-week dietary study in mice reported some reduction in RBCs at the lowest dose tested (10 mg/kg bw/day), and more significant effects (reduced packed cell volume and haemoglobin, increased mean corpuscular volume at 100 mg/kg bw/day. In long-term dietary studies in rats, there was a slight increase in urinary porphyrins, together with red fluorescence in the liver, correlating to porphyrin deposits, at 12 mg/kg bw/day. The lowest NOEL was 3 mg/kg bw/day in the rat study and this is the basis for the current ADI. A 52-week oral study in dogs showed an increased level of urinary porphyrins from 150 mg/kg bw/day.

Carcinogenicity: Based on long-term exposure studies in mice, rats and dogs, there is no evidence of carcinogenicity for carfentrazone-ethyl.

Genotoxicity*:* Carfentrazone-ethyl is not considered to be genotoxic, based on *in vitro* and in vivo short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive performance or on foetal development at below maternotoxic dose levels.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Carfentrazone-ethyl is considered not to require control by scheduling due to its low toxicity and is therefore in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for carfentrazone-ethyl was determined as follows:

$$0.1 \text{ mg/L} = \frac{3 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 3 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Chloral hydrate

(Trichloroacetaldehyde)

CAS NO 302-17-0

(endorsed 2014)

GUIDELINE

Based on health considerations, the concentration of chloral hydrate in drinking water should not exceed 0.1 mg/L.

Action to reduce chloral hydrate is encouraged, but must not compromise disinfection, as non-disinfected water poses significantly greater risk than chloral hydrate.

GENERAL DESCRIPTION

Chloral hydrate may be formed as a byproduct during chlorination of water containing naturally occurring organic material. Contamination of drinking water due to industrial spills is unlikely in Australia but has occurred overseas. In the United States, chloral hydrate has been detected in a small number of supplies, with concentrations ranging from 0.00001 mg/L (10 ng/L) to 0.1 mg/L.

Chloral hydrate has been used as a sedative and hypnotic drug in humans at oral doses up to 14 mg/kg body weight. A typical adult dose as a sedative is 250 mg, three times per day (WHO 2005). However, therapeutic use is generally short-term.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Testing undertaken of drinking water in South Australia between 2000 and 2012 detected up to 0.088 mg/L chloral hydrate (Amis 2012) while a survey conducted in Victoria in 2010 detected up to 0.04 mg/L (Department of Health 2011). Another study found concentrations of chloral hydrate in Australian drinking waters ranged from 0.0002 to 0.019 mg/L (Simpson and Hayes 1998).

LIMITING FORMATION IN DRINKING WATER

The presence of chloral hydrate in drinking water can be minimised by removing naturally occurring organic matter from the source water, by reducing the amount of chlorine added, or by the use of alternative disinfectants.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of chloral hydrate (USEPA Method 551.1 1995). Chloral hydrate is extracted using methyl tert-butyl ether and analysed using gas chromatography with an electron capture detector. The limit of determination is approximately 0.000005 mg/L (5 ng/L). Standard Method 5710 D of the 21st edition of the *Standard Methods for the Examination of Water and Wastewater* can be used to analyse chloral hydrate as well as trihalomethanes (APHA *et al.* 2012).

HEALTH CONSIDERATIONS

Chloral hydrate is known to be rapidly absorbed in humans and quickly oxidised to trichloroacetic acid or reduced to trichloroethanol.

In its wide use as a sedative or hypnotic drug in humans, concentrated solutions have proved quite

irritating to the gastrointestinal tract, and have caused nausea and vomiting. Side effects of the drug have included central nervous system depression, minor sensitivity reactions, and central nervous system excitement. Chronic use may result in development of tolerance, physical dependence and addiction. Addicts have been reported to take as much as 12 grams per day.

There have been a number of animal toxicity studies using rats and mice varying in duration from a few days to 2 years. In a 90-day drinking water study using mice, some enlargement of the liver was reported at doses from 16 mg/kg body weight per day. Other studies have reported that higher doses cause some liver toxicity.

A number of chronic studies have provided equivocal evidence for carcinogenicity (WHO 2005; Health Canada 2008). In a 2-year drinking water study in mice, the incidence of proliferative lesions in the liver was increased at concentrations of 120 mg/L (13.5 mg/kg/d, LOAEL) and above.

Chloral hydrate was mutagenic in tests with some strains of bacteria but did not bind to mouse liver DNA. It increased the frequency of chromosome aberrations in cultured cells and of bone marrow micronuclei in mice.

DERIVATION OF GUIDELINE

The guideline value for chloral hydrate in drinking water was determined as follows:

$$0.1 \text{ mg/L} = \frac{13.5 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day} \times 3000}$$

where:

- 13.5 mg/kg body weight per day is the lowest effect level based on a 2-year drinking water study using mice where the incidence of liver proliferative lesions was increased at the lowest dose (George *et al.* 1982).
- 70 kg is the average weight of an adult.
- 0.8 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 3000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variation, 10 for intraspecies variation, 10 for the use of a lowest effect level instead of a no-effect level, and 3 for limitations in the data relating to carcinogenicity).

The World Health Organization has no formal guideline value but notes a value of 0.1 mg/L could be calculated (WHO 2011).

An allocation factor of 80% is used as, except for therapeutic use, exposure is predominantly from chlorinated drinking water. This is the same approach taken by WHO (2011) and Health Canada (2008).

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorantraniliprole

(endorsed 2011)

GUIDELINE

Based on human health concerns, chlorantraniliprole in drinking water should not exceed 6 mg/L.

RELATED CHEMICALS

Chlorantraniliprole (CAS 500008-45-7) is in the anthranilic diamide class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, chlorantraniliprole would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chlorantraniliprole is an insecticide used to control pests on turf, cotton and a variety of fruits and vegetables. It is also used on residential lawns.

There are registered products containing chlorantraniliprole in Australia. These products are for professional and home garden use and are applied using ground boom sprayers, hand-held sprayers or aerial spraying. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to chlorantraniliprole are the use of the home garden products, and residues in food. Residue levels in crops grown according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of sources waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No sufficient monitoring data in drinking water are available. Modelling incorporating data on environmental fate and physico-chemical characteristics has been used to estimate concentrations of chlorantraniliprole. Environmental concentrations of chlorantraniliprole from long-term exposure are estimated to be 3.65 µg/L for surface water and 1.06 µg/L for groundwater in the USA (USEPA 2008a) and 63 µg/L for groundwater in Canada (Health Canada 2008). There are no published reports on chlorantraniliprole occurrence in Australian drinking water supplies.

TREATMENT OF DRINKING WATER

There are no published reports on methods of removal of chlorantraniliprole from drinking water. However, granular activated carbon, reverse osmosis and advanced oxidation process would be probably effective. Photodegradation and alkaline-catalysed hydrolysis may also reduce chlorantraniliprole concentrations in water (USEPA 2008a)

MEASUREMENT

High performance liquid chromatography–ultraviolet detection, gas chromatography/electron capture detection, and liquid chromatography with tandem mass spectrometry (LC-MS-MS) have all been reported for the determination of chlorantraniliprole in water matrices (USEPA 2008b). LC-MS-MS is the most commonly used method. The LC-MS-MS DuPont-11374 method can achieve a limit of quantitation of 0.01 mg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for chlorantraniliprole is 1.58 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 158 mg/kg bw/day 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 and it was established in 2008.

A health value has not been previously set for chlorantraniliprole by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Chlorantraniliprole is rapidly absorbed (5-12 hours) from the gastrointestinal tract and is widely distributed throughout the body. Metabolism is extensive and there is a low potential for accumulation. Excretion is substantially complete by 48-72 hours, mainly via bile and faeces.

Acute effects: Chlorantraniliprole has low acute oral and dermal toxicity. It is a slight eye irritant but is not a skin irritant or a skin sensitiser.

Short-term and long-term effects: Short-term and long-term dietary studies in mice, rats and dogs produced adaptive liver changes including increases in liver weights (at ≥658 mg/kg bw/day in mice; at ≥128 mg/kg bw/day in rats; and at ≥1163 mg/kg bw/day in dogs) and cytochrome P450 levels (at ≥658 mg/kg bw/day in female mice) and microvesiculation of the adrenal cortex (at ≥7.71 mg/kg bw/day in rats). Additional studies demonstrated that this microvesiculation did not adversely affect adrenal gland function. Long-term studies also revealed eosinophilic foci accompanied by hepatocellular hypertrophy at high dose levels. The NOEL was 158 mg/kg bw/day, and this NOEL is the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for chlorantraniliprole.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: Chlorantraniliprole is not considered to be genotoxic, based on short-term *in vitro* and *in vivo* studies.

Reproductive and developmental effects: A reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or on foetal development.

Neurotoxicity, immunotoxicity: In medium-term studies in mice and rats, there was no evidence of neurotoxicity. In 28-day studies in mice and rats, there was no evidence of effects on the immune system.

Poison Schedule: Chlorantraniliprole is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 6 mg/L for chlorantraniliprole was determined as follows:

$$6 \text{ mg/L} = \frac{158 \text{ mg/kg bodyweight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 158 mg/kg bw/day is a NOEL based on a long-term (18-month) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the average maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Chlordane

(endorsed 2011)

GUIDELINE

Based on human health concerns, chlordane in drinking water should not exceed 0.002 mg/L.

RELATED CHEMICALS

Chlordane (CAS 57-74-9) belongs to the cyclodiene organochlorine class of chemicals. A currently used pesticide in this class is endosulfan. Chlordane is also classified as a persistent organic pollutant (POP). Other cyclodiene organochlorines that were previously used as pesticides include aldrin, dieldrin and heptachlor (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present as a contaminant in drinking water, chlordane would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chlordane was used previously as an insecticide for the control of termites and soil insects.

There are no registered products that contain chlordane in Australia, but de-registered compounds may still be detected in water.

Exposure sources: The general public may be exposed to low levels of chlordane and its metabolites through residues in food and/or contaminated source waters from previous insecticidal use of chlordane.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No specific reports of chlordane in Australian drinking waters have been identified. However, chlordane is a relatively commonly identified water contaminant in many parts of the world (Yamashita *et al.* 2000, Fatoki and Awofolu 2004, Singh *et al.* 2007, Kumari *et al.* 2008, Mmualefe *et al.* 2009).

TREATMENT OF DRINKING WATER

No specific data on the treatment of chlordane in drinking water have been identified. It is expected that treatment by activated carbon should be effective under optimal conditions (WHO 2004).

MEASUREMENT

Chlordane is commonly measured in drinking waters by gas chromatography–electron capture detection, with a limit of detection of 0.014 µg/L (WHO 2004).

HISTORY OF THE HEALTH VALUES

The current tolerable daily intake (TDI) for chlordane is 0.0005 mg per kg bodyweight (mg/kg bw), 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.

When chlordane was previously used, the acceptable daily intake (ADI) was 0.0005 mg/kg bw/day, based on a NOEL of 0.045 mg/kg bw/day from the same long-term dietary study.

The previous health value was 0.001 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Chlordane is readily absorbed via the gastrointestinal tract and is extensively metabolised to oxychlordane and heptachlor epoxide. It is mainly excreted in the faeces.

Acute effects: Chlordane has low/moderate acute oral toxicity and moderate dermal toxicity. It is not a skin sensitiser.

Short-term effects: A 30-day dietary study in mice reported histopathological changes in the liver at 1.4 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies conducted in mice, rats and dogs showed the liver to be the target organ of toxicity. Effects on the liver were observed at 0.13 mg/kg bw/day in mice and 0.27 mg/kg bw/day in dogs. In a 130-week study in rats, increased absolute and relative liver weights, liver enlargement, hepatocellular swelling and necrosis were seen at dose levels above 0.045 mg/kg bw/day. The NOEL of 0.045 mg/kg bw/day is the basis for the current TDI.

Carcinogenicity: Carcinogenicity studies were conducted in mice and rats. There was evidence of liver tumours in mice at dose levels of 0.65 mg/kg bw/day and above. There was no evidence of carcinogenicity in rats.

Genotoxicity: Chlordane is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Reproduction studies in rats and mice reported reduced viability of offspring during weaning at 3 mg/kg bw/day and 7.5 mg/kg bw/day, respectively. Developmental studies in rabbits showed no effects on foetal development at doses up to 50 mg/kg bw/day.

Poisons Schedule: Chlordane is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.002 mg/L for chlordane was determined as follows:

$$0.002 \text{ mg/L} = \frac{0.045 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.045 mg/kg bw/day is the NOEL based on a long-term (130-week) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the TDI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization established a health-based guideline value of 0.0002 mg/L for chlordane in 2003 (WHO 2006).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorfenvinphos

(endorsed 2011)

GUIDELINE

Based on human health concerns, chlorfenvinphos in drinking water should not exceed 0.002 mg/L.

RELATED CHEMICALS

Chlorfenvinphos (CAS 470-90-2) belongs to the organophosphate class of chemicals. There are many other pesticides in this class including fenthion, parathion, profenofos and ethoprophos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, chlorfenvinphos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chlorfenvinphos is an insecticide that is used primarily as a parasiticide treatment for cattle, sheep, horses and to a lesser extent, deer, goats and working dogs. Agricultural use of chlorfenvinphos was cancelled and veterinary use restricted following a review in 2000 (AVPMA 2000).

There are registered products containing chlorfenvinphos in Australia. These products are intended for veterinarian or farm worker use and are applied as a topical suspension or spray, or as a dip for cattle. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to chlorfenvinphos is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The veterinary use of chlorfenvinphos provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on the concentrations of chlorfenvinphos in Australian drinking water.

TREATMENT OF DRINKING WATER

Relatively high removal rates of chlorfenvinphos have been achieved using conventional flocculation, adsorption onto activated carbon and ozonation (Ormad *et al.* 2008).

MEASUREMENT

Several methods have been reported for the analysis of chlorfenvinphos in water including solid phase extraction with gas chromatography–tandem mass spectrometry, with a limit of detection (LOD) of 4 ng/L (Ruiz-Gill *et al*. 2008), solid phase extraction with liquid chromatography–tandem mass spectrometry (LOD 10 ng/L, Greulich *et al*. 2008) and stir-bar sorptive extraction with gas chromatography–mass spectrometry (LOD 4.3 ng/L, Ochiai *et al*. 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for chlorfenvinphos is 0.0005 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.05 mg/kg bw/day from a 4-week dietary study in rats, a 2-year dietary study in rats and a 2-generation reproduction study in rats. This NOEL is based on plasma and/or brain cholinesterase inhibition. The ADI incorporates a safety factor of 100 and was established in 1998.

The previous Australian ADI for chlorfenvinphos was 0.002 mg/kg bw, based on a NOEL of 0.15 mg/kg bw/day for plasma cholinesterase inhibition seen in a 2-year rat dietary study and using a 100-fold safety factor.

The acute reference dose (ARfD) of 0.02 mg/kg bw/day for chlorfenvinphos was established in 2000, 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.

The previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Chlorfenvinphos is absorbed readily and extensively via the gastrointestinal tract. The rate of metabolism of chlorfenvinphos is species-specific, with dogs much higher than rats. In a human volunteer study, there was rapid excretion in the urine (94% in 26 hours). The main metabolite was desethyl chlorfenvinphos.

Acute effects: Chlorfenvinphos has low to high acute toxicity depending on the species. In rats, the acute oral and dermal toxicity was high. It was not a skin sensitiser. Clinical signs of acute poisoning were typical of cholinesterase inhibition and included hyperexcitability, salivation, bronchoconstriction, headache, vomiting and other behavioural changes. These have been observed in humans as well as animals.

Short-term and long-term effects: Short-term and long-term dietary studies with chlorfenvinphos reported symptoms indicative of nervous system toxicity caused by depression of cholinesterase activity. Short-term studies in mice reported brain cholinesterase inhibition at 0.2 mg/kg bw/day and plasma cholinesterase inhibition at 1.9 mg/kg bw/day. In a 2-year mouse study, plasma cholinesterase levels were depressed at 3.9 mg/kg bw/day. Both plasma and brain cholinesterase had similar level of sensitivity in the rat. Four-week and 2-year studies in rats reported plasma cholinesterase inhibition at dose levels of 0.15 mg/kg bw/day and above. The NOEL of 0.05 mg/kg bw/day from the rat studies is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for chlorfenvinphos.

Genotoxicity: Chlorfenvinphos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: Multigeneration reproduction studies in rats reported decreased fertility and decreased pup survival, but only at dose levels causing cholinesterase inhibition. In developmental toxicity studies in rats and rabbits, foetal development was impaired only at dose levels caused significant cholinesterase inhibition.

Poisons Schedule: Chlorfenvinphos is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.002 mg/L for chlorfenvinphos was determined as follows:

$$0.002 \text{ mg/L} = \frac{0.05 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.05 mg/kg bw/day is the NOEL based on a short-term (4-week) dietary study in rats, a long-term (2-year) dietary study in rats, and a 2-generation reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Chloride

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations, the chloride concentration in drinking water should not exceed 250 mg/L.

No health-based guideline value is proposed for chloride.

GENERAL DESCRIPTION

Chloride is present in natural waters from the dissolution of salt deposits, and contamination from effluent disposal.

Sodium chloride is widely used in the production of industrial chemicals such as caustic soda, chlorine, and sodium chlorite and hypochlorite. Potassium chloride is used in the production of fertilisers.

The taste threshold of chloride in water is dependent on the associated cation but is in the range 200–300 mg/L. The chloride content of water can affect corrosion of pipes and fittings. It can also affect the solubility of metal ions.

In surface water, the concentration of chloride is usually less than 100 mg/L and frequently below 10 mg/L. Groundwater can have higher concentrations, particularly if there is salt water intrusion.

Food is the major source of chloride intake. All plants and animals contain chloride. The addition of salt during processing or cooking can markedly increase the chloride content.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies chloride concentrations range up to 350 mg/L. Typical values depend to a large extent on local conditions but concentrations of 150 mg/L are not uncommon in some areas.

TREATMENT OF DRINKING WATER

Chloride cannot be removed from drinking water by conventional water treatment processes. It can be removed by distillation or reverse osmosis but these are expensive to operate.

MEASUREMENT

The chloride concentration in drinking water can be determined with titrimetric techniques using silver nitrate or mercuric nitrate and colorimetric or potentiometric end-point detection (APHA Method 4500-Cl^- Parts B or C 1992). The limit of determination is approximately 1 mg/L. Ion chromatography can also be used (APHA Method 4500-Cl^- Part F 1992), with a limit of determination of 0.1 mg/L.

HEALTH CONSIDERATIONS

Chloride is essential for humans and animals. It contributes to the osmotic activity of body fluids. A normal 70 kg human body contains approximately 80 g of chloride.

Chloride is absorbed almost completely by the gastrointestinal tract. Healthy individuals can tolerate the intake of large quantities of chloride provided there is a corresponding intake of fresh water.

Little is known about the prolonged intake of large amounts of chloride by humans. Large salt intake has been reported to increase blood pressure but this is attributed to the sodium content rather than chloride. Similar results have been reported in studies with animals, although long-term data are not available.

No data are available on carcinogenic or genotoxic effects for chloride.

DERIVATION OF GUIDELINE

The guideline value is based on the taste threshold in drinking water of approximately 250 mg/L.

There are no data to suggest that chloride causes health problems; hence, no guideline value based on health considerations is warranted.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorinated furanones
3-chloro-4-(dichloromethyl)-5-hydroxy-2(5H)-furanone (MX)

(endorsed 1996)

GUIDELINE

Data are inadequate to set a guideline value for MX in drinking water.

GENERAL DESCRIPTION

The organic compound known as MX can be formed by the reaction between chlorine and naturally occurring organic matter in water. It has been identified in chlorinated humic acid solutions, after the chlorination of pulp mill effluent, and chlorinated drinking water. No other sources of MX are known.

The stability of MX is dependent on pH. Below pH 7 it is relatively stable but above pH 7 it rapidly breaks down.

Studies in the United States, the United Kingdom and Finland have found extremely low MX concentrations in drinking water. Concentrations range up to 0.000067 mg/L (67 ng/L).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Preliminary investigations indicate that concentrations of MX in Australian drinking water are likely to be similar to those found overseas.

LIMITING FORMATION IN DRINKING WATER

The presence of MX in drinking water can be minimised by removing naturally occurring organic matter from the source water, by reducing the amount of chlorine added, by the use of alternative disinfectants, or by ensuring that the pH is kept above 7.

MEASUREMENT

MX is extremely difficult to detect because of the very low concentrations and the masking effects of other substances. Analysis is by extraction on XAD resin, methylation of the concentrate, and detection on a gas chromatography/mass spectrometer system employing selected ion monitoring techniques. The procedure is not suitable for routine analysis.

HEALTH CONSIDERATIONS

There are no data on the health effects of MX in humans, nor are there any long-term or lifetime toxicity data for animals.

Studies have shown that MX is an extremely potent mutagen when applied to some strains of bacteria, and about a third of the mutagenicity of chlorinated drinking water has been attributed to this compound. Genotoxic activity has also been observed *in vitro* using cultured mammalian cells, although *in vivo* experiments showed no evidence of genotoxic activity. No carcinogenicity data are available for MX.

Chlorine

CAS NO 7782-50-5

(endorsed 2014)

GUIDELINE

Based on health considerations, the guideline value for total chlorine in drinking water is 5 mg/L.

GENERAL DESCRIPTION

Chlorine dissociates in water to form free chlorine, which consists of aqueous molecular chlorine, hypochlorous acid and hypochlorite ion. Chlorine and hypochlorites are toxic to microorganisms and are used extensively as disinfectants for drinking water supplies. Chlorine is also used to disinfect sewage and wastewater, swimming pool water, in-plant supplies, and industrial cooling water.

Chlorine has an odour threshold in drinking water of about 0.6 mg/L, but some people are particularly sensitive and can detect amounts as low as 0.2 mg/L. Water authorities may need to exceed the odour threshold value of 0.6 mg/L in order to maintain an effective disinfectant residual.

In the food industry, chlorine and hypochlorites are used for general sanitation and for odour control. Large amounts of chlorine are used in the production of industrial and domestic disinfectants and bleaches, and it is used in the synthesis of a large range of chemical compounds.

Free chlorine reacts with ammonia and certain nitrogen compounds to form combined chlorine. With ammonia, chlorine forms chloramines (monochloramine, dichloramine and nitrogen trichloride or trichloramine) (APHA 2012). Chloramines are used for disinfection but are weaker oxidising agents than free chlorine.

Free chlorine and combined chlorine may be present simultaneously (APHA 2012). The term total chlorine refers to the sum of free chlorine and combined chlorine present in a sample.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

When used as a disinfectant, the free chlorine residual in major Australian reticulated supplies ranges from 0.1 mg/L to 4 mg/L, with typical concentrations in the reticulation of about 0.2 to 0.5 mg/L.

TREATMENT OF DRINKING WATER

Chlorine can be removed from drinking water by aeration, by exposure to sunlight, or by the addition of reducing agents such as sodium bisulfite.

MEASUREMENT

The concentration of chlorine in drinking water can be determined by several methods including the amperometric titration method (APHA Method 4500-Cl Part D 2012), DPD ferrous titrimetric method (APHA Method 4500-Cl Part F 2012) and the DPD colorimetric method (APHA Method 4500-Cl Part G 2012). The methods are subject to interferences and vary in complexity, sensitivity, precision and accuracy. Water utilities should consider Standard Methods when selecting a method (APHA 2012). The chlorine concentration should be determined immediately after sampling as chlorine is not stable in water.

HEALTH CONSIDERATIONS

Chlorine and hypochlorites are strong oxidising agents that readily react with organic molecules to produce a wide variety of chlorinated compounds. This reactivity makes it difficult to separate the effects of chlorine from those of its metabolites. In animal studies using a naturally occurring non-radioactive chlorine isotope, chlorine was rapidly absorbed by the gastrointestinal tract, and highest concentrations of the isotope were found in blood plasma.

It is assumed that the toxicities of aqueous solutions containing chlorine, hypochlorous acid or hypochlorite are similar since they are in dynamic equilibrium. Chlorine concentrations therefore refer to free available chlorine.

Very few toxic effects have been associated with drinking water containing high chlorine concentrations. In one report, 150 people drank water with 50 mg/L during a period of mains disinfection, with no adverse effects. Several instances have been reported where military personnel drank water with chlorine concentrations up to 32 mg/L for several months with no ill effects. Mouth irritation and momentary constriction of the throat were observed when the chlorine concentration exceeded 90 mg/L. Most people would refuse to drink water with a chlorine concentration over 25 mg/L (Muegge 1956).

A number of studies have suggested an association between water chlorination and various cancers or adverse reproductive outcomes. However, results of analytical epidemiological studies are insufficient to support a causal relationship for any of the observed associations (IPCS 2004). (See Section 6.3.2 for a discussion of disinfection by-products, and Section V - Fact Sheets on specific disinfection by-products.)

Long-term animal toxicity studies have shown no specific effects from the ingestion of chlorine. Chlorine, hypochlorous acid and hypochlorite did not act as carcinogens or tumour initiators.

Assessment of the mutagenicity of chlorine is complicated by the reactivity of chlorine. Hypochlorite was found to be mutagenic in tests with one strain of bacteria but not with another. Chromosome aberrations were reported in tests with mammalian cells.

The International Agency for Research on Cancer has concluded that hypochlorites are not classifiable as to their carcinogenicity in humans (Group 3, no human data and inadequate evidence in animals) (IARC 1991).

DERIVATION OF GUIDELINE

The guideline value for chlorine in drinking water was determined as follows:

$$5 \text{ mg/L} = \frac{15 \text{ mg/kg body weight per day} \times 70 \text{ kg}}{2 \text{ L/day} \times 100}$$

where

- 15 mg/kg body weight per day is the no-effect level from a 2-year drinking water study using rodents (NTP 1992).
- 70 kg is the average weight of an adult.
- 2 L/day is the average amount of water consumed by an adult.
- 100 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations and 10 for intraspecies variations).

It is assumed that all chlorine intake is from drinking water.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

APHA Method 4500-Cl Part A (2012). Chlorine (residual): Introduction. *Standard Methods for the Examination of Water and Wastewater*, 22nd edition. APHA (American Public Health Association), AWWA (American Water Works Association) and WEF (Water Environment Federation), Washington, DC.

APHA Method 4500-Cl Part D (2012). Chlorine (residual): Amperometric titration method. *Standard Methods for the Examination of Water and Wastewater*, 22nd edition. APHA (American Public Health Association), AWWA (American Water Works Association) and WEF (Water Environment Federation), Washington, DC.

APHA Method 4500-Cl Part F (2012). Chlorine (residual): DPD Ferrous Titrimetric method. *Standard Methods for the Examination of Water and Wastewater*, 22nd edition. APHA (American Public Health Association), AWWA (American Water Works Association) and WEF (Water Environment Federation), Washington, DC.

APHA Method 4500-Cl Part G (2012). Chlorine (residual): DPD colorimetric method. *Standard Methods for the Examination of Water and Wastewater*, 22nd edition. APHA (American Public Health Association), AWWA (American Water Works Association) and WEF (Water Environment Federation), Washington, DC.

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorine dioxide

Chlorite

Chlorate

(endorsed 2011)

GUIDELINE

Chlorine dioxide: Based on aesthetic considerations, the concentration in drinking water should not exceed 0.4 mg/L.

Chlorite: Based on health considerations, the concentration in drinking water should not exceed 0.8 mg/L.

Chlorate: Data are insufficient to set a guideline value in drinking water.

Action to reduce chlorite is encouraged, but must not compromise disinfection, as non-disinfected water poses significantly greater risk than chlorite.

GENERAL DESCRIPTION

Chlorine dioxide is used as a disinfectant for drinking water supplies. When added to water, it dissociates into chlorite and, to a lesser extent, chlorate. It is usually generated on site due to handling and transportation difficulties.

Chlorine dioxide is used commercially as a bleaching agent in paper production, paper pulp, and cleaning and tanning of leather. Chlorite is used in the production of paper, textiles and straw products, and in the manufacture of waxes, shellacs and varnishes. Chlorates have been used as herbicides and defoliants, and in the manufacture of dyes, matches, and explosives. Chlorate is also generated by the dissociation of hypochlorite solutions, which are used for disinfection of drinking water. Use of such solutions has become more common in Australia in recent years as use of chlorine gas has declined due to occupational health and safety considerations. Chlorate levels can be minimised by restricting storage times for hypochlorite solution (7 days maximum storage is recommended), and storing the solution under cool dark conditions.

The taste and odour threshold for chlorine dioxide in water is 0.4 mg/L. No data are available on taste and odour thresholds for chlorite and chlorate.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Chlorine dioxide (chlorite) is rarely used as a disinfectant in Australian reticulated supplies. When used, the chlorite residual is generally maintained between 0.2 mg/L and 0.4 mg/L. It is particularly effective in the control of manganese-reducing bacteria. Few data are available on chlorate levels in Australian water supplies.

TREATMENT OF DRINKING WATER

Chlorine dioxide can be removed from drinking water by the addition of reducing agents such as sodium bisulfite (although some studies indicate that the chlorate concentration increases as a result), by exposure to sunlight, or by the use of granular activated carbon.

NOTE: Important general information is contained in PART II, Chapter 6

MEASUREMENT

Methods are available for the determination of chlorine dioxide, chlorite and chlorate and total available chlorine (APHA *et al.* 2005 a,b).

HEALTH CONSIDERATIONS

Chlorine dioxide, chlorite, and chlorate are all absorbed rapidly by the gastrointestinal tract into blood plasma and distributed to the major organs. All compounds appear to be rapidly metabolised.

Chlorine dioxide has been shown to impair neurobehavioural and neurological development in rats exposed before birth. Experimental studies with rats and monkeys exposed to chlorine dioxide in drinking water have shown some evidence of thyroid toxicity; however, because of the studies' limitations, it is difficult to draw firm conclusions (WHO 2005)

The primary concern with chlorite and chlorate is oxidative stress resulting in changes in red blood cells. This end point is seen in laboratory animals and, by analogy with chlorate, in humans exposed to high doses in poisoning incidents (WHO 2005).

In a study with human volunteers, no adverse effects were observed after drinking water with either chlorine dioxide or chlorite concentrations up to 5 mg/L for periods of 12 weeks (Lubbers *et al.* 1981).

The International Agency for Research on Cancer has concluded that chlorite is not classifiable as to its carcinogenicity in humans (Group 3, no human data and inadequate evidence in animals) (IARC 1991).

DERIVATION OF GUIDELINES

The guideline values were determined as follows:

i) Chlorine dioxide:

A health based guideline value has not been established for chlorine dioxide because of its rapid hydrolysis to chlorite and chlorate. The guideline for chlorite is adequately protective for potential toxicity from chlorine dioxide (the no-observed-adverse-effect level [NOAEL] of 2.9 mg/kg bw/day used to derive the tolerable daily intake for chlorite is similar to the lowest NOAELs observed for effects of chlorine dioxide on neurobehavioral and neurological development and on thyroid hormone levels). The taste and odour threshold for chlorine dioxide is 0.4 mg/L.

ii) Chlorite:

$$0.8 \text{ mg/L} = \frac{2.9 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day} \times 100}$$

where

- 2.9 mg/kg body weight per day is the no-effect level from a two-generation study using rats (CMA 1997, TERA 1998).
- 0.8 is the proportion of total daily intake attributable to the consumption of water, based on the occasional use of chlorite in the food industry.
- 100 is the safety factor applied in using the results of an animal study as a basis for human exposure (10 for interspecies variations and 10 for intraspecies variations).

The World Health Organization (WHO) guideline value of 0.7 mg/L was determined using an adult body weight of 60 kg (WHO 2005). The difference is not significant.

NOTE: Important general information is contained in PART II, Chapter 6

iii) Chlorate:

Data are currently considered insufficient to set a guideline value for chlorate in Australian drinking water supplies. A provisional guideline value for chlorate of 0.7 mg/L was published by WHO in 2004 based on limited data from human volunteer studies and a short-term study in rats. Data from a long-term study in rats was subsequently published (NTP 2005) and has been used to derive a new TDI value (JECFA 2007). Given the importance of maintaining adequate disinfection of water supplies and limited options for reducing chlorate levels in supplies treated with hypochlorite, further information on the occurrence and sources of chlorate in Australian waters is needed before a guideline value can be developed.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Chloroacetic acids
chloroacetic acid
dichloroacetic acid (DCA)
trichloroacetic acid (TCA)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentrations of chloroacetic acids in drinking water should not exceed the following values:

chloroacetic acid	***0.15 mg/L***
dichloroacetic acid	***0.1 mg/L***
trichloroacetic acid	***0.1 mg/L***

GENERAL DESCRIPTION

Chloroacetic acids are produced in drinking water as by-products of the reaction between chlorine and naturally occurring humic and fulvic acids. Concentrations reported overseas range up to 0.16 mg/L, and are typically about half the chloroform concentration.

The chloroacetic acids are used commercially as reagents or intermediates in the preparation of a wide variety of chemicals. Monochloroacetic acid can be used as a pre-emergent herbicide, dichloroacetic acid as an ingredient in some pharmaceutical products, and trichloroacetic acid as a herbicide, soil sterilant and antiseptic.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Based on preliminary data, concentrations of chloroacetic acids in Australian drinking waters range from 0.01 mg/L to 0.1 mg/L for chloroacetic acid, from 0.003 mg/L to 0.05 mg/L for dichloroacetic acid, and from 0.001 mg/L to 0.1 mg/L for trichloroacetic acid.

LIMITING FORMATION IN DRINKING WATER

The formation of chloroacetic acids in drinking water can be minimised by removing naturally occurring organic matter from the source water, reducing the amount of chlorine added, or using alternative disinfectants.

MEASUREMENT

The chloroacetic acids can be analysed by a liquid–liquid extraction procedure (USEPA Draft Method 552 1990). In this method the sample is adjusted to pH 11.5 and extracted with methyl tert-butyl ether (MTBE) to remove neutral and basic compounds. The sample is then acidified to pH 0.5 and the chloroacetic acids extracted into MTBE. The dried extracts are methylated, and the esters analysed by gas chromatography using electron capture detection. Limits of determination are lower than 0.001 mg/L.

HEALTH CONSIDERATIONS

Chloroacetic acids would be expected to be absorbed after ingestion in view of their water solubility, but there are no data to confirm this assumption. Dichloroacetate is rapidly metabolised to glyoxylate and oxalate by the liver, but no data are available on how the other chloroacetic acids are metabolised.

Dichloroacetic acid has been used in humans to control blood sugar and cholesterol levels. There are no studies on the short- or long-term exposure of humans to chloroacetic acid or trichloroacetic acid.

In rats and mice fed chloroacetic acid for two years, survival was decreased in rats at doses of 15–30 mg/kg body weight per day, whereas in mice, survival was affected at 100 mg/kg body weight per day (males) but not at 50 mg/kg body weight per day. There was no evidence of carcinogenic activity.

Rats given dicholoroacetic acid by gavage at 3 months developed brain lesions and increases in mean liver, kidney and adrenal weight at doses from 125 mg/kg body weight per day. Similar effects were observed at 3 months in dogs fed encapsulated dichloroacetate at 50 mg/kg body weight per day. Mice receiving dichloroacetate in their drinking water for a year had decreased body weight at doses from 410 mg/kg body weight per day, increased liver weight at doses from 77 mg/kg body weight per day, and an increase in the incidence of hepatocellular carcinomas and adenomas at doses from 295 mg/kg body weight per day.

Trichloroacetic acid administered in drinking water to rats for 90 days significantly increased liver peroxisomal activity at a dose of 355 mg/kg body weight per day. A 12-month drinking water study in mice reported increases in liver weight and hepatocellular carcinomas at doses from 178 mg/kg body weight per day.

No data are available on the genotoxicity of dichloroacetic acid. Trichloroacetic acid and chloroacetic acid are not mutagenic in tests using bacteria, but have shown some mutagenic activity in some mammalian cells.

DERIVATION OF GUIDELINES

The guideline values for the chloroacetic acids in drinking water were determined as follows:

i) Chloroacetic acid:

$$0.15 \text{ mg/L} = \frac{15 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.2}{2 \text{ L/day} \times 500} \times \frac{5}{7}$$

where:

- 15 mg/kg body weight per day is the lowest effect level based on a 2-year feeding study using rats (NTP 1992).
- 70 kg is the average weight of an adult.
- 0.2 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 500 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 5 for use of the low-effect level, which is close to the no-effect level).
- 5/7 is used to convert data based on a 5-day week feeding study to a 7-day week equivalent.

The 2004 World Health Organization (WHO) Guidelines do not have a health-based guideline for chloroacetic acid.

NOTE: Important general information is contained in PART II, Chapter 6

ii) Dichloroacetic acid:

$$0.1 \text{ mg/L} = \frac{7.6 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.2}{2 \text{ L/day} \times 500}$$

where:

- 7.6 mg/kg body weight per day is the no-effect level based on a 90-day drinking water study using mice (DeAngelo *et al*. 1991).
- 500 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 5 for limited evidence of carcinogenicity).
- Other factors are as above.

The 2004 WHO provisional guideline value of 0.05 mg/L includes a factor of 10 for carcinogenicity. On review this was considered to be excessive and a lower factor was used.

iii) Trichloroacetic acid:

$$0.1 \text{ mg/L} = \frac{36 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.2}{2 \text{ L/day} \times 2000}$$

where:

- 36 mg/kg body weight per day is the no-effect level based on a 90-day drinking water study using male rats (Mather *et al*. 1990).
- 2000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations, 10 for evidence of carcinogenicity in animals and 2 because a less than lifetime study was used but chronic studies are available).
- Other factors are as above.

The 2004 WHO has a health-based guideline value of 0.2 mg/L for trichloroacetic acid.

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorobenzene

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (taste), the concentration of chlorobenzene in drinking water should not exceed 0.01 mg/L.

Chlorobenzene would not be a health concern unless the concentration exceeded 0.3 mg/L.

GENERAL DESCRIPTION

Chlorobenzene is used as a solvent and may be present in drinking water through contamination of water sources by spills or discharges. It has occasionally been detected in drinking water supplies in Canada and the United States at concentrations up to 0.005 mg/L. Inhalation from the atmosphere is believed to be the major route of environmental exposure.

Chlorobenzene has a low taste and odour threshold in water of about 0.01 mg/L.

It is used primarily as a solvent for pesticide formulations, in di-isocyanate manufacture, as a degreasing agent for mechanical parts, and in the production of nitrochlorobenzene. It is also used in the production of other halogenated organic compounds.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Chlorobenzene has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

Aeration or adsorption onto granular activated carbon will remove chlorobenzene from water.

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for analysis (USEPA Draft Method 502.1 1986). An inert gas is bubbled through the sample and chlorobenzene trapped on an adsorbent. The adsorbent is then heated and chlorobenzene analysed using gas chromatography with electron capture detection. The limit of determination is 0.0002 mg/L.

HEALTH CONSIDERATIONS

In humans, chlorobenzene is absorbed after ingestion or inhalation, and distributed primarily to adipose tissue and to the liver and kidney. It is metabolised into 4-chlorocatechol, which is excreted in urine.

An extensive review and summary of the human and animal toxicity data for chlorobenzenes is available (IPCS 1991).

There are few data on the effects of chlorobenzene on humans, and those that are available are of poor quality. They consist mainly of cases of poisoning and occupational exposure, with the principal effect being disturbances to the central nervous system.

Studies over 2 years using rats and mice reported adverse effects to the liver, kidneys, and blood-cell formation at high doses (250 mg/kg body weight per day). There is evidence of an increase of liver

NOTE: Important general information is contained in PART II, Chapter 6

tumours in male rats fed doses of 120 mg/kg body weight per day of monchlorobenzene for 2 years. No increases were observed in female rats, or in male and female mice. Chlorobenzene was not mutagenic in tests with bacteria, but may bind to RNA and DNA.

DERIVATION OF GUIDELINE

The health-based guideline value for chlorobenzene in drinking water was determined as follows:

$$0.3 \text{ mg/L} = \frac{60 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 500} \times \frac{5}{7}$$

where:

- 60 mg/kg body weight per day is the no-effect level from a 2-year gavage study using rats (NTP 1985).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 500 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 5 for limited evidence of carcinogenicity).
- 5/7 is used to convert data based on a 5 day per week feeding study to a 7-day week equivalent.

This health-based guideline value is greater than the taste and odour threshold of 0.01 mg/L.

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NOTE: Important general information is contained in PART II, Chapter 6

Chloroketones
1,1-dichloropropanone (dichloroacetone)
1,3-dichloropropanone
1,1,1-trichloropropanone (trichloroacetone)
1,1,3-trichloropropanone

(endorsed 1996)

GUIDELINE

Data are inadequate to set guideline values for chloroketones in drinking water.

GENERAL DESCRIPTION

The chloroketones are produced in drinking water as by-products of the reaction between naturally occurring organic matter and chlorine. No data are available on other sources or uses for these compounds.

Concentrations of chloroketones in drinking water reported overseas are very low and are estimated at less than 0.01 mg/L.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies 1,1,1-trichloropropanone has been recorded in concentrations up to 0.02 mg/L, but it is usually below the limit of determination of 0.0005 mg/L. No data are available for other chloroketones.

LIMITING FORMATION IN DRINKING WATER

The presence of chloroketones in drinking water can be minimised by removing naturally occurring organic matter from the source water, by reducing the amount of chlorine added, or by the use of alternative disinfectants.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of chloroketones (USEPA Draft Method 551 1990). Sodium chloride is added to the sample and the chloroketones extracted using methyl tert-butyl ether. The extracts are then analysed using gas chromatography with an electron capture detector. Limits of determination are less than 0.0005 mg/L.

HEALTH CONSIDERATIONS

No data are available on absorption from the gastrointestinal tract, metabolism or health effects in humans.

Acute oral toxicity studies in mice using 1,1-dichloropropanone and 1,3-dichloropropanone have found no toxic effects with single doses of 130 mg/kg and 20 mg/kg respectively. No long-term toxicity studies have been reported.

Both 1,1-dichloropropanone and 1,3-dichloropropanone were direct-acting mutagens in tests with bacteria. There was some evidence that 1,3-dichloropranone initiated skin tumours in mice when applied at 50 mg/kg body weight per day for two weeks. There was no evidence that either 1,1-dichloropropanone or 1,1,1-trichloropropanone acted in this way.

The NHMRC Standing Committee on Toxicity reviewed the available data for chloroketones in 1991.

It was concluded that data were insufficient to set no-effect levels for these compounds.

REFERENCE

USEPA Draft Method 551, (1990). Determination of chlorination disinfection by-products and chlorinated solvents in drinking water by liquid–liquid extraction and gas chromatography with electron capture detection. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Chlorophenols
2-chlorophenol
2,4-dichlorophenol
2,4,6-trichlorophenol

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations, the concentration of chlorophenols in drinking water should not exceed the following values.

Chlorophenols would not be a health concern unless concentrations exceeded the health-based guideline values listed.

	Health-based guideline value	*Aesthetic value guideline (odour and taste)*
2-chlorophenol	***0.3 mg/L***	***0.0001 mg/L***
2,4-dichlorophenol	***0.2 mg/L***	***0.0003 mg/L***
2,4,6-trichlorophenol	***0.02 mg/L***	***0.002 mg/L***

GENERAL DESCRIPTION

Chlorophenols may be present in drinking water as a result of chlorination of water that contains phenol or lower chlorophenols, or from contamination of water sources. Chlorination of water containing natural organic compounds can produce very low concentrations of chlorophenols. Degradation of phenoxy herbicides such as 2,4,5-T and 2,4-D also generates chlorophenols. The limited data available from overseas studies indicate that concentrations in drinking water are very low.

Chlorophenols have taste and odour thresholds in the range 0.0001 mg/L to 0.002 mg/L, with a characteristic antiseptic smell.

Chlorophenols are used commercially as preservatives, moth-proofing agents, germicides and anti-mildew agents. Exposure to chlorophenols via tap water has been estimated to be less than 10% of total dietary exposure.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on concentrations of chlorophenols in Australian drinking waters. If present at all, it is likely that concentrations would be extremely low.

TREATMENT OF DRINKING WATER

In pilot studies, granular activated carbon has successfully removed over 90% of 2-chlorophenol from water. It would probably be similarly effective in removing the other chlorophenols.

MEASUREMENT

Sensitive and isomer-specific procedures for the analysis of chlorophenols are available (USEPA Method 604 1986). The chlorophenols are derivatised with pentafluorobenzyl ether, and analysed using gas chromatography with electron capture detection. Limits of determination are 0.01 mg/L for monochlorophenol, 0.0005 mg/L for dichlorophenol and 0.00001 mg/L (10 ng/L) for trichlorophenol.

HEALTH CONSIDERATIONS

Chlorophenols are known to be efficiently absorbed and metabolised when administered orally to laboratory animals. Highest concentrations occur in the liver, brain and fat.

An extensive review and summary of the human and animal toxicity data for chlorophenols is available (IPCS 1989).

People occupationally exposed to chlorophenols often complain of irritation to the skin, mucous membranes and respiratory tract as a result of direct airborne contact. In addition, chronic ailments, skin lesions and ulcerations (particularly chloracne), and clinical indications of liver damage and neurological effects have also been reported, particularly in association with high exposures.

There have been a number of studies on the toxic effects of chlorophenols in rats and mice. Short-term exposure to high doses results in an increased respiration rate, motor weakness, tremors, convulsion, coma and death. Long-term studies over 2 years could not determine any specific dose-related effects using either 2-chlorophenol or 2,4-dichlorophenol, but 2,4,6-trichlorophenol induced leukaemia and lymphomas in male rats, and liver cancer in male and female mice.

No information is available on the mutagenic effects of 2-chlorophenol. Mutagenic tests on bacteria were negative for 2,4-dichlorophenol. Separate tests gave weakly positive and negative results for 2,4,6-trichlorophenol.

The International Agency for Research on Cancer has concluded that 2,4,6-trichlorophenol is possibly carcinogenic to humans (group 2B, sufficient evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline values for the chlorophenols in drinking water, based on health considerations, were determined as follows:

i) 2-chlorophenol:

$$0.3 \text{ mg/L} = \frac{7.5 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 7.5 mg/kg body weight per day is the no-effect level based on a 2-year drinking water study using rats (Exon and Koller 1985).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 100 is the safety factor in using the results of an animal study as a basis for human. exposure (10 for interspecies variations and 10 for intraspecies variations). The use of this safety factor was recommended by the NHMRC Standing Committee on Toxicity.

The World Health Organization (WHO) Guidelines do not have a health-based guideline for 2-chlorophenol.

ii) 2,4-dichlorophenol:

$$0.2 \text{ mg/L} = \frac{4.5 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 4.5 mg/kg body weight per day is the no-effect level based on a 2-year drinking water study using rats (Exon and Koller 1985). The use of this value was recommended by the NHMRC Standing Committee on Toxicity following a review of the available toxicity data for the chlorophenols.
- Other factors are as above.

The WHO Guidelines do not have a health-based guideline for 2,4-dichlorophenol.

iii) 2,4,6-trichlorophenol:

$$0.02 \text{ mg/L} = \frac{4.5 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 4.5 mg/kg body weight per day is the no-effect level based on a 2-year drinking water study using rats (Exon and Koller 1985). The use of this value was recommended by the NHMRC Standing Committee on Toxicity following a review of the available toxicity data for the chlorophenols.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for carcinogenic effects).
- Other factors are as above.

The WHO guideline value of 0.2 mg/L for 2,4,6-trichlorophenol was based on a calculation that estimated an additional lifetime risk of one fatal cancer per hundred thousand people (WHO 2006).

As the guideline values based on health considerations are greater than the taste thresholds for these compounds, the taste thresholds should be used as the guideline values.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Chloropicrin

(endorsed 2011)

GUIDELINE

Data are inadequate to set a health-based guideline for chloropicrin in drinking water.

RELATED CHEMICALS

Chloropicrin (CAS 76-06-2) belongs to the fumigant class of chemicals. Other pesticides in this class include methyl bromide and sulfuryl fluoride (Tomlin 2006).

HUMAN RISK STATEMENT

There are currently insufficient data on which to base a human risk statement.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chloropicrin is a fumigant used in soil to control soil-borne fungi, diseases and nematodes. It is also used to fumigate stored products and to treat wood poles and timbers for internal decay by fungi and insects. Because of its pungent odour, it is also used as a warning agent in combination with other fumigants. Chloropicrin, or trichloronitromethane (Cl_3CNO_2), is a liquid that volatilises readily when released into the atmosphere.

There are registered products containing chlorpicrin in Australia. The products are all for professional use and are applied either by hand equipment or machinery. Currently, the only products containing chlorpicrin that are applied to stored food commodities also contain methyl bromide, which is in the phase-out stage (except for quarantine uses). Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure: Public exposure is unlikely as residues are not allowed in food and are at the level of detection in cereal grains. It is also unlikely to be found in drinking water due to its physicochemical properties.

Since chloropicrin is highly soluble in water and has low adsorption in soil, it can potentially leach into groundwater and to surface water through run-off under a flooded condition. The low octanol/water partition coefficient of chloropicrin also indicates that it is not likely to be bioconcentrated in tissues of aquatic organisms (USEPA 2008).

A major route of exposure to chloropicrin is likely to be inhalation from gaseous sources, such as leaking and venting from fumigation chambers, and gas escape when using the product.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on concentrations of chloropicrin in Australian drinking waters. Chloropicrin has been detected in drinking water supplies in the USA at concentrations of less than 0.005 mg/L (USEPA 1990) and in Korea at concentrations less than 0.003 mg/L (Lee *et al*. 2001).

TREATMENT OF DRINKING WATER

There are no reports of the treatment of chloropicrin in drinking water.

However, given that chloropicrin may be formed in water as a chlorination disinfection by-product, the presence of chloropicrin in drinking water can be minimised by removing naturally occurring organic matter from the source water, by optimising disinfection practices, or by using alternative disinfectants. Most importantly, adequate disinfection must remain the primary concern and should not be compromised in response to a perceived need to lower levels of chloropicrin that may be detected.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of chloropicrin (USEPA method 551 1990). Sodium chloride is added to the sample, and the chloropicrin extracted using methyl tert-butyl ether. The extract is then analysed using gas chromatography with an electron capture detector. The limit of detection is approximately 20 ng/L. Other methods include purge and trap-gas chromatography-mass spectrometry, with detection limits reported as 250 ng/L (Lee *et al*. 2001).

HISTORY OF THE HEALTH VALUES

No acceptable daily intake (ADI) or acute reference dose (ARfD) values have been established for chloropicrin.

The available toxicity data on chloropicrin have not been evaluated to establish a health value.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Chloropicrin has had only limited toxicological assessment by Australian authorities. The Australian Government Department of Health and Ageing proposed chloropicrin for a review by the Australian Pesticides and Veterinary Medicines Authority in 2008, based on the absence of data to determine a safe level of exposure, especially to workers.

The United States Environmental Protection Agency (USEPA) selected a reversible acute endpoint using a human sensory irritation study with a benchmark concentration level ($BMCL_{10}$) of 0.073 parts per million (0.073 mg/L). At this level, the USEPA does not expect eye or nose irritation, upper respiratory changes, or any other health effects (USEPA 2008).

Poisons Schedule: Chloropicrin is included in Schedule 6 or 7 and Appendix J (Conditions for availability and use of Schedule 7 poisons) of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on concentration Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

As a no-observed-effect level (NOEL) for repeat exposure to chloropicrin has not been determined, it is not possible to determine a health-based guideline value for chloropicrin in drinking water.

The World Health Organization has not established a guideline value for chloropicrin because of inadequate data (WHO 2004).

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorothalonil

(endorsed 2011)

GUIDELINE

Based on human health concerns, chlorothalonil in drinking water should not exceed 0.05 mg/L.

RELATED CHEMICALS

Chlorothalonil (CAS 1897-45-6) belongs to the chloronitrile class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, chlorothalonil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chlorothalonil is a fungicide used for the control of fungal diseases in fruits and vegetables, as well as in turf, ornamentals, freshly sawn *Pinus* spp timber, and in various tress and vine crops.

There are registered products that contain chlorothalonil in Australia. These products are intended for professional and for home garden use and are available as concentrated solutions to be applied in diluted form using ground or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to chlorothalonil and its metabolites are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of chlorothalonil may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of chlorothalonil in Australian drinking waters have been identified. However, chlorothalonil has been occasionally identified in drinking source waters in the USA (Walker *et al*. 2000).

TREATMENT OF DRINKING WATER

No specific data on the treatment of chlorothalonil in drinking water have been identified.

MEASUREMENT

Chlorothalonil can be measured in surface waters by liquid chromatography with ultraviolet (UV) detection, with a practical limit of quantitation of 25 ng/L (Ozhan and Alpertunga 2007). Similar detection limits may alternatively be achieved by solid-phase microextraction and gas chromatography coupled with electron-capture and mass spectrometric detection (Lambropoulou *et al*. 2000).

Chlorothalonil can be measured in surface waters by liquid chromatography with UV analysis

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for chlorothalonil is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.5 mg/kg bw/day from a long-term (2-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 and was established in 1991.

The previous ADI was 0.4 mg/kg bw/day based on a NOEL of 800 mg/kg bw/day. The ADI incorporated a safety factor of 2000 and was set in 1973. In 1986, the Joint FAO/WHO Meeting on Pesticide Residues, recommended a temporary ADI of 0.0005 mg/kg bw based on a NOEL of 0.5 mg/kg bw and a safety factor of 1000. The NOEL was based on an increased incidence of renal tumours at high doses in a 2-year rat study. The transitional ADI was pending additional studies on carcinogenicity in mice and rats.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Chlorothalonil is absorbed via the gastrointestinal tract. It is largely eliminated in the faeces (95%) within 24 hours, with minor excretion of the parent compound or its metabolites in the urine. The major metabolite identified was 4-hydroxy-2,3,5-trichloroisophthalonitrile.

Acute effects: Chlorothalonil has low acute oral and dermal toxicity. Chlorothalonil is not a skin sensitiser.

Short-term effects: In a 90-day dietary study in mice and rats, kidney and liver weights were increased at doses of 71.4 and 75 mg/kg bw/day, respectively. The incidence of hyperplasia and hyperkeratosis of stomach epithelial cells was also increased at doses of 7.1 mg/kg bw/day and above in mice and at the lowest dose tested of 40 mg/kg bw/d and above (tested up to 1500 mg/kg bw/d) in rats. A separate medium-term dietary study in rats reported increased kidney weight at 3 mg/kg bw/day.

Long-term effects: Two-year dietary studies were conducted in mice, rats and dogs. The mouse study reported histopathological findings in the kidney at dose levels above 1.5 mg/kg bw. The rat study reported renal toxicity at 40 mg/kg bw/day. The dog study reported slight nephrotoxicity at 3 mg/kg bw. The overall NOEL was 1.5 mg/kg bw/day in the mouse and dog studies, and this was the basis for the ADI.

Carcinogenicity: There was evidence of carcinogenicity in both the mouse and rat studies. In mice, forestomach tumours occurred at 26 mg/kg bw/day as a result of increased hyperplasia and hyperkeratosis at 6 mg/kg bw/day and above. In rats, renal tumours and effects indicative of renal toxicity occurred at the lowest dose of 40 mg/kg bw/day. This dose level was considered well in excess of the likely level of human exposure.

Genotoxicity: There was equivocal evidence of genotoxicity from *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 3-generation reproduction study in rats did not produce any evidence of reproductive effects. In developmental toxicity studies in rats and rabbits, there was evidence of maternotoxicity in rats and foetotoxicity in rabbits at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Chlorothalonil is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.05 mg/L for chlorothalonil was determined as follows:

$$0.05 \text{ mg/L} = \frac{1.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.5 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in mice and dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for chlorothalonil and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Lambropoulou DA, Konstantinou IK, Albanis TA (2000). Determination of fungicides in natural waters using solid-phase microextraction and gas chromatography coupled with electron-capture and mass spectrometric detection. *Journal of Chromatography A,* 893(1):143-156.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Chlorpyrifos

(endorsed 2011)

GUIDELINE

Based on human health concerns, chlorpyrifos in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Chlorpyrifos (CAS 39475-55-3) is in the organophosphate class of chemicals. There are many other pesticides in this class, including fenthion, parathion, profenofos and ethoprofos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, chlorpyrifos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chlorpyrifos is a broad-spectrum insecticide used to control a broad range of insect pests in many crops, the home and commercial sites.

There are approximately 100 products containing chlorpyrifos. These products are intended for professional and home garden use and are available in many different formulations for the large variety of use patterns. The most common application methods include vehicle-mounted equipment, hand-held equipment, and aircraft for spraying and soil injection. Aerial ultra-low volume (ULV) application is permitted.

Exposure sources: The main sources of public exposure to chlorpyrifos and its metabolites are home and garden uses, and residues in food. Residue levels in food produced according to good agricultural practice are anticipated to be generally low.

Agricultural use of chlorpyrifos may potentially lead to contamination of source waters through processes such as run-off, spray drift (especially from aerial application) or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Surface water contamination arising from agricultural uses of chlorpyrifos are generally below 1 µg/L on the rare occasions that chlorpyrifos is detected in Australian surface waters (APVMA 2000). Extensive monitoring has been conducted in the cotton areas of northern New South Wales and the irrigation areas in southern New South Wales. There are a few high outliers, reaching 26 µg/L in northern rivers and 25 µg/L in irrigation drainage adjacent to rice bays in southern New South Wales, but these appear to be isolated occurrences, with such levels seldom detected because of the limited aquatic persistence of chlorpyrifos (APVMA 2000).

TREATMENT OF DRINKING WATER

Chlorpyrifos has been shown to be completely removed from water by chlorination when the chlorine dose is adjusted to match chlorine demand. Nanofiltration has also been shown to be highly effective (Kiso *et al*, 2000).

Ozonation and activated carbon adsorption for chlorpyrifos removal has also been reported to have moderate success (Ormad *et al*. 2008). Conventional coagulation/flocculation has been shown to provide a relatively low removal rate.

More research is required to investigate the effectiveness of adsorption or oxidation methods. Jar testing to identify the effectiveness of various removal methods in specific waters is recommended if chlorpyrifos is detected.

MEASUREMENT

The practical limit of quantification for chlorpyrifos in water is 0.001 mg/L by liquid chromatography with tandem mass spectrometry (Alder *et al*. 2006).

HISTORY OF THE HEALTH VALUES

The acceptable daily intake (ADI) for chlorpyrifos is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.03 mg/kg bw/day. The NOEL is 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 acute reference dose (ARfD) of 0.1 mg/kg bw/day for chlorpyrifos was established in 2000, based on a NOEL of 1 mg/kg bw/day. The NOEL was based on inhibition of red blood cell acetylcholinesterase inhibition from a 3-day human volunteer oral study. The ARfD incorporates a safety factor of 10.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Chlorpyrifos is readily absorbed from the gastrointestinal tract, widely distributed throughout the body, and excreted rapidly in the urine and faeces. Only low tissue residues have been detected. The major urinary metabolite of chlorpyrifos identified was 3,5,6-trichloro-2-pyridinol (TCP).

Acute effects: Chlorpyrifos has moderate to high acute oral toxicity and low dermal toxicity. It is not a skin sensitiser. Clinical signs of acute poisoning were typical of cholinesterase inhibition and included hyperexcitability, salivation, bronchoconstriction, headache, vomiting and other behavioural changes.

Short-term and long-term effects: Short-term and long-term studies in mice, rats, dogs and monkeys resulted in symptoms indicative of central nervous system toxicity. The most sensitive effect observed was inhibition of plasma acetylcholinesterase in rats at an oral dose of 0.03 mg/kg bw/day. Effects at higher doses included reductions in bodyweight, and increased adrenal and liver weights. In a 28-day human study, the NOEL based on cholinesterase inhibition was 0.03 mg/kg bw/day. This NOEL was the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for chlorpyrifos.

Genotoxicity: There was no evidence of genotoxicity in short-term *in vitro* or *in vivo* studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: There was no evidence of delayed neurotoxicity in chicken and rat studies, nor was there any evidence of developmental neurotoxicity in a developmental study in rats.

Poisons Schedule: Chlorpyrifos is included in Schedule 5 or 6 in the Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) No.1 (2010), depending on the concentration, formulation type or use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for chlorpyrifos was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.03 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.03 mg/kg bw/day is the NOEL based on a short-term (28-day) volunteer study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is a safety factor applied to the NOEL derived from human studies to allow for intraspecies variation.

The World Health Organization has a guideline value of 0.03 mg/L for chlorpyrifos (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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WHO (World Health Organization) (2004). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Chlorsulfuron

(endorsed 2011)

GUIDELINE

Based on human health concerns, chlorsulfuron in drinking water should not exceed 0.2 mg/L.

RELATED CHEMICALS

Chlorsulfuron (CAS 64902-72-3) belongs to the sulfonylurea herbicide class of chemicals. Other pesticides in this class include azimsulfuron, etametsulfuron-methyl, ethoxysulfuron, metsulfuron-methyl, halosulfuron-methyl, iodosulfuron methyl-sodium salt, sulfometuron methyl, sulfosulfuron, triasulfuron, tribenuron methyl and trifloxysulfuron (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, chlorsulfuron would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Chlorsulfuron is a selective post-emergence herbicide used for control of broad-leaf weeds in cereal crops.

There are currently products containing chlorsulfuron registered in Australia. These products are intended for professional use and are available in wettable powder and granular formulations. Product labels indicate products are to be diluted and applied directly to crops and soil by ground and aerial spray application methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to chlorsulfuron and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of chlorsulfuron may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on chlorsulfuron in Australian waters. In the USA, modelling by the United States Environmental Protection Agency suggests maximum concentrations of 41.3 µg/L and 3.5 µg/L in surface water and groundwater, respectively (USEPA, 2005).

TREATMENT OF DRINKING WATER

No specific data on the treatment of chlorsulfuron in drinking water have been identified.

MEASUREMENT

Chlorsulfuron in water can be measured by high performance liquid chromatography with ultraviolet detector, with a limit of detection of 1 µg/L (Sarmah and Kookana 1999).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for chlorsulfuron is 0.05 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day from a long-term (2-year dietary) study. This NOEL is based on haematological changes observed in rats. The ADI incorporates a safety factor of 100 and was established in 1982.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Chlorsulfuron is not extensively metabolised, and is rapidly excreted mostly unchanged in the urine. A small portion is metabolised to a sulfonamide and a triazine residue.

Acute effects: Chlorsulfuron has low acute oral and dermal toxicity and is not a skin sensitiser. The minor amounts of sulfonamide and triazine metabolites formed also have low acute oral toxicity and are not skin sensitisers.

Short-term effects: Medium-term dietary studies in mice and rats reported haematological changes and decreased urine pH at doses above 8 mg/kg bw/day.

Short-term dietary studies in rats indicated that chlorsulfuron metabolites are less toxic than their parent compound.

Long-term effects: Long-term dietary studies in mice and rats reported reduced bodyweight as the major effect, occurring markedly at 120 mg/kg bw/day in rats, with the only effect noted in mice at 750 mg/kg bw/day. In addition, male rats had minor changes in haematological parameters (increased red blood cell volume, mean cell haemoglobin and haematocrit) in addition to reduced bodyweight from 25 mg/kg bw/day, but only at the 1-year interim. The NOEL for the rat study was 5 mg/kg bw/day, and this is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in rats, there is no evidence of carcinogenicity for chlorsulfoton

Genotoxicity: Chlorsulfuron and its metabolites are not considered genotoxic, based on a variety of *in vitro* and *in vivo* short-term tests.

Reproductive and developmental effects: Three-generation reproductive studies in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Poisons Schedule: Chlorsulfuron is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.2 mg/L for chlorsulfuron was determined as follows:

$$0.2 \text{ mg/L} = \frac{5 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 5 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation. No additional safety was considered necessary.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety. This includes the NDPSC and PACC references below.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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NOTE: Important general information is contained in PART II, Chapter 6

Chromium

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of hexavalent chromium (Cr(VI)) in drinking water should not exceed 0.05 mg/L. If the concentration of total chromium exceeds this value then a separate analysis for hexavalent chromium should be undertaken.

GENERAL DESCRIPTION

Chromium is present in the environment in the trivalent (Cr(III)) and hexavalent (Cr(VI)) states.

Trivalent chromium is the most common naturally occurring state. Most soils and rocks contain small amounts of chromium oxide, and weathering, oxidation and bacterial action convert this insoluble compound into soluble Cr(III) salts.

Trivalent chromium salts are used in leather tanning, manufacture of catalysts, paint pigments, fungicides, and ceramic and glass manufacture.

Trivalent chromium is an essential trace element for humans, with food being the major source of intake.

Hexavalent chromium occurs infrequently in nature. Its presence in water is generally the result of industrial and domestic chromium waste discharges. Hexavalent chromium compounds are used in the metallurgical industry for chrome alloy and chrome metal production, and in the chemical industry as oxidising agents.

Hexavalent chromium is not considered to be an essential nutrient and harmful effects due to chromium have been attributed to this form.

Total chromium concentrations in drinking water are usually less than 0.005 mg/L although concentrations between 0.06 mg/L to 0.12 mg/L have been reported overseas.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies concentrations of total chromium range up to 0.03 mg/L, with typical concentrations usually less than 0.005 mg/L.

TREATMENT OF DRINKING WATER

Chromium can be removed from drinking water sources by coagulation/filtration, ion exchange, reverse osmosis and lime softening. Trivalent chromium can be oxidised to hexavalent chromium with disinfectants, particularly chlorine, chlorine dioxide and ozone.

MEASUREMENT

The total chromium concentration in drinking water can be determined by inductively coupled plasma emission spectroscopy or graphite furnace atomic absorption spectroscopy (APHA Method 3500-Cr Parts B or C 1992). The limit of determination is approximately 0.01 mg/L.

Hexavalent chromium (Cr(VI)) can be determined with a colorimetric method using diphenylcarbizide (APHA Method 3500-Cr part D 1992). The limit of determination is 0.005 mg/L.

HEALTH CONSIDERATIONS

The absorption of chromium after ingestion is low and depends on the valence state. Hexavalent chromium is more readily absorbed from the gastrointestinal tract than trivalent compounds. It is able to penetrate cell membranes, and within cells it is reduced to Cr(III) and forms complexes with proteins and genetic material.

An extensive review and summary of the human and animal toxicity data for chromium is available (IPCS 1988).

Epidemiological studies have found an association between inhalation of hexavalent chromium compounds and lung cancer, especially in humans occupationally exposed during chromate production. There is no evidence that organs other than the lung are affected or that ingestion of hexavalent chromium compounds can cause cancer.

There are sufficient animal data to indicate that many hexavalent chromium compounds are carcinogenic. Hexavalent chromium compounds also cause mutations and chromosome aberrations in a variety of test systems. The mutagenic activity can be decreased or abolished by reducing agents, such as gastric juice.

In animal studies, orally administered trivalent chromium compounds have not been shown to induce cancer or to induce mutations in genetic material.

The International Agency for Research on Cancer has concluded that hexavalent chromium is carcinogenic to humans (Group 1, sufficient evidence of carcinogenicity in humans); and that trivalent chromium is not classifiable as to its carcinogenicity to humans (Group 3, inadequate evidence in humans and inadequate evidence in animals) (IARC 1990).

DERIVATION OF GUIDELINE

The guideline value for chromium in drinking water is based on a World Health Organization assessment and should be reviewed when more toxicological data become available. It was adopted after consideration of the following points:

- The guideline value of 0.05 mg/L has been used in many countries for a number of years with no known cases of chromium toxicity.
- The value was originally set following a conservative assessment of studies on the toxicity of hexavalent chromium to rats (Mackenzie *et al.* 1958).
- Trivalent chromium is essential for human health and has no known toxic effects.
- Data are insufficient to determine whether a higher value would be equally safe.

Analysis for the separate valence states of chromium is time consuming and hence the guideline value applies to total chromium. If concentrations of total chromium exceed the guideline value, it is recommended that separate analyses for Cr(VI) and Cr(III) be undertaken.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Clopyralid

(endorsed 2011)

GUIDELINE

Based on human health concerns, clopyralid in drinking water should not exceed 2 mg/L.

RELATED CHEMICALS

Clopyralid (CAS 1702-17-6) belongs to the pyridinecarboxylic acid class of chemicals. Other pesticides in this class include aminopyralid, fluroxypyr, picloram, picolinafen and triclopyr (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, clopyralid would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Clopyralid is used as a herbicide for the control of broad-leaf weeds in turf, industrial situations and agricultural crops.

There are currently products registered in Australia that contain clopyralid, its potassium salt, its trisopropanolamine salt or its monoethanolamine salt. Clopyralid products are intended for professional use. Products are not intended for use in the home garden. Clopyralid is available as concentrated solutions, powder and granular formulations to be applied in diluted form using boom, aerial or hand-held spray equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to clopyralid and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of clopyralid may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of clopyralid in Australian drinking waters have been identified. However, an estimated mean annual calculated concentration of 24 ng/L and a maximum concentration of 1 µg/L has been reported in drinking water supplies of the northern Great Plains of the USA (Donald *et al*. 2007).

TREATMENT OF DRINKING WATER

No specific data on the treatment of clopyralid in drinking water have been identified.

MEASUREMENT

Clopyralid can be measured in drinking waters by solvent extraction followed by gas-chromatography with mass spectrometry detection. The practical limit of detection is 0.6 ng/L (Donald *et al.* 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for clopyralid is 0.5 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 50 mg/kg bw/day from a long-term (2-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 and was established in 1982.

The previous health value was 1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

The toxicological database for clopyralid consists of toxicity studies on the parent compound.

Metabolism: No metabolism studies in animals are available for clopyralid. A short-term human volunteer study reported elimination of clopyralid to be rapid and occur mainly via the urine. Metabolites were not measured in this study.

Acute effects: Clopyralid has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: Two- and four-week dietary studies in rats and dogs indicate the kidney and liver are target organs of clopyralid toxicity. Decreased bodyweight was reported at the highest dose level of 1500 mg/kg bw/day. The most sensitive toxicological effects observed were increased blood urea nitrogen levels and proliferative changes in the stomach epithelium at dose levels above 150 mg/kg bw/day in rats.

Medium-term (90-day) dietary studies were conducted in mice, rats and dogs. In rats, increased kidney and liver weights were observed at doses of 300 mg/kg bw/day. There were no treatment-related effects observed in dogs at the highest dose tested (150 mg/kg bw/day).

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. In mice, decreased bodyweight gain was observed at the high dose of 2000 mg/kg bw/day. In dogs, changes in haematological parameters and increased liver and kidney weights were observed above a dose level of 100 mg/kg bw/day. In rats, hyperplasia in stomach epithelium and decreased bodyweight gain were observed at a dose of 100 mg/kg bw/day. The NOEL based on decreased bodyweight gain and effects on the gastric epithelium was 50 mg/kg bw/day, and is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for clopyralid.

Genotoxicity: Clopyralid is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits produced no evidence of adverse effects on reproduction or the developing foetus.

Poisons Schedule: Clopyralid is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 2 mg/L for clopyralid was determined as follows:

$$2 \text{ mg/L} = \frac{50 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 50 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Donald DB, AJ Cessna, E Sverko, NE Glozier (2007). Pesticides in surface drinking-water supplies of the northern Great Plains (Research). *Environmental Health Perspectives*, 115(8):1183(9).

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

Colour (True)

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations, true colour in drinking water should not exceed 15 HU.

GENERAL DESCRIPTION

Two terms are used to describe colour. 'True colour' is the colour after particulate matter has been removed (usually by filtration through a 0.45 micrometer pore size filter). 'Apparent colour' is what one actually sees; it is the colour resulting from the combined effect of true colour and any particulate matter, or turbidity. In turbid waters, the true colour is substantially less than the apparent colour.

In natural waters, colour is due mainly to the presence of dissolved organic matter including humic and fulvic acids, which originate from soil and decaying vegetable matter. Surface water can also be coloured by waste discharges, for example from dyeing operations in the textile industry, and paper manufacture.

The dissolution of metals in pipes and fittings can also discolour drinking water. Badly corroded iron pipes can produce a brownish colour whereas corrosion of copper pipes can produce a blue-green colouration on sanitary ware and a faint blue colour in water in extreme cases. The condition of household pipes can significantly influence water colour.

In bore water, 'red water' is a frequent problem, caused by the oxidation of iron. In addition, a black discolouration in reservoirs and distribution systems can result from the action of bacteria on dissolved manganese to produce insoluble oxides. Some of these compounds form fine suspensions, or are only partially dissolved, and so contribute to apparent rather than true colour. (See Section 5.6 *Nuisance organisms*.)

As a guide, tea has a colour of about 2500 Hazen units (HU, see below). A true colour of 15 HU can be detected in a glass of water, and a true colour of 5 HU can be seen in larger volumes of water, for instance in a white bath. Few people can detect a true colour level of 3 HU, and a true colour of up to 25 HU would probably be accepted by most people provided the turbidity was low. Some examples of drinking water with differing turbidity and colour are shown in Plate 1.

True colour is preferred analytically, as the measurement is more precise than for apparent colour, and not as dependent on site or time. If both true colour and turbidity are at the guideline values (i.e. true colour of 15 HU and turbidity of 5 NTU[Nephelometric Turbidity Units]), the apparent colour could be 20 HU. This is considered to be acceptable.

Variations in colour are likely to lead to more complaints than a high but consistent colour.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies true colour ranges from 1 HU to 25 HU for filtered or fully treated supplies, and from 1 HU to 85 HU for unfiltered supplies.

MEASUREMENT

Colour can be measured spectrophotometrically or using a visual comparator. In both cases, the standard unit of measurement is the Hazen unit (HU). (True colour is often quoted as True Colour Units, or TCU; however, the numerical values are identical.) Hazen units are defined in terms of a platinum–cobalt standard (APHA Method 2120B 1992). This standard was developed for the analysis of colour in natural

waters with a yellow-brown appearance, and is not applicable to waters with different colours.

It is advisable to record the pH with the colour measurement, as the colour of natural surface waters increases with pH.

Colour values obtained using a spectrophotometer are dependent on the wavelength used for the measurement. There is no standard wavelength used in Australia, but values ranging from 395 nm to 465 nm are generally used. In the absence of a suitable Australian Standard, the British Standard, which uses 436 nm (BSI Method BS6068 1986), is suitable.

TREATMENT OF DRINKING WATER

Constituents of natural colour derived from humic and fulvic acids can be reduced by coagulation followed by filtration (AWWA 1990). Oxidation by chlorine or ozone will also reduce colour but may produce undesirable by-products.

HEALTH CONSIDERATIONS

Colour is generally related to organic content, and while colour derived from natural sources such as humic and fulvic acids is not a health consideration, chlorination of such water can produce a variety of chlorinated organic compounds as by-products (see Section 6.3.2 on disinfection by-products). If the colour is high at the time of disinfection, then the water should be checked for disinfection by-products. It should be noted, however, that low colour at the time of disinfection does not necessarily mean that the concentration of disinfection by-products will be low.

Reactions between naturally occurring humic and fulvic material and water disinfectants (such as chlorine, ozone, chloramines and chlorine dioxide) can also cause difficulties in maintaining an adequate level of disinfectant, thus creating the opportunity for bacterial reinfection or regrowth.

The solubility of some organic pollutants can also be increased through complex formation with humic material.

Coloured water may prompt people to seek other, perhaps less safe, sources of drinking water.

DERIVATION OF GUIDELINE

The guideline value is based on the colour that is just noticeable in a glass of water. This is generally accepted as being 15 HU.

GUIDELINES IN OTHER COUNTRIES

The Canadian Guidelines and the 1984 World Health Organization (WHO) Guidelines both recommend a value of 15 HU. The 1993 WHO Guidelines indicate that a colour above 15 TCU may give rise to consumer complaints.

The United States EPA Secondary Drinking water Regulations have a maximum concentration for colour of 15 HU.

The European Economic Community Standards for colour are a maximum admissible value of 20 HU and a guideline value of 1 HU.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

APHA Method 2120B (1992). Colour: Visual comparison method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

AWWA (American Water Works Association) (1990). *Water Quality and Treatment: A handbook of community water supplies*. AWWA, 4th edition, McGraw-Hill Inc.

BSI Method BS6068 (1986). Examination and determination of colour. British Standards Institution, British Standard for Water Quality, Section 2.22.

WHO (World Health Organization) (2006). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

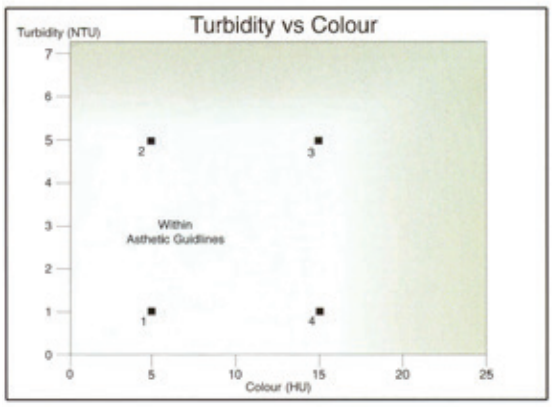
Colour and Turbidity

1. Colour = 5 HU
   Turbidity = 1 NTU

2. Colour = 5 HU
   Turbidity = 5 NTU

3. Colour = 15 HU
   Turbidity = 5 NTU

4. Colour = 15 HU
   Turbidity = 1 NTU



NOTE: Important general information is contained in PART II, Chapter 6

Copper

(endorsed 2001)

GUIDELINE

Based on health considerations, the concentration of copper in drinking water should not exceed 2 mg/L.

Based on aesthetic considerations, the concentration of copper in drinking water should not exceed 1 mg/L.

GENERAL DESCRIPTION

Copper is widely distributed in rocks and soils as carbonate and sulfide minerals.

Copper is relatively resistant to corrosion and is used in domestic water supply pipes and fittings. It is also used in the electroplating and chemical industries, and in many household goods. Copper sulfate is used extensively to control the growth of algae in water storages.

Copper is present in uncontaminated surface waters at very low concentrations, usually less than 0.01 mg/L. The concentration can rise substantially when water with a low pH and hardness remains in stagnant contact with copper pipes and fittings. Under these conditions, the concentration of copper can reach 5 mg/L or higher. In one extreme case overseas, a concentration of 22 mg/L was reported.

The taste threshold for copper is in the range 1–5 mg/L, depending on the water purity. Concentrations above 1 mg/L may cause blue or green stains on sanitary ware. Such stains may also be due to slowly leaking taps, where copper corrosion occurs over a long time, and are not necessarily due to high concentrations of copper in drinking water.

Food is the main source of copper intake. Intake from water would normally be less than 10% of total intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, total copper concentrations range up to 0.8 mg/L, with typical concentrations of about 0.05 mg/L.

TREATMENT OF DRINKING WATER

Copper can be removed from drinking water by increasing the pH, and then using the water treatment processes of coagulation followed by filtration. Aggressive water, which is likely to induce corrosion of copper pipes, should be stabilised with respect to pH and hardness as part of the treatment process prior to distribution in order to minimise copper leaching.

MEASUREMENT

The copper concentration can be determined by inductively coupled plasma emission spectroscopy (APHA Method 3500-Cu Part C 1992) with an estimated limit of determination of 0.01 mg/L. Alternatively, flame or graphite furnace atomic absorption spectroscopy can be used (APHA 3500-Cu Part B 1992) with limits of determination of 0.05 mg/L and 0.005 mg/L respectively.

HEALTH CONSIDERATIONS

Copper is an essential trace element for humans. It is estimated that adult requirements are about 2–3 mg per person per day. High doses of copper (above 50 mg/kg bodyweight) can be lethal.

The absorption of copper by the gastrointestinal tract is in the range of 25–60%, depending on a number of factors, including copper speciation and copper dietary status (Olivares *et al.* 1998). Copper is stored in the liver, brain and muscle tissue. High concentrations can also be found in the kidneys, heart and hair. Copper is eliminated from the body mainly in the bile.

Many cases of copper poisoning have been reported, including cases involving the poisoning of children who had their food prepared in copper or brass pots (Tanner 1998). Copper poisoning has resulted in cirrhosis of the liver and, in extreme cases, death. Other less severe symptoms associated with the consumption of water containing 3–5 mg/L copper (but not 1 mg/L) are gastrointestinal symptoms such as nausea, abdominal pain and vomiting (Pizarro *et al.* 1999). Infants are thought to be most susceptible, though in one study of 3-month-old infants given water containing 2 mg/L copper over 9 months there were no acute or chronic adverse consequences (Olivares *et al.* 1998). In the genetic disorders Wilson's disease and idiopathic copper toxicosis, sufferers are particularly susceptible to copper (Lönnerdal and Uauy 1998).

Apart from humans, sheep are the most susceptible animals to the toxic effects of copper, with a daily intake of 1–2 mg/kg body weight resulting in serious illness and death.

Copper was not found to be carcinogenic in tests with mice and dogs. The results of mutagenicity tests with different strains of bacteria were generally negative. Tests for mutagenicity using mammalian cells, both *in vitro* and *in vivo*, gave predominantly positive results.

DERIVATION OF GUIDELINE

The health-based guideline value of 2 mg/L (rounded up) for copper in drinking water was derived as follows:

$$2\ \text{mg/L} = \frac{0.5\ \text{mg/kg bodyweight per day} \times 70\ \text{kg} \times 0.1}{2\ \text{L/day}}$$

where:

- 0.5 mg/kg body weight per day is the provisional maximum tolerable daily intake for humans (WHO 1982).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.

In this derivation, which others have also used and which is still endorsed by the World Health Organization (2006), there is considerable uncertainty (Fitzgerald 1998). Nevertheless, on the basis of recent copper investigation studies, the derived guideline value appears to be a safe level for infants and is just below a level where minor symptoms were observed in adults.

In premises with a history of copper corrosion, water that has been in stagnant contact (6 hours or more) with copper pipes and fittings should not be used in the preparation of food or drink. Copper levels can be effectively reduced by flushing the taps for 1 minute.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

APHA Method 3500-Cu Part B (1992). Copper: Atomic Absorption Spectrometric method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

APHA Method 3500-Cu Part C (1992). Copper: Inductively Coupled Plasma method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

Fitzgerald DJ (1998). Safety guidelines for copper in water. *American Journal of Clinical Nutrition*, 67(suppl):1098S–1102S.

Lönnerdal B, Uauy R (1998). Genetic and environmental determinants of copper metabolism. *American Journal of Clinical Nutrition*, 67(5S).

Olivares M, Pizarro F, Speisky H, Lönnerdal B, Uauy R (1998). Copper in infant nutrition: Safety of World Health Organization provisional guideline value for copper content of drinking water. *Journal of Pediatric Gastroenterology and Nutrition*, 26:251–257.

Pizarro F, Olivares M, Uauy R, Contreras P, Rebelo A, Gidi V (1999). Acute gastrointestinal effects of graded levels of copper in drinking water. *Environmental Health Perspectives*, 107:117–121.

Tanner MS (1998). Role of copper in Indian childhood cirrhosis. *American Journal of Clinical Nutrition*, 67(suppl):1074S–1081S.

WHO (World Health Organization) (1982). Toxicological evaluation of certain food additives: copper. WHO, Joint Food and Agriculture Organization of the United Nations/WHO Expert Committee on Food Additives, 17, 265–296, Geneva, Switzerland.

WHO (World Health Organization) (2006). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Cyanide

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of cyanide in drinking water should not exceed 0.08 mg/L.

GENERAL DESCRIPTION

Cyanide can be present in drinking water through the contamination of source water, or through the natural decomposition of some plants that synthesise cyanoglycosides. Some microorganisms, such as the cyanobacterium *Anacystis nidulans* and the bacterium *Chromobacterium violaceum*, produce free cyanide. In uncontaminated water sources, free cyanide concentrations are usually less than 0.01 mg/L.

Sodium cyanide is used in the extraction of gold and silver from low-grade ores. It is also used in the electroplating, steel and chemical industries.

Some foods can contain quite high concentrations of cyanide. Green almonds and improperly treated cassava are of particular concern.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies cyanide concentrations range up to 0.05 mg/L, with typical concentrations usually less than 0.02 mg/L.

TREATMENT OF DRINKING WATER

There are no published reports on methods for the removal of cyanide from drinking water. Chlorine gas or hypochlorite will react with cyanide to form cyanate. Ozone is also an effective oxidant.

MEASUREMENT

The cyanide concentration in drinking water can be determined with a colorimetric method using chloramine-T (APHA Method 4500-CN Part E 1992). The limit of determination is 0.02 mg/L.

HEALTH CONSIDERATIONS

Cyanide is highly toxic. It is rapidly absorbed by the gastrointestinal tract and metabolised to thiocyanate.

In humans, long-term consumption of improperly prepared cassava in the tropics has been linked with effects on the thyroid gland and particularly the nervous system. Cyanide may deplete vitamin B12 and result in a deficiency that can cause goitre and cretinism. People most at risk are those with a nutritionally inadequate diet.

Animal studies indicate that pigs may be more sensitive than rats to the effects of long-term exposure to cyanide. In a six-month study using pigs, exposure to cyanide was reported to increase ambivalence (sic) and result in slower response times to stimuli. Behaviour demanding high energy appeared to be more readily affected by cyanide exposure than low-energy behaviour.

No data are available on the carcinogenic properties of cyanide. Tests for mutagenicity with different strains of bacteria have been mostly negative.

DERIVATION OF GUIDELINE

The guideline value for cyanide in drinking water was derived as follows:

$$0.08 \text{ mg/L} = \frac{1.2 \text{ mg/kg body weight per day } 70 \text{ kg} \times 0.2}{2 \text{ L/day} \times 100}$$

where:

- 1.2 mg/kg body weight per day is the no-effect level from 6-month feeding studies using pigs Jackson *et al*. 1986, (Jackson 1988).
- 70 kg is the average weight of an adult.
- 0.2 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 100 is the safety factor in applying the results of animal studies to humans (10 for interspecies variations and 10 for intraspecies variations).

The World Health Organization guideline of 0.07 mg/L was based on an adult weight of 60 kg. The difference in guideline values is not significant.

REFERENCES

APHA Method 4500-CN Part E (1992). Cyanide: Colorimetric method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

Jackson LC, Chandler JP, Jackson RT (1986). Inhibition and adaptation of red cell glucose-6-phosphate dehydrogenase *in vivo* to chronic sublethal dietary cyanide in an animal model. *Human Biology*, 58:67–77.

Jackson LC (1988). Behavioural effects of chronic sub-lethal dietary cyanide in an animal model: Implications for humans consuming cassava (*Manihot esculenta*). *Human Biology*, 60:597–614.

NOTE: Important general information is contained in PART II, Chapter 6

Cyanogen chloride

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of total cyanogenic compounds in drinking water should not exceed 0.08 mg/L.

GENERAL DESCRIPTION

Cyanogen chloride is a by-product of chloramination. It can be formed as a by-product of the reaction between organic precursors with hypochlorous acid in the presence of the ammonium ion. Concentrations reported overseas in chloraminated supplies are typically 0.004 mg/L.

Cyanogen chloride may be used commercially in chemical synthesis, and for fumigation.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on concentrations of cyanogen chloride in Australian drinking waters.

LIMITING FORMATION IN DRINKING WATER

The presence of cyanogen chloride in drinking water can be minimised by removing naturally occurring organic matter from the source water, by reducing the amount of chloramine added, or by the use of alternative disinfectants.

MEASUREMENT

A suitable method for analysis involves extraction from water using the purge and trap technique followed by gas chromatography/mass spectrometry (USEPA Draft Method 524.2 1986). The limit of determination is 0.0003 mg/L.

HEALTH CONSIDERATIONS

Cyanogen chloride is highly irritant and very poisonous, as it is rapidly metabolised to cyanide in the body and has similar toxicity.

Effects of ingested cyanogen chloride in humans have not been reported. A concentration of 1 ppm in air causes irritation on inhalation.

Only acute toxicity data are available on the health effects of cyanogen chloride in animals.

No data are available on the carcinogenicity or mutagenicity of cyanogen chloride.

The NHMRC Standing Committee on Toxicity reviewed available toxicity data for cyanogen chloride in 1991. It was considered that data were insufficient to set a no-effect level.

DERIVATION OF GUIDELINE

As cyanogen chloride is rapidly converted to cyanide by the body, the guideline value is based on the cyanide value of 0.08 mg/L (see also Fact Sheet on Cyanide).

REFERENCE

USEPA Draft Method 524.2 (1986). Volatile organic compounds in water by purge and trap capillary column gas chromatography/mass spectrometry. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Cyfluthrin, Beta-cyfluthrin

(endorsed 2011)

GUIDELINE

Based on human health concerns, cyfluthrin or beta-cyfluthrin in drinking water should not exceed 0.05 mg/L.

RELATED CHEMICALS

Cyfluthrin and beta-cyfluthrin (CAS 68359-37-5) are in the pyrethroid class of chemicals. Cyfluthrin is a mixture of 8 isomers, comprising 4 diastereoisomeric pairs. Beta-cyfluthrin contains the two active diastereoisomers. Other pesticides in this class include cypermethrin, alpha-cypermethrin, deltamethrin and permethrin (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, cyfluthrin or beta-cyfluthrin would not be a health concern unless the concentration exceeded 0.05 mg/L. 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Cyfluthrin and beta-cyfluthrin are broad-spectrum insecticides used for the control of spiders, ants, fleas, flies, silverfish, cockroaches, bedbugs and mosquitoes.

There are registered products containing and registered products containing beta-cyfluthrin in Australia. The majority of those containing cyfluthrinvare household insecticide sprays, of both the knock-down and surface spray varieties. Some products are also used to impregnate mosquito nets. Cyfluthrin is not applied to crops. Products containing beta-cyfluthrin are used on a variety of fruits, vegetables, cereals and pastures. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure are the use of household insecticide sprays, and residues in food. Residue levels in crops grown according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of sources waters through processes such as run-off, spray drift, or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of cyfluthrin or beta-cyfluthrin in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No reports of the treatment of cyfluthrin or beta-cyfluthrin in drinking water have been identified.

MEASUREMENT

Several methods have been reported for the analysis of cyfluthrin and beta-cyfluthrin in water, including gas chromatography with micro-electron capture detection (limit of detection [LOD] 0.85 ng/L, Casas *et al*. 2006; LOD 2 ng/L, Mekebri *et al*. 2008) and gas chromatography with high resolution mass spectrometry (LOD 0.10 ng/L, Woudneh and Oras 2006).

HISTORY OF THE HEALTH VALUES

For cyfluthrin, the current acceptable daily intake (ADI) is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.5 mg/kg bw/day from a 2-year dietary study in rats. The NOEL is based on decreased bodyweight gain and a small increase in fluorine content of bones. The ADI incorporates a safety factor of 100 and was established in 1985.

For beta-cyfluthrin, the current ADI is 0.01 mg/kg bw, based on a NOEL of 1.5 mg/kg bw/day from a 13-week dietary study in dogs. The NOEL is based on vomiting, diarrhoea and effects on motor function. The ADI incorporates a safety factor of 100 and was established in 1990.

A health value has not previously been established for cyfluthrin or beta-cyfluthrin.

HEALTH CONSIDERATIONS

Metabolism: Absorption of cyfluthrin and beta-cyfluthrin via the gastrointestinal tract is rapid and extensive (86-100%). Metabolism occurs via ester hydrolysis, oxidation of the alcohol moiety, hydroxylation and conjugation. The metabolites are excreted in urine (66%) and faeces (33%).

Acute effects: Cyfluthrin has low to moderate acute oral toxicity and low acute dermal toxicity. It does not cause skin sensitisation. Experience in the use of cyfluthrin has shown that skin irritation and peripheral sensory nerve excitation can result from human exposure, but these effects are reversible.

Beta-cyfluthrin has moderate acute oral toxicity and low dermal toxicity. It is not a skin sensitiser.

Short-term effects: In a 28-day dietary study in rats, cyfluthrin significantly decreased weight gain, elevated serum alanine amino transferase levels, increased absolute and relative liver and adrenal weights, and caused increased mortality at 80 mg/kg bw/day.

Medium-term dietary studies with cyfluthrin were conducted in rats and dogs. In the 3-month rat study, no toxicity was observed up to the highest dose of 25 mg/kg bw/day. A 6-month dog study reported decreased weight gain at 6.2 mg/kg bw/day, and vomiting, diarrhoea, trembling and poor motor co-ordination at 18.5 mg/kg bw/day.

A 28-day dietary study in rats with beta-cyfluthrin reported behavioural changes and increased mortality at 4 mg/kg bw/day and above, and salivation, apathy, changes in gait, respiratory distress and body rolling at 16 mg/kg bw/day.

Medium-term dietary studies were conducted in rats and dogs with beta-cyfluthrin. In a 90-day rat study, head and neck necrosis, uncoordinated gait, poor general condition, reduced bodyweight gain, and decreased cholesterol and triglyceride levels were observed at 50 mg/kg bw/day. A 13-week study in dogs reported toxic effects on motor function, vomiting and diarrhoea at 9 mg/kg bw/day. The NOEL of 1.5 mg/kg bw/day in this dog study is the basis for the current ADI for beta-cyfluthrin.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: Long-term studies with cyfluthrin in mice, rats and dogs produced decreased bodyweight gain at dose levels of 220 mg/kg bw/day, 6 mg/kg bw/day and 24 mg/kg bw/day, respectively. A 2-year rat study reported a small increase in fluoride concentration in bones at 6 mg/kg bw/day. In a 12-month dietary study in dogs, clinical signs of toxicity were observed at a dose of 24 mg/kg bw/day. The NOEL of 2.5 mg/kg bw/day in the rat study is the basis for the current ADI for cyfluthrin.

Carcinogenicity: Based on long-term studies in rodents, there is no evidence of carcinogenicity for cyfluthrin.

Genotoxicity: Cyfluthrin and beta-cyfluthrin are not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats with cyfluthrin showed evidence of reduced fertility and pup survival at dose levels of 6 mg/kg bw/day and above. A developmental toxicity study in rats did not produce any evidence of effects on foetal development.

Neurotoxicity: There was no evidence of delayed neurotoxicity with cyfluthrin in studies in hens.

Poisons Schedule: Cyfluthrin is included in Schedule 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Beta-cyfluthrin is included in Schedules 5, 6 and 7 , depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.05 mg/L for beta-cyfluthrin was determined as follows:

$$0.05 \text{ mg/L} = \frac{1.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.5 mg/kg bw/day is a NOEL based on a medium-term (13-week) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the average maximum amount of water consumed by an adult
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

Casas V, Llompart M, Garcia-Jares C, Cela R, Dagnac T (2006). Multivariate optimisation of the factors influencing the solid-phase microextraction of pyrethroid pesticides in water. *Journal of Chromatography A*, 1124:148-156.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Cypermethrin isomers

(endorsed 2011)

GUIDELINE

Based on human health concerns, cypermethrin in drinking water should not exceed 0.2 mg/L.

RELATED CHEMICALS

Cypermethrin (CAS 52315-07-8) belongs to the pyrethroid class of chemicals. Cypermethrin is a mixture of 8 isomers, comprising 4 diastereoisomeric pairs. Alpha-, beta- or zeta-cypermethrin each contain different amounts of the isomers. There are many other pesticides in this class including allethrin, bifenthrin, deltamethrin, permethrin, phenothrin and tetramethrin (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, cypermethrin would not be a health concern unless the concentration exceeded 0.2 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 medium- to long-term effects.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Cypermethrin is an insecticide used to control a broad range of insect and rodent pests in domestic, commercial and industrial areas, and in crops. It is also used as an ectoparasiticide in cattle and domestic pets, and as a fungicide in crop seeds.

There are many registered products containing cypermethrin in Australia; some contain alpha-cypermethrin, and a small number contain beta-cyperemethrin or zeta-cypermethrin. Cypermethrin products are intended for professional and home garden use, and include insecticide dusts, sprays and bait, rodent pellets, sheep drenches, cattle ear tags and pet shampoos. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to cypermethrin are the use of household products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of cypermethrin may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

The veterinary use of cypermethrin provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of cypermethrin in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No reports of the treatment of cypermethrin in drinking water have been identified.

MEASUREMENT

Several methods have been reported for the analysis of cypermethrin in water, including gas chromatography with micro-electron capture detection (limit of detection [LOD] 1 ng/L, Casas *et al*. 2006; LOD 2 ng/L, Mekebri *et al*, 2008) and gas chromatography with high resolution mass spectrometry (LOD 0.1 ng/L, Woudneh and Oras 2006).

HISTORY OF THE HEALTH VALUES

The acceptable daily intake (ADI) for cypermethrin, alpha-cypermethrin, and beta-cypermethrin is 0.05 mg per kg of bodyweight (mg/kg bw). For cypermethrin, the ADI is based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day from a 2-year rat study. This NOEL is based on increased liver weights, and haematological and biochemical effects. For alpha-cypermethrin, the ADI is based on a NOEL of 4.7 mg/kg bw/day from a 13-week dog study. This NOEL is based on neurological effects. The ADIs for both cypermethrin and alpha-cypermethrin incorporate a safety factor of 100 and were established in 1988 and 1994, respectively.

For beta-cypermethrin, the 2-year rat study used for establishing the cypermethrin ADI was considered appropriate to use for the beta-cypermethrin ADI.

For zeta-cypermethrin, the ADI is 0.07 mg/kg bw, 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. The ADI incorporates a safety factor of 100 and was established in 1996.

An acute reference dose (ARfD) of 0.05 mg/kg bw/day for beta-cypermethrin was established in 2002, based on a NOEL of 4.7 mg/kg bw/day from a 3-month dog study. The NOEL was based on neurological effects. The ARfD incorporates a safety factor of 100.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Cypermethrin and alpha-cypermethrin are both well absorbed via the gastrointestinal tract and readily metabolised in rats and humans. Excretion is rapid and mainly via the urine. In humans, cyclopropane carboxylic acid is the major urinary metabolite.

Acute effects: Cypermethrin has moderate acute oral toxicity and low acute dermal toxicity. There is some evidence of skin sensitisation. Alpha-cypermethrin has moderate to high acute oral toxicity. Beta-cypermethrin has low acute oral and dermal toxicity. Zeta-cypermethrin has moderate acute oral toxicity and low dermal toxicity.

Short-term effects: In 13-week dietary studies in rats and dogs with cypermethrin, there was nervous system toxicity in both species at doses above 7.5 mg/kg bw/day. Changes indicative of kidney and liver toxicity were also observed in rats at higher dose levels.

In 5- and 13-week dietary studies in rats and dogs with alpha-cypermethrin, there were clinical signs indicative of neurotoxicity (hypersensitivity to noise and abnormal gait) as well as increased organ weights for brain, liver and kidney at 21.9 mg/kg bw/day and above in rats and at 14 mg/kg bw/day in dogs. The NOEL of 4.7 mg/kg bw/day in this dog study is the basis for the current alpha-cypermethrin ADI.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: Long-term (2-year) studies in mice, rats and dogs with cypermethrin reported increased organ weights and haematological and biochemical changes in all species. The rat was the most sensitive species, with effects observed at 50 mg/kg bw/day and above. The NOEL of 5 mg/kg bw/day in this rat study is the basis for the current cypermethrin ADI.

There were no long-term studies conducted on alpha-cypermethrin or other isomers; however, the data for cypermethrin are considered representative of other isomers in relation to potential long-term effects.

Carcinogenicity: On the basis of long-term studies in mice and rats, there is no evidence of carcinogenicity for cypermethrin.

Genotoxicity: Cypermethrin and alpha-cypermethrin are not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A multigenerational reproduction study in rats and developmental studies in rats and rabbits with cypermethrin reported no evidence of effects on reproductive parameters or on foetal development. There are no reproduction or developmental studies available for the other cypermethrin isomers; however, the data for cypermethrin are considered representative of other isomers for these endpoints.

Neurotoxicity/immunotoxicity: Studies in rats and hamsters with cypermethrin reported no evidence of delayed neurotoxicity or toxicity to the immune system.

Poisons Schedule: Cypermethrin and alpha-, beta- and zeta-cypermethrin are in Schedules 5, 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard) (DoHA 2010), depending on the concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.2 mg/L for cypermethrin was determined as follows:

$$0.2 \text{ mg/L} = \frac{5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 5 mg/kg bw/day is the NOEL for cypermethrin and alpha-cypermethrin based on a long-term (2-year) study in rats and a medium-term (13-week) study in dogs, respectively. This NOEL is considered to be protective for other cypermethrin isomers.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has included cypermethrin in the list of chemicals from agricultural activities excluded from guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

Casas V, Llompart M, Garcia-Jares C, Cela R, Dagnac T (2006). Multivariate optimisation of the factors influencing the solid-phase microextraction of pyrethroid pesticides in water, *Journal of Chromatography A*, 1124, 148-156.

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Mekebri A, Crane DB, Blondina GJ, Oros DR, Rocca JL (2008) Extraction and analysis methods for the determination of pyrethroid insecticides in surface water, sediments and biological tissues at environmentally relevant concentrations, *Bulletin of Environmnetal Contamination and Toxicology*, 80, 455-460.

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NOTE: Important general information is contained in PART II, Chapter 6

Cyprodinil

(endorsed 2011)

GUIDELINE

Based on human health concerns, cyprodinil in drinking water should not exceed 0.09 mg/L.

RELATED CHEMICALS

Cyprodinil (CAS 121552-61-2) belongs to the anilinopyrimidine class of chemicals. Another pesticide in this class is pyrimethanil (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, cyprodinil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Cyprodinil is a fungicide for the control of black spot in apples and pears; the control of blossom blight and brown rot in apricots, peaches, plums and nectarines; and, in combination with fludioxonil, the control of grey mould in grapes.

There are registered products that contain cyprodinil in Australia. These are intended for professional use and are available as water-dispersible granules to be applied as concentrated or dilute solutions, commonly using air blast, misters or hand-held equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to cyprodinil is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of cyprodinil may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for cyprodinil in Australian waters were found.

TREATMENT OF DRINKING WATER

No data on drinking water treatment removal efficiency were found for cyprodinil.

MEASUREMENT

Cyprodinil in water can be analysed by adapting a solid-phase microextraction gas chromatrography mass spectrometry method developed for white wine (Otero *et al.* 2002), with a limit of detection of 0.2 µg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for cyprodinil is 0.02 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.7 mg/kg bw/day from a long-term (2-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 and was established in 1994.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Cyprodinil is rapidly absorbed via the gastrointestinal tract in rats. The parent compound is completely metabolised and excreted mainly as conjugated derivatives. These are excreted mainly in the urine within 48 hours.

Acute effects: Cyprodinil has low acute oral and dermal toxicity. It is a skin sensitiser in guinea pigs.

Short-term effects: In 1- to 3-month studies in mice, rats and dogs, the liver was the main target of toxicity, although most effects occurred only at very high dose levels. In mice, liver necrosis was observed at 257 mg/kg bw/day. In dogs, increased liver weights were observed at 46 mg/kg bw/day. Rats showed increased plasma cholesterol and phospholipid levels at 3 mg/kg bw/day, and effects on the thyroid and kidney at 19 mg/kg bw/day.

Long-term effects: Long-term dietary studies conducted in mice, rats and dogs showed the liver to be the main target organ of toxicity. Effects on the liver were noted at 600 mg/kg bw/day in mice (increased relative liver weight), at 36 mg/kg bw/day in male rats (spongiosis hepatitis) and at 446 mg/kg bw/day in dogs (pigmentation of hepatocytes). The lowest NOEL was 2.7 mg/kg bw/day in the rat study and this is the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for cyprodinil.

Genotoxicity: Cyprodinil is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats did not produce any evidence of reproductive effects. Developmental studies in rats and rabbits showed effects on foetal development in rats only, at dose levels above the maternotoxic dose, which are well in excess of the likely level of human exposure.

Poisons Schedule: Cyprodinil is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.09 mg/L for cyprodinil was determined as follows:

$$0.09 \text{ mg/L} = \frac{2.7 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 2.7 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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2,4-D [(2,4-Dichlorophenoxy) acetic acid]

(endorsed 2011)

GUIDELINE

Based on human health concerns, 2,4-D in drinking water should not exceed 0.03 mg/L.

RELATED CHEMICALS

2,4-D (CAS 94-75-7) belongs to the phenoxycarboxylic class of chemicals. Other pesticides in this class include dicloprop-p, MCPA, and mecoprop-p (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, 2,4-D would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking-water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: 2,4-D is a systemic herbicide used for the control of broad-leaf and aquatic weeds.

There are registered products containing 2,4-D in its various forms (free acid, alkali and amine salts and esters) in Australia. These products are intended for professional and home garden use and are used in food crops, in forestry, on turf and on non-crop land including industrial/commercial areas. They may be applied to these uses by a boom spray and aircraft. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to 2,4-D is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The agricultural use of 2,4-D can involve direct application into waterways or sewage systems, which may then enter source waters for drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Reported concentrations of 2,4-D in Queensland potable water supplies range from 0.2 to 0.0004 mg/L (0.4 µg/L) (Mitchell *et al.* 2005), and in Victoria range from 0.00002 to 0.34 mg/L (0.02 to 34 µg/L) (Amis 2008). Other river systems for which data exist have reported concentrations of up to 0.0156 mg/L (15.6 µg/L) (Hunter 2001).

NOTE: Important general information is contained in PART II, Chapter 6

TREATMENT OF DRINKING WATER

Common water treatment processes are not effective in removing 2,4-D from water. Activated carbon adsorption, either powdered or granulated, is the method of choice for removing 2,4-D from drinking water supplies (Health Canada 1991). Powdered activated carbon removed 90% of an initial dose of 1.0 mg/L (Canadian Department of National Health and Welfare 1993). Laboratory tests or expert advice should be sought to ensure that an effective activated carbon is selected for use. Membrane filtration treatments, ultraviolet (UV) irradiation, ozone, and the combination of UV and peroxide are also effective in removing 2,4-D (Benitez *et al*. 2004).

MEASUREMENT

Residues of 2,4-D and its salts and esters in water are commonly measured by solid-phase extraction, chemical derivatisation, separation by liquid or gas chromatography and electron capture detection (WHO 2004). Analytical detection limits for this approach range from 0.00005 to 0.0005 mg/L (0.05 to 0.5 µg/L). High performance liquid chromatography with ultraviolet detector is also commonly used and can achieve a limit of detection (LOD) of 0.001 mg/L (1 µg/L). High performance liquid chromatography–mass spectrometry can reach a lower LOD (0.00001 mg/L [0.01 µg/L]). Measurement of 2,4-D is also described in EPA methods 515.1, 555.2, 555.3, 55.4, and 555 and ASTM International methods D5317-93 and D5317-98 (USEPA 2008). Enzyme-linked immunosorbent assay (ELISA) has been also used for the quantification of 2,4-D and its salts and typical reported LODs from immunoassays are 0.0001 to 0.0007 mg/L (0.1 to 0.7 µg/L) (USEPA 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for 2,4-D is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observation-effect level (NOEL) of 1 mg/kg bw/day from a long-term (2-year) rat study. The NOEL is based on effects on the kidney. The ADI incorporates a safety factor of 100 and it was initially established in 1989 and re-confirmed in 2006.

An acute reference dose (ARfD) of 0.8 mg/kg bw/day was established for 2,4-D in 2006 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 previous health value was 0.03 mg/L (NHMRC & NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Both the free acid and the salt form of 2,4-D are rapidly absorbed from the gastrointestinal tract and distributed to tissues, with highest concentrations in kidney, liver and brain. There is no evidence for accumulation in fat. More than 70% of the oral dose was recovered in urine in animals and humans.

Acute effects: 2,4-D has low acute oral and dermal toxicity, and is not a skin sensitizer.

Short-term effects: Three-month dietary studies in mice, rats and dogs reported effects on the kidney at dose levels of 45 mg/kg bw/day, 5 mg/kg bw/day and 3 mg/kg bw/day, respectively.

Long-term effects: Long-term dietary studies in rats reported abnormal kidney histopathology at doses of 5 mg/kg bw/day and above. Effects on the rat thyroid were also noted at 45 mg/kg bw/day. The NOEL of 1 mg/kg bw/day is the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for 2,4-D.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: 2,4-D is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a 2-generation reproduction study in rats, decreased offspring viability and malformations were seen only at maternotoxic doses. Developmental studies in rats and rabbits did not produce any evidence of effects on foetal development.

Neurotoxicity: In a 15-day dietary study, 2,4-D induced neurological effects that included changes in gait, coordination and decreased motor activity at doses of 250 mg/kg bw/day. The NOEL was 75 mg/kg bw/day and was the basis for the ARfD. These effects were not noted in other acute and/or repeat-dose studies in rats and dogs.

Poisons Schedule: 2,4-D is included in Schedule 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010)., depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.03 mg/L for 2,4-D was determined as follows:

$$0.03 \text{ mg/L} = \frac{1.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.0 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

This guideline value applies to 2,4-D as well as salts and esters of 2,4-D, as these are rapidly hydrolysed to the free acid in water.

The World Health Organization has established a health-based guideline value of 0.03 mg/L for 2,4-D in 1993 (WHO 2004).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

DDT (1,1,1-trichloro-di-(4-chlorophenyl) ethane)

(endorsed 2011)

GUIDELINE

Based on human health concerns, DDT in drinking water should not exceed 0.009 mg/L.

RELATED CHEMICALS

DDT (CAS 50-29-3(p.p')/CAS 789-02-6 (o.p')) belongs to the organochlorine class of chemicals and is classified as a persistant organic pollutant (POP). Other POPs that were previously used as pesticides include aldrin, dieldrin and heptachlor (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present as a contaminant in drinking water, DDT would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: DDT is a contact insecticide used in some parts of the world for the control of insects, including those carrying diseases that are infectious to humans such as malaria.

There are no registered products that contain DDT in Australia, but de-registered compounds may still be detected in water.

Exposure sources: DDT persists in the environment as a result of previous use as an insecticide. The general public may be exposed to low levels of DDT through residues in food and/or contaminated source waters.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Since banning in the 1980s, DDT has not been commonly reported in Australian drinking waters. Evidence suggests that the concentrations of DDT in Australian rivers have progressively declined, as indicated by water in the Brisbane River, which consistently fell from maximum concentrations of about 1.7 µg/L in 1972-1973 to not detectable in 1986-1987 (Connell *et al.* 2001).

TREATMENT OF DRINKING WATER

DDT can be effectively removed from drinking waters by activated carbon treatment (Thacker *et al.* 1997, Ormad *et al.* 2008). Flocculation-coagulation can also be effective under suitable conditions (Ormad *et al.* 2008).

MEASUREMENT

DDT can be measured in drinking water using gas chromatography with electron caption detection (WHO 2004). The limit of detection for this technique is 0.01 µg/L.

HISTORY OF THE HEALTH VALUES

The current tolerable daily intake (TDI) for DDT is 0.002 mg per kg bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.25 mg/kg bw/day 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. The TDI was established in 2003.

When DDT was used previously, the ADI was 0.02 mg/kg bw based on a NOEL of 0.25 mg/kg bw/day from the same epidemiological study. The ADI was not maintained, as DDT is no longer used in agricultural practice.

The previous health value was 0.02 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: DDT is absorbed moderately well via the gastrointestinal tract in rats, and absorption is enhanced in the presence of fat. DDT and its metabolite DDE accumulate and are stored in adipose tissue and in organs containing large amounts of fat. DDT is also able to cross the placental barrier in rats and rabbits and accumulate in the foetus. It is excreted mainly unchanged in the faeces, with some excretion of the metabolite DDE occurring in urine and bile. DDT and its metabolites are also excreted in the milk of lactating animals. DDT residues have been found in human breastmilk.

Acute effects: DDT has moderate acute oral toxicity in mice, rats, guinea pigs and rabbits. Data are not available on its potential dermal toxicity or skin sensitisation.

Short-term effects: A short-term oral study in rabbits reported liver and kidney damage, and increased mortality, at 50 mg/kg bw/day. A 1-year oral study in monkeys reported hyperglycaemia, liver enlargement and hepatitis at 0.2 mg/kg bw/day. A 21-month oral study in human volunteers at 0.5 mg/kg bw/day of DDT did not produce any obvious signs of toxicity.

Long-term effects: Long-term oral studies were conducted in mice, rats, guinea pigs, dogs and monkeys. The liver was the main target organ of toxicity, with mice and rats showing particular sensitivity. In mice, there were increased benign and malignant liver tumours at dose levels above 3 mg/kg bw/day. In rats, there was hypertrophy, formation of lipospheres and cell proliferation at 0.25 mg/kg bw/day, and benign hepatocellular tumours at 12.5 mg/kg bw/day. In dogs, jaundice and haemorrhagic symptoms were reported at 50 mg/kg bw/day. In monkeys, loss of appetite, decreased bodyweight gain and convulsions were reported at 55 mg/kg bw/day.

In an epidemiological study of workers exposed to 0.25 mg/kg bw/day for 25 years, there was no association between adverse health outcomes and exposure to DDT. The NOEL of 0.25 mg/kg bw/day from this study is the basis for the current TDI. Two other epidemiological studies reported an association between the incidence of liver and pancreatic cancer and exposure to DDT, however, there were significant confounding factors in these studies.

Carcinogenicity: Long-term dietary studies in mice and rats reported evidence of liver cancer following exposure to DDT. In lifetime studies in hamsters and monkeys, there was no evidence of cancer from exposure to DDT. Epidemiological studies in humans produced only limited evidence of liver and pancreatic cancers following exposure to DDT.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: DDT is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2- and 3-generation reproduction study in rats and dogs respectively did not produce evidence of adverse effects on reproductive parameters at 10 mg/kg bw. Developmental studies in mice and rabbits have produced conflicting results but the weight of evidence indicates no effects on foetal development, except at high dose levels, well in excess of the likely level of human exposure.

Poisons Schedule: DDT is included in Appendix C of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). This appendix is for 'Substances, other than those included in schedule 9, of such danger to health as to warrant prohibition of sale, supply and use'. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.009 mg/L for DDT was determined as follows:

$$0.009 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.25 mg/kg bw/day is the NOEL based on a 25-year study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the
- TDI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for intraspecies variation and 10 for the uncertainty arising from the lack of detail in the epidemiological study.

The World Health Organization has a health-based guideline value of 0.001 mg/L for DDT (WHO 2004).

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Deltamethrin

(endorsed 2011)

GUIDELINE

Based on human health concerns, deltamethrin in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

Deltamethrin (CAS 52918-63-5) is in the pyrethroid class of chemicals. Other pesticides in this class include cyfluthrin, cypermethrin, alpha-cypermethrin and permethrin (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, deltamethrin would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Deltamethrin is an insecticide and parasiticide used for the control of a range of insects in various situations.

There are 70 products containing deltamethrin. They are intended for both professional and home garden use. For professional use, deltamethrin may be applied either as a pour-on, or as a spray, using ground or aerial methods of application. For home garden use, deltamethrin is generally available as pre-prepared spray or aerosol.

Exposure sources: The main source of public exposure to deltamethrin is residues in food. Residues levels in food produced according to good agricultural practice are generally low.

Agricultural use of deltamethrin may potentially lead to the contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on the concentrations of deltamethrin in Australian drinking waters or in drinking water overseas.

TREATMENT OF DRINKING WATER

There are no reports of the treatment of deltamethrin in drinking water.

MEASUREMENT

Several methods have been reported for the analysis of deltamethrin in water including liquid chromatography with electrospray ionisation mass spectrometry, with a limit of detection (LOD) of 0.2 ng/L in groundwater and 0.3 ng/L in sea water (Gil-Garcia *et al*. 2006); gas chromatography with micro-electron capture detection, LOD 0.81 ng/L (Casas *et al*. 2006); and gas chromatography-high resolution mass spectrometry, LOD 0.74 ng/L (Woudneh and Oras 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for deltamethrin is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1 mg/kg bw/day from a long-term dog study. This NOEL is based on clinical effects, including dilation of the pupils, decreased weight gain, vomiting and diarrhoea. The ADI incorporates a safety factor of 100 and was established in 1980.

A health value has not previously been established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Deltamethrin is rapidly absorbed via the gastrointestinal tract. It is extensively metabolised and excreted. The principal routes of metabolism are ester cleavage and oxidation at the 4-position of the alcohol moiety.

Acute effects: Deltamethrin has moderate to high acute oral toxicity and low acute dermal toxicity. It is not a skin sensitiser. Production and agricultural workers have reported irritation to the skin and mucous membranes, which last for several days.

Short-term effects: Medium-term dietary exposure in rats and dogs resulted in decreased bodyweight gain at the highest doses tested, namely, 2.5 mg/kg bw/day and 1 mg/kg bw/day, respectively. This was not accompanied by any pathological changes.

Long-term effects: Long-term dietary studies in mice, rat and dogs reported no significant toxic effects at dose levels of 15, 2.1 and 1.0 mg/kg bw/day, respectively.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for deltamethrin.

Genotoxicity: Deltamethrin is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a multigenerational reproduction study in rats and in developmental studies in mice, rats and rabbits, there was no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Deltamethrin is included in Schedule 5, 6 or 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on the concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.04 mg/L for deltamethrin was determined as follows:

$$0.04 \text{ mg/L} = \frac{1.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.0 mg/kg bw/day is the NOEL based on a long-term (2-year) toxicity dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

Deltamethrin is excluded from the World Health Organization drinking water guidelines because it is "unlikely to occur in drinking water" (WHO 2006).

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NOTE: Important general information is contained in PART II, Chapter 6

Diazinon

(endorsed 2011)

GUIDELINE

Based on human health concerns, diazinon in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Diazinon (CAS 333-41-5) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, including chlorpyrifos, malathion, and temephos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, diazinon would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Diazinon is a insecticide used on sheep and cattle and companion animals; on fruit, vegetables, mushrooms and field crops; and in horticulture for nursery plants and ornamentals, including quarantine use. It is also used on lawns and turf, and in commercial, public and domestic buildings and surrounds.

There are registered products containing diazinon in Australia. These are intended for professional use and are available as soluble concentrates to be diluted and applied by ground and aerial sprays to crops, or as impregnated flea collars (pets) and ear tags (cattle). Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to diazinon and its metabolites are its use in public or domestic buildings, in the garden, or on companion animals; and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural and veterinary use of diazinon may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of diazinon in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Diazinon can be readily removed by various oxidation processes including ultraviolet radiation, oxidation, advanced oxidation and ozone (Real *et al*. 2007). However, oxidation can result in the formation of unwanted by-products, therefore a by-product management plan is also recommended before implementing any oxidation processes.

Activated carbon is effective in the removal of diazinon (Ohno *et al*. 2008). However, in the presence of chlorine, unwanted diazinon by-products were shown to desorb from the activated carbon surface (Ohno *et al*. 2008).

Nanofiltration has also been shown to be effective in the removal of Diazinon. (Kiso *et al*. 2000).

MEASUREMENT

The practical limit of quantification for diazinon in water is 0.0001 µg/L by liquid chromatography–tandem mass spectrometry (Alder *et al*. 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for diazinon is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observable-effect level (NOEL) of 0.02 mg/kg bw/day 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 and was established in 1999.

The acute reference dose (ARfD) of 0.01 mg/kg bw/day for diazinon was established in 2002, 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 previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Diazinon is rapidly absorbed from the gastrointestinal tract, extensively metabolised and rapidly excreted mainly in urine (97%) within 24 hours. The highest tissue concentrations are in fat, with no evidence of accumulation.

Acute effects: Diazinon has moderate acute oral and dermal toxicity, and is a skin sensitiser in guinea pigs. It can also cause delayed neuropathy 24-96 hours after acute exposure. Clinical symptoms of toxicity were typical of cholinesterase inhibition and included tremors, prostration, coma, piloerection, ataxia, and salivation.

Short-term effects: Short-term dietary studies in rats reported inhibition of plasma cholinesterase at doses of 0.2 mg/kg bw/day. Inhibition of erythrocyte cholinesterase activity was seen at 2.5 mg/kg bw/day, while brain cholinesterase activity was inhibited at 23 mg/kg bw/day. In a 37-43 day dietary study in humans, the NOEL for cholinesterase inhibition was 0.02 mg/kg/ bw/day, and this is the basis for the ADI.

Long-term effects: In long-term dietary studies in rats, mice and dogs, plasma cholinesterase inhibition was seen at doses of 0.018 mg/kg bw/day and above (dogs). Decreased brain cholinesterase activity (rats) and decreased bodyweight gain (dogs) was seen at 5 mg/kg bw/day. Clinical symptoms of nervous system toxicity were seen at 15 mg/kg bw/day (mice). The overall lowest NOEL was 0.0037 mg/kg bw/day (dogs) in these studies.

NOTE: Important general information is contained in PART II, Chapter 6

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for diazinon.

Genotoxicity: Diazinon is not considered to be genotoxic, based on *in vitro* and *in vivo* short term studies.

Reproductive and developmental effects: Reproduction studies in rats and developmental studies in rats and rabbits produced no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Diazinon is included in Schedule 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010)., depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.004 mg/L for diazinon was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.02 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 20}$$

where:

- 0.02 mg/kg bw/day is the NOEL based on a short-term (37-43 day) repeat-dose study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 20 is the safety factor applied to the NOEL from a study conducted in humans. The safety factor of 20 incorporates a factor of 10 for intraspecies variation and 2 for the closeness of the NOEL and LOEL.

The World Health Organization has not established a health-based guideline value for diazinon and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Dicamba

(endorsed 2011)

GUIDELINE

Based on human health concerns, dicamba in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Dicamba (CAS 1918-00-9) belongs to the chlorophenoxy chemical class. Other pesticides in this class include 2,4-D, MCPA and mecoprop (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, dicamba would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Dicamba is used as a herbicide for the control of annual and perennial broad-leaf weeds in home garden lawns, turf and agricultural crops.

There are currently products registered in Australia that contain dicamba, its acid derivative, its dimethylamine salt or its sodium salt. Dicamba products are intended for professional or home garden use. Products are available as concentrated solutions to be applied diluted and undiluted using boom spray, aerial spray, and hand-held sprays or watering cans. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to dicamba and its metabolites are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of dicamba may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Dicamba is a very polar herbicide and results of its analysis in water have traditionally been negative. This may be a factor in the absence of reliable data on the presence of dicamba in Australian waters. A survey of pesticides including dicamba in New South Wales drinking water reported in 1989 (Ang *et al.* 1989) did not find detectable levels of dicamba in any sample. A recent published paper (Tran *et al.* 2006)

reported use of state-of-the-art analytical techniques to determine the presence of a range of herbicides including dicamba in agricultural drainage waters in Australia. While a range of herbicides was detected, no dicamba was found in the samples.

One of the main studies on dicamba incidence in water was from Canada, to derive Canadian Water Quality Guidelines (Caux *et al*. 1993). Dicamba was detected in less than 8% of surface water samples, with a maximum concentration of 13 µg/L; and in groundwater, it was detected in 2% of samples but at concentrations to 517 µg/L.

TREATMENT OF DRINKING WATER

Dicamba has been shown to be completely removed when water undergoes advanced oxidation with iron-catalysed ultraviolet irradiation and peroxide (Fenton reaction) (Huston and Pignatello 1999).

MEASUREMENT

Dicamba is a very polar herbicide that is not amenable to direct analysis by gas chromatographic techniques. It is commonly extracted from water via solid phase extraction techniques and determined by high performance liquid chromatography using ultraviolet detection. This approach leads to limits of detection of approximately 1 µg/L (Krzyszowska and Vance 1994). This process has recently been refined in a study investigating a range of hydrophilic solid phase extraction techniques (Tran *et al*. 2006).

HISTORY OF THE HEALTH-BASED GUIDELINE

The current acceptable daily intake (ADI) for dicamba is 0.03 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 3 mg/kg bw/day 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 and was established in 1991.

The previous ADI for dicamba was 0.05 mg/kg bw/day. This ADI was established in 1986; however, there is no information indicating how it was derived.

The previous NHMRC health-based guideline value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Dicamba is readily and extensively absorbed via the gastrointestinal tract in all species studied. It does not undergo significant metabolism and is excreted rapidly, predominantly in urine, largely unchanged.

Acute effects: Dicamba has low acute oral and dermal toxicity. Dicamba is a moderate skin sensitiser in guinea-pigs.

Short-term effects: A 13-week dietary study in rats reported decreased bodyweight gain and elevated liver enzyme levels at 500 mg/kg bw/day.

Long-term effects: A 2-year dietary study in mice reported increased male mortality and reduced female bodyweight gain at the high dose (450 mg/kg bw/day). The NOEL for this study was 150 mg/kg bw/day.

Carcinogenicity: Based on long-term dietary studies in mice, there is no evidence of carcinogenicity for dicamba.

Genotoxicity: There is evidence of genotoxicity but only at dose levels well in excess of the likely level of human exposure.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 3-generation reproduction study in rats did not report any evidence of toxicity in adult rats or offspring at doses up to 25 mg/kg bw/day. In developmental studies in rats and rabbits, there was no evidence of delayed development or teratogenicity. Maternotoxicity (decreased bodyweight gain in rats and neurotoxicity in rabbits) was reported. The most sensitive NOEL for maternotoxicity was 3 mg/kg bw/day in rats, which was used to establish the current ADI.

Poisons Schedule: Dicamba is included in Schedule 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for dicamba was determined as follows:

$$0.1 \text{ mg/L} = \frac{3 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 3 mg/kg bw/day is the NOEL based on a short-term (developmental) study in rabbits.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Dichlorobenzenes
1,2-dichlorobenzene (1,2-DCB)
1,3-dichlorobenzene (1,3-DCB)
1,4-dichlorobenzene (1,4-DCB)

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations, the concentrations of dichlorobenzenes in drinking water should not exceed the values shown below.

Dichlorobenzenes would not be a health concern unless concentrations exceeded the health-based guildeine values shown below:

	Health-based guideline value	*Aesthetic guideline value*
1,2-dichlorobenzene	*1.5 mg/L*	*0.001 mg/L*
1,3-dichlorobenzene	*inadequate data*	*0.02 mg/L*
1,4-dichlorobenzene	*0.04 mg/L*	*0.0003 mg/L (300 ng/L)*

GENERAL DESCRIPTION

Dichlorobenzenes are widespread in the environment and may be present in drinking water though spills and discharges, from atmospheric deposition, or by contact with contaminated soils. Studies in Japan, England, Canada and the United States have reported concentrations in the range 0.0000005 mg/L (0.5 ng/L) to 0.013 mg/L. Most supplies tested are below 0.00001 mg/L (10 ng/L), with 1,2-DCB and 1,4-DCB the most widely detected isomers. Sources of human exposure to DCBs are mainly food and air.

The dichlorobenzenes impart an offensive taste and odour to water, with thresholds between 0.0003 mg/L and 0.02 mg/L.

1,4-DCB is used in toilet blocks to deodorise air, and as a moth repellent, and is widely diffused in the environment. 1,3-DCB is a minor fumigant and insecticide and can be formed from incomplete combustion of waste. 1,2-DCB is used primarily as a chemical intermediate for dyestuffs and pesticides.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

DCBs have not been found in Australian drinking waters. They are included here to provide guidance in the unlikely event of contamination, and because they have been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

It is unlikely that DCB concentrations are reduced significantly during conventional water treatment processes. Removal using packed tower aeration or by the use of granular activated carbon is more than 90% effective and it is likely that concentrations below 0.001 mg/L can be achieved using these methods.

NOTE: Important general information is contained in PART II, Chapter 6

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for analysis (USEPA Draft Method 502.1 1986). An inert gas is bubbled through the sample and the dichlorobenzenes trapped on an adsorbent. The adsorbent is then heated and the dichlorobenzenes analysed using gas chromatography with electron capture detection. The limit of determination is approximately 0.0002 mg/L.

HEALTH CONSIDERATIONS

DCBs are absorbed rapidly through the lungs and from the gastrointestinal tract, and then distributed to tissues, primarily to fat or fatty tissue, and the lungs and kidneys. They are metabolised by the liver to the respective chlorophenols and eliminated in urine.

An extensive review and summary of the human and animal toxicity data for chlorobenzenes is available (IPCS 1986).

In the various reported cases of human exposure to DCBs, inhalation is the primary route. Toxic effects include liver damage, blood disorders, and disturbances to the immune system, the central nervous system or the respiratory tract. Skin pigmentation and allergic dermatitis have followed skin contact.

In rodents, long-term gavage (measured force-feeding) studies showed high doses of 1,2-DCB (120 mg/kg body weight per day) to affect mainly the liver and kidney, but found no adverse effects at lower doses. On balance, the available evidence suggests that 1,2-DCB is neither mutagenic in tests with bacteria nor carcinogenic in rodents.

No data are available on chronic toxicity for 1,3-DCB. No mutagenic activity was seen in tests with bacteria.

Long-term gavage studies involving 1,4-DCB produced similar results to the 1,2-DCB studies. In addition, there is evidence that 1,4-DCB increases the incidence of kidney tumours in male rats and liver tumours in mice after long-term exposure. It did not exhibit mutagenic activity in tests with bacteria or mammalian cells.

The International Agency for Research on Cancer has concluded that 1,4-DCB is possibly carcinogenic to humans (Group 2B, inadequate evidence in humans but sufficient evidence in animals), but that 1,2-DCB is unclassifiable as to its carcinogenicity (Group 3, inadequate evidence in humans and animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline values for dichlorobenzenes in drinking water were determined as follows:

i) 1,2-dichlorobenzene:

The health-based guideline value of 1.5 mg/L was determined as follows:

$$1.5\ \text{mg/L} = \frac{60\ \text{mg/kg body weight per day} \times 70\ \text{kg} \times 0.1}{2\ \text{L/day} \times 100} \times \frac{5}{7}$$

where:

- 60 mg/kg body weight per day is the no-effect level from a 2-year gavage study using mice (NTP 1985).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.

NOTE: Important general information is contained in PART II, Chapter 6

FACT SHEETS

- 100 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations and 10 for intraspecies variations).
- 5/7 is used to convert data based on a 5 day per week gavage study to a 7-day week equivalent.
- Other factors are as above.

This health-based guideline value exceeds the taste and odour threshold of 0.001 mg/L. The World Health Organization (WHO) guideline value of 1 mg/L was based on an adult body weight of 60 kg. The difference in the guideline values is not significant.

ii) 1,3-dichlorobenzene

There are insufficient long-term data to set a guideline value for 1,3-DCB in drinking water based on health considerations. The maximum concentration guideline of 0.02 mg/L is based on the aesthetic considerations of taste and odour.

iii) 1,4-dichlorobenzene

The health-based guideline value of 0.04 mg/L was determined as follows:

$$0.04\ \text{mg/L} = \frac{150\ \text{mg/kg body weight per day} \times 70\ \text{kg} \times 0.1}{2\ \text{L/day} \times 10{,}000} \times \frac{5}{7}$$

where:

- 150 mg/kg body weight per day is the lowest effect level based on the appearance of kidney tumours in a 2-year gavage study using rats (NTP 1987).
- 10,000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations, 10 because a lowest effect level was used instead of a no-effect level, and 10 because carcinogenic effects were observed at the lowest doses used).
- Other factors are as above.
- 5/7 is used to convert data based on a 5 day per week gavage study to a 7-day week equivalent.

This health-based value exceeds the taste and odour threshold of 0.0003 mg/L. The WHO guideline value of 0.3 mg/L did not include the additional factor of 10 for possible carcinogenic effects.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

IPCS (International Programme on Chemical Safety) (1991). Chlorobenzenes other than hexachlorobenzene. Environmental Health Criteria, 128. World Health Organization, IPCS.

NTP (National Toxicology Program) (1985). Toxicology and carcinogenesis studies of 1,2-dichlorobenzene (o-dichlorobenzene) in F344/N rats and B6C3F1 mice (gavage studies). NTP Technical Report No. 255, Publication No. 86-2511. United States Department of Health and Human Services, National Institute of Health.

NTP (National Toxicology Program) (1987). Toxicology and carcinogenesis gavage studies of 1,4-dichlorobenzene in F344/N rats and B6C3F1 mice. NTP, Technical Report Series No. 319, Publication No. 87-2575, National Institute of Health, Bethesda, United States.

USEPA Draft Method 502.1 (1986). Volatile halogenated organic compounds in water by purge and trap gas chromatography. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (ESML), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Dichloroethanes
1,1-dichloroethane
1,2-dichloroethane

(endorsed 1996)

GUIDELINE

1,1-dichloroethane: data are inadequate to set a drinking water guideline value.

1,2-dichloroethane: based on health considerations, the concentration in drinking water should not exceed 0.003 mg/L.

GENERAL DESCRIPTION

Dichloroethanes are present in some industrial effluent and have occasionally been found in drinking water supplies in the United States at concentrations below 0.006 mg/L.

The major use for 1,2-dichloroethane is in the production of vinyl chloride. It is also used in the production of other solvents, and can be used as a lead scavenger in petrol. 1,1-dichloroethane is used in the commercial production of 1,1,1-trichloroethane, as a solvent in paints, and as a varnish and finish remover.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Dichloroethanes have not been found in Australian drinking waters. They are included here to provide guidance in the unlikely event of contamination, and because they have been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

The dichloroethanes can be removed from drinking water using packed tower aeration, or by adsorption onto granular activated carbon.

MEASUREMENT

The dichloroethanes can be analysed by the purge and trap method (USEPA Method 502.1 1986). In this method an inert gas is bubbled through the sample and the dichloroethanes trapped on an adsorbent. The adsorbent is then heated and the dichloroethanes analysed using gas chromatography with electron capture detection. The limit of determination is approximately 0.0002 mg/L.

HEALTH CONSIDERATIONS

1,2-dichloroethane is absorbed through the lungs and gastrointestinal tract. Highest concentrations occur in the kidney and liver where it is metabolised to 2-chloroethanol. There are few data for 1,1-dichloroethane but it could be absorbed faster as it is more lipophilic (fat soluble).

An extensive review and summary of the human and animal toxicity data for 1,2-dichloroethane is available (IPCS 1987).

A number of cases of poisoning following consumption of high doses of 1,2-dichloroethane have been reported. While not all cases have been fatal, death is attributed to circulatory and respiratory failure.

1,1-dichloroethane has been used as an anaesthetic. Its use was discontinued because of problems associated with heart rhythm.

A 13-week inhalation study with 1,1-dichloroethane reported elevated blood-urea nitrogen concentrations in cats but not in rats, rabbits or guinea pigs. No other adverse effects were observed. A 78-week feeding study reported a marginally significant increase in the incidence of tumours of the mammary glands of female rats. No statistically significant increase in tumours was observed in male rats, or male and female mice. 1,1-dichloroethane has exhibited mutagenic activity in tests with bacteria and mammalian cells.

A 13-week feeding and drinking water study with 1,2-dichloroethane using rats and mice reported increased kidney and liver weights at high doses (4000 mg/L). No increase in the incidence of tumours or lesions was observed in mice or male rats, but female rats exhibited an increase in the incidence of kidney lesions.

A significant increase in tumours of the fore-stomach and circulatory system was reported in male rats fed 1,2-dichloroethane five times per week for 78 weeks. The same study reported tumours of the mammary glands in female rats. 1,2-dichloroethane has exhibited mutagenic activity in tests with different strains of bacteria, and metabolites are known to be strongly mutagenic.

The International Agency for Research on Cancer has concluded that 1,2-dichloroethane is possibly carcinogenic to humans (Group 2B, no data in humans but sufficient evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The assessment of the toxicological data of these compounds by the World Health Organization (WHO) has been used without review; however, the guideline value has been adjusted to a risk level of one in one million.

i) 1,1-dichloroethane

There are insufficient long-term data to set a health-based guideline value for 1,1-dichloroethane in drinking water.

ii) 1,2-dichloroethane

The guideline value for 1,2-dichloroethane in drinking water has been set at 0.003 mg/L. The WHO has conservatively calculated, using an extrapolation model based on a 78 week study in rats (NCI 1978), that consumption of water containing 0.003 mg/L of 1,2-dichloroethane would pose a lifetime risk of one additional cancer per million people.

The guideline value should be reviewed when more data are available.

The WHO guideline value of 0.03 mg/L was based on a calculation that estimated an additional lifetime risk of one fatal cancer per 100,000 people.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

IPCS (International Programme on Chemical Safety) (1987). 1,2-Dichloroethane. Environmental Health Criteria, 62. World Health Organization, IPCS.

NCI (National Cancer Institute) (1978). Bioassay of 1,2-dichloroethane for possible carcinogenicity. NCI, Department Health Education and Welfare, Washington DC, Report NCI-CG-TR-55.

USEPA Draft Method 502.1 (1986). Volatile halogenated organic compounds in water by purge and trap gas chromatography. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (ESML), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Dichloroethenes
1,1-dichloroethene (1,1-DCE)
1,2-dichloroethene (1,2-DCE)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentrations of dichloroethenes in drinking water should not exceed the following values:

1,1-dichloroethene	***0.03 mg/L***
1,2-dichloroethene	***0.06 mg/L***

GENERAL DESCRIPTION

Available data indicate that the dichloroethenes are rarely found in drinking water. Studies in the United States have very occasionally reported DCEs in groundwater, usually from wells heavily contaminated with other chlorinated solvents.

1,1-DCE is used as a chemical intermediate in the manufacture of chloroform and polyvinylidene (PVDE) polymers. 1,2-DCE is also used as an intermediate in the manufacture of chlorinated solvents, and as a solvent. It can occur as two isomers, the *cis* and *trans* forms.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

DCEs have not been found in Australian drinking waters. They are included here to provide guidance in the unlikely event of contamination, and because they have been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

The DCEs can be removed from drinking water by aeration, or by adsorption onto granular activated carbon.

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for analysis (USEPA Draft Method 502.1 1986). An inert gas is bubbled through the sample and the dichloroethenes trapped on an adsorbent. The adsorbent is then heated and the dichloroethenes analysed using gas chromatography with electron capture detection. The limit of determination is approximately 0.0002 mg/L.

HEALTH CONSIDERATIONS

The DCEs can be readily absorbed through the lungs and the gastrointestinal tract. They are distributed primarily to the liver and kidneys, and are metabolised to chloroacetic acid, chloroacetyl chloride, dichloroacetaldehyde and reactive epoxides.

In humans, exposure to high concentrations in air can lead to central nervous system depression. The DCEs have been used as anaesthetics.

NOTE: Important general information is contained in PART II, Chapter 6

A long-term study where rats were exposed to 1,1-DCE in their drinking water for 2 years reported minimal swelling to liver cells but no other adverse effects. No changes were observed in tissues taken from dogs after 97 days of exposure. 1,1-DCE induced tumours in mice in one inhalation study, but was not carcinogenic in other studies, including one drinking water study. It has exhibited some mutagenic activity in tests with bacteria but not with cultured mammalian cells.

The International Agency for Research on Cancer has concluded that 1,1-DCE is not classifiable as to its carcinogenicity (Group 3, evidence inadequate in humans and limited in animals) (IARC 1987).

No long-term data are available for 1,2-DCE; however, a 90-day immunotoxicity study with mice using the *trans* isomer reported increases in glutathione levels and aniline hydroxylase activity. No data are available on carcinogenicity bioassays with animals. The *cis* isomer, but not the *trans* isomer, has exhibited some mutagenic activity *in vivo* in tests with bacteria. Neither isomer induced chromosomal aberrations in hamster lung cells *in vitro*.

DERIVATION OF GUIDELINE

The assessment of the toxicological data of these compounds by the World Health Organization (WHO) has been used without review. The guideline values were determined as follows:

i) 1,1-dichloroethene

$$0.03 \text{ mg/L} = \frac{9 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 70.1}{2 \text{ L/day} \times 1000}$$

where:

- 9 mg/kg body weight per day is the lowest effect level based on a 2-year drinking water study using rats (Quast *et al.* 1983).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 because a lowest effect level was used instead of a no-effect level).

ii) 1,2-dichloroethene

$$0.06 \text{ mg/L} = \frac{17 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 17 mg/kg body weight per day is the no-effect level based on a 90-day drinking water study using mice (Barnes *et al.* 1985).
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for the less than lifetime study).
- other factors apply as above.

The WHO guideline value of 0.05 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

Barnes DW, Sanders VM, White KL, Shopp GM, Munson AE (1985). Toxicology of trans-1,2-dichloroethylene in the mouse. *Drug and Chemical Toxicology*, 8:373–392.

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

Quast JF, Humiston CG, Wade CE, Ballard J, Beyer JE, Schwetz RW, Norris JM (1983). A chronic toxicity and oncogenicity study in rats and subchronic toxicity study in dogs on ingested vinylidene chloride. *Fundamental and Applied Toxicology*, 3:55–62.

USEPA Draft Method 502.1 (1986). Volatile halogenated organic compounds in water by purge and trap gas chromatography. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (ESML), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Dichloromethane (methylene chloride)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of dichloromethane in drinking water should not exceed 0.004 mg/L.

GENERAL DESCRIPTION

Dichloromethane releases into the environment are substantial and widely dispersed. In overseas studies it has been found in the parts-per-trillion range in air and is a common contaminant of ground and surface waters, with higher concentrations found in groundwater. In surface waters it can volatilise into air and will degrade in the atmosphere.

Dichloromethane is a widely used organic solvent. It can be found in paints, insecticides, degreasing agents, cleaning fluids and paint strippers.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Dichloromethane has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

Dichloromethane concentrations in drinking water can be reduced using aeration, or by adsorption onto granular activated carbon.

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for analysis (USEPA Draft Method 502.1 1986). An inert gas is bubbled through the sample and dichloromethane trapped on an adsorbent. The adsorbent is then heated and dichloromethane analysed using gas chromatography with electron capture detection. The limit of determination is approximately 0.0003 mg/L.

HEALTH CONSIDERATIONS

Studies indicate that dichloromethane is completely absorbed after ingestion and distributed primarily to the liver. It is metabolised to carbon monoxide, carbon dioxide and formic acid.

An extensive review and summary of the human and animal toxicity data for dichloromethane is available (IPCS 1984).

Inhalation of high doses has induced narcosis in humans, and acute exposure has caused impairment of sensory and motor functions.

In animals, a 2-year drinking water study on rats reported some changes to the liver at doses from 52 mg/kg body weight per day. Studies have shown mice to be less sensitive than rats to the toxic effects of dichloromethane.

Epidemiological investigations have failed to demonstrate a correlation between dichloromethane exposure and increased cancer incidence.

Overall, carcinogenicity of dichloromethane given in water to rodents is borderline and not conclusive. By inhalation there is clear evidence of carcinogenicity in rodents (IARC 1987).

The International Agency for Research on Cancer has concluded that dichloromethane is possibly carcinogenic to humans (Group 2B, inadequate evidence in humans but sufficient evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline value for dichloromethane in drinking water of 0.004 mg/L was determined as follows:

$$0.004 \text{ mg/L} = \frac{6 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 5000}$$

where:

- 6 mg/kg body weight per day is the lowest effect level based on a 2-year drinking water study using rats (Serota *et al.* 1986).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 5000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations, 10 for genotoxicity and 5 for lowest effect level).

The World Health Organization guideline of 0.02 mg/L did not include a safety factor for the use of a lowest effect level. The need to use this additional factor arose after a statistical evaluation of the data in the referenced study indicating that the end point was a lowest effect level, not a no-effect level.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

IPCS (International Programme on Chemical Safety) (1984). Methylene chloride. Environmental Health Criteria, 32. World Health Organization, IPCS.

Serota DG, Thakur AK, Ulland BM, Kirschman JC, Brown NM, Coots RH, Morgareidge K (1986). A two-year drinking water study of dichloromethane in rodents: I. Rats. *Food and Chemical Toxicology*, 24:951–958.

USEPA Draft Method 502.1 (1986). Volatile halogenated organic compounds in water by purge and trap gas chromatography. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (ESML), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

1,3-Dichloropropene

(endorsed 2011)

GUIDELINE

Based on human health concerns, 1,3-dichloropropene in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

1,3-Dichloropropene (CAS 542-75-6) does not belong to a recognised class of chemicals. The commercial product is a mixture of the *cis* and *trans* isomers (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, 1,3-dichloropropene would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: 1,3-Dichloropropene is a nematocide for the control of soil pests including plant parasitic nematodes.

There are registered products that contain 1,3-dichloropropene in Australia. These products are intended for professional use only by authorised or licensed persons as a pre-plant soil fumigant. 1,3-dichloropropene is available as a concentrated solution to be applied in undiluted form using soil injection equipment, or in diluted form by drip irrigation, and applied as either a broadacre or row soil treatment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to 1,3-dichloropropene is contamination of water. No residues are expected in food.

Agricultural use of 1,3-dichloropropene may potentially lead to contamination of source waters through absorption into the soil moisture and subsequent leaching into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of 1,3-dichloropropene in Australian drinking waters have been identified. However, laboratory experiments indicate that leaching 1,3-dichloropropene residues through soil to water is likely to be significant (Guo *et al.* 2003). Therefore there is some risk of contamination of groundwaters in areas where 1,3-dichloropropene is applied to agricultural soils.

TREATMENT OF DRINKING WATER

No reports have been identified for the targeted treatment of 1,3-dichloropropene in drinking water supplies.

MEASUREMENT

Analysis of 1,3-dichloropropene by solid-phase micro-extraction followed by gas chromatography with electron capture detection has been reported, with a limit of quantitation of 0.5 μg/L (Fuster *et al.* 2005). Further optimisation of this approach has been reported to achieve method detection limits of 0.5 ng/L for cis-1,3-dichloropropene and 1.0 ng/L for trans-1,3-dichloropropene (Antelo *et al.* 2007). An on-line purge and trap gas chromatography mass spectrometry has been developed with a reported limit of quantitation of 0.1 μg/L (Frenich *et al.* 2009).

HISTORY OF THE HEALTH VALUES

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.

A health value has not previously been established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: 1,3-dichloropropene is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, and the metabolites are rapidly excreted in the urine, almost completely within 48 hours. The primary metabolite of 1,3-dichloropropene in the urine is N-acetyl-S-(3-chloroprop-2-enyl)cysteine.

Acute effects: 1,3-dichloropropene (both the *cis* isomer and a mixture of the *cis* and *trans* isomers) has moderate acute oral and dermal toxicity in rats, and is a skin sensitiser in guinea pigs.

Short-term effects: Short-term studies in mice and rats reported reduced bodyweight gain, decreased clinical chemistry parameters, hyperplasia of the gastric mucosa and decreased organ weights at 15 and 5 mg per kg body weight per day (mg/kg bw/day), respectively. At higher doses in mice, there was decreased vacuolation of the renal tubules at 175 mg/kg bw/day. In a short-term study in dogs, vomiting occurred at 10 mg/kg bw/day. The lowest overall no-observed-effect level (NOEL) was 3 mg/kg bw/day in rats.

Long-term effects: Two-year dietary studies in mice and rats reported reduced bodyweight gain, decreased serum triglycerides and decreased organ weights at 25 mg/kg bw/day and 12.5 mg/kg bw/day respectively. In rats, there was also an increased incidence of liver adenomas and hyperplasia of the gastric mucosa at 12.5 mg/kg bw/day. A 1-year dietary study in dogs reported anaemia, with increased haematopoiesis from 15 mg/kg bw/day. The lowest NOEL was 2.5 mg/kg bw/day in rats, mice and dogs.

Carcinogenicity: Tumour formation was observed in long-term studies in mice and rats. In rats, there was an increase in primary hepatocellular adenomas at 12.5 mg/kg bw/day, and squamous cell papillomas and some carcinomas of the forestomach at 50 mg/kg bw/day. In mice, there was an increase in bladder and lung tumours at 50 mg/kg bw/day. These effects occurred at doses well in excess of the likely level of human exposure through drinking water. In male mice exposed via inhalation to 60 ppm technical-grade 1,3-dichloropropene for 24 months, an increased incidence of bronchioalveolar adenomas was seen.

Genotoxicity: 1,3-dichloropropene was positive in some *in vitro* short-term assays but negative in most *in vivo* assays. Overall, it was not considered to be genotoxic.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: Reproduction studies and developmental toxicity studies via the inhalation route in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development. No dietary studies were available.

Poisons Schedule: 1,3-dichloropropene is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), with an Appendix J rider limiting availability to authorised or licensed persons. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for 1,3-dichloropropene was determined as follows:

$$0.1 \text{ mg/L} = \frac{2.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 1}{2 \text{ L/day} \times 1000}$$

where:

- 2.5 mg/kg bw/day is the NOEL based on long-term (1- and 2-year) studies in rats, mice and dogs.
- 70 kg is taken as the average weight of an adult.
- The proportionality factor is 1, since 1,3-dichoropropene has no residues in food and therefore the assumption is that 100% of the ADI (nominal in this case) will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation and an additional 10 for the uncertainty associated with the potential carcinogenic risk.

The World Health Organization has established a health-based guideline value of 0.02 mg/L for 1,3-dichloropropene in 1993 (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Dichlorprop/Dichlorprop-P

(endorsed 2011)

GUIDELINE

Based on human health concerns, dichlorprop in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Dichlorprop (CAS 7547-66-2/CAS 15165-67-0) is in the phenoxycarboxylic acid group of chemicals. Dichlorprop possesses a single asymmetric carbon and is a chiral molecule. Dichlorprop is a racemic mixture of stereoisomers and dichlorprop-P is the R-isomer of dichlorprop. Other pesticides in this group include 2,4-D, MCPA and mecoprop (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, dichlorprop would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate

inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Dichlorprop is a herbicide used for the control of weeds and as a plant growth regulator for citrus fruits.

There are registered product containing either dichlorprop (as the potassium salt) or dichlorprop-P (as the 2-ethylhexyl ester) in Australia. These are for professional use and applied by spray (backpack, boom spray or helicopter) to citrus fruits or non-crop areas. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to dichlorprop is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

There are few available data for dichlorprop in Australian drinking water. In Australian treated sewage, dichlorprop was below 0.5 µg/L (supporting data, NRMMC/EPHC/NHMRC 2008). In Canada, the maximum concentration in drinking water was 0.10 µg/L (Donald *et al.* 2007).

TREATMENT OF DRINKING WATER

Although no empirical data are currently available, it is likely that activated carbon would provide efficient removal based on its chemical structure.

MEASUREMENT

Dichlorprop in water can be analysed by gas chromatography with mass spectrometry, with a detection limit of 0.42 ng/L (Donald *et al*. 2007).

HISTORY OF THE HEALTH VALUES

The acceptable daily intake (ADI) for dichlorprop (R and S isomers) is 0.03 mg per kg of bodyweight (mg/kg bw), 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 and was established in 1998.

The ADI for dichlorprop-P is 0.03 mg/kg bw, 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 and was established in 2006.

An acute reference dose (ARfD) has not been set for dichlorprop. An acute reference dose (ARfD) of 0.20 mg/kg bw/day for dichlorprop-P was established based on a NOEL of 20 mg/kg bw/day from a developmental study in rats. The ARfD incorporates a safety factor of 100.

A health value has not been previously established by NHMRC for dichlorprop-P.

HEALTH CONSIDERATIONS

The toxicology data on dichlorprop-P largely form the basis for the public health standards for both of these chemicals.

Metabolism: Dichlorprop-P is rapidly and extensively absorbed via the gastrointestinal tract in rats. There is limited metabolism of dichlorprop and no evidence of tissue accumulation. It is largely excreted unchanged in the urine within 24-48 hours. Metabolism and toxicokinetic data are similar for the dichlorprop-P acid and 2-ethylhexylester forms.

Acute effects: Dichlorprop-P has low acute oral and dermal toxicity in rats. It is not a skin sensitiser.

Short-term effects: Short-term studies in mice reported effects on the liver and on blood cholesterol at very high dose levels only. Studies in rats and dogs also reported effects on the kidney and liver at high dose levels. Blood lipids were decreased in dogs at 17 mg/kg bw/day.

Long-term effects: Long-term dietary studies in mice and dogs reported the kidney as the main target organ. The lowest NOEL was 6 mg/kg bw/day in mice and this NOEL is the basis of the ADI.

Carcinogenicity: Based on long-term studies in mice, there is no evidence of carcinogenicity for dichlorprop-P.

Genotoxicity: Dichlorprop-P is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Neurotoxicity: In an oral single dose and a dietary repeat dose study in rats, there was no evidence of delayed neurotoxicity.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Dichlorprop and dichlorprop-P are included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for dichlorprop and dichlorprop-P was determined as follows:

$$0.1 \text{ mg/L} = \frac{6 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 200}$$

where:

- 6 mg/kg bw/day is the NOEL for dichlorprop-P based on a long-term (18-month) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 200 is a safety factor applied to the NOEL derived from a study conducted in animals. The safety factor incorporates a factor of 10 for interspecies extrapolation, a factor of 10 for intraspecies variation, and an additional factor of 2 for uncertainty in the toxicology database.

The World Health Organization has established a health-based guideline value of 0.1 mg/L for dichlorprop, in 1993 (WHO 2004).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Dichlorvos

(endorsed 2011)

GUIDELINE

Based on human health concerns, dichlorvos in drinking water should not exceed 0.005 mg/L.

RELATED CHEMICALS

Dichlorvos (CAS 62-73-7) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, including acephate, chlorpyrifos, diazinon, fenitrothion, profenofos and trichlorfon (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, dichlorvos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Dichlorvos is an insecticide and acaricide for the control of insects in a wide range of situations, including in domestic and public health situations, as well as in warehouses and storerooms and in animal houses. Dichlorvos is also used to control pests in a wide range of crops and is used as a veterinary anthelmintic.

There are registered products containing dichlorvos in Australia. These products are intended for professional and home garden use. The products used as insecticides are generally available as emulsifiable concentrates to be diluted and applied by spray. The veterinary products containing dichlorvos are formulated as an oral paste for veterinary use. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to dichlorvos are the use of home garden products and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of dichlorvos may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

The veterinary use of dichlorvos provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Dichlorvos has been routinely monitored by some water utilities in Australia. No detections above analytical limits of detection have been reported in the reviewed reports.

TREATMENT OF DRINKING WATER

Coagulation achieves only 10-20% removal of organophosphorus pesticides. Ozone treatment can achieve complete degradation of dichlorvos under experimental conditions (Liu *et al.* 2009). Kim *et al.* (2002) reported a complete reduction of dichlorvos (initial concentration of 220 mg/L) by batch treatment with ozone at 1 mg/L. Good photocatalytic degradation/oxidation of dichlorvos has been reported using ultraviolet (UV) irradiation (Lu 1994, Liu *et al.* 2009) and UV/titanium dioxide (Evgenidou *et al.* 2005, Senthilnathan *et al.* 2009). A challenger advanced oxidation process test using ozone and hydrogen peroxide was able to reduce by 49% the influent concentration of dichlorvos, and the combination of advance oxidation and activated carbon filter reduced dichlorvos by 99% (USEPA 2007).

Nanofiltration using different membranes gave 4–87% removal from a 1 mg/L solution; adsorption onto the membrane was an important contributor to removal (Ozaki *et al.* 2000). A concentration of 0.01 µg/L was reduced by 98–99% by different ultra-low reverse osmosis membranes (Hofman *et al.* 1998). Reverse osmosis challenger test with an initial concentration of 1300 µg/L was efficient in removing dichlorvos (95% removal) (USEPA 2005).

MEASUREMENT

Dichlorvos is included in the United States Environmental Protection Agency (USEPA) gas chromatographic Method 622. The extract is concentrated and analyzed by gas chromatography using a flame photometric or phosphorus/nitrogen detector (Pressley *et al.* 2002). Hollow fibre-liquid phase microextraction with gas chromatography by flame thermionic detection can achieve a limit of detection of 32 ng/L for dichorvos (Lambropoulou *et al.* 2005). Enzyme-linked immunosorbent assay (IC-ELISA) method can achieve a limit of quantitation of 0.048 µ/mL for dichlorvos (Tang *et al.* 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for dichlorvos is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.014 mg/kg bw/day from a short-term (28-day) human study. The NOEL is based on plasma cholinesterase inhibition. The ADI incorporates a safety factor of 10, and was established in 2004.

The previous ADI was 0.0005 mg/kg bw based on a NOEL of 0.05 mg/kg bw/day for cholinesterase inhibition in a dog study, and using a safety factor of 100.

The acute reference dose (ARfD) of 0.1 mg/kg bw for dichlorvos was established in 2004, 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 previous health value was 0.001 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Dichlorvos is readily absorbed from the gastrointestinal tract. It is extensively metabolised and rapidly excreted in the urine and as exhaled CO_2 within 24 hours.

Acute effects: Dichlorvos has moderate to high acute oral and dermal toxicity in rats. It is a skin sensitiser in both humans and guinea pigs.

NOTE: Important general information is contained in PART II, Chapter 6

Short-term effects: In a 28-day dietary study in humans, there was inhibition of plasma cholinesterase activity at 0.021 mg/kg bw/day. The NOEL of 0.014 mg/kg bw/day in humans is the basis for the current ADI.

Inhibition of plasma and red blood cell cholinesterase activity was reported at 0.9 mg/kg bw/day and above in a 90-day dietary study in dogs, and at 1.5 mg/kg bw/day in a 13-week oral study in rats.

Long-term effects: In a 2-year rat study, inhibition of plasma and red blood cell cholinesterase activity was reported from 2.3 mg/kg bw/day. In a 2-year dog study, inhibition of red blood cell cholinesterase activity in males was reported at 0.08 mg/kg bw/day and above.

Carcinogenicity: The weight of evidence from long-term studies in rodents indicates that dichlorvos is not carcinogenic.

Genotoxicity: Dichlorvos was positive in some *in vitro* short-term assays, but not genotoxic *in vivo*.

Reproductive and developmental effects: A 2-generation reproduction study in rats reported effects on reproductive parameters at high dose levels, which were well in excess of the likely human exposure levels. Developmental studies in mice, rats and rabbits did not produce any evidence of effects on foetal development.

Neurotoxicity: Short-term oral studies in chickens and rats did not report any evidence of delayed neurotoxicity.

Poisons Schedule: Dichlorvos is included in Schedules 5, 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.005 mg/L for dichlorvos was determined as follows:

$$0.005 \text{ mg/L} = \frac{0.014 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.014 mg/kg bw/day is the NOEL based on a short-term (28-day) study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from human studies to allow for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Diclofop-methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, diclofop-methyl in drinking water should not exceed 0.005 mg/L.

RELATED CHEMICALS

Diclofop-methyl (CAS 51338-27-3) belongs to the aryloxyphenoxy propionate and chlorophenoxy class of chemicals. Other pesticides in these classes include dichlorprop, fenoprop, 2,4-D, 2,4,5-T and MCPA (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, diclofop-methyl would not be a health concern unless the concentration exceeded 0.005 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Diclofop-methyl is used as a post-emergence herbicide for the control of grass weeds in turf and agricultural crops.

There are currently products registered in Australia that contain diclofop-methyl. All of these are intended for professional use and not for use in the home garden. Diclofop-methyl is available in concentrated solutions to be applied in diluted form using aircraft, ground sprayers or knapsack spray equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to diclofop-methyl and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of diclofop-methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of diclofop-methyl in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of diclofop in drinking water have been identified.

MEASUREMENT

Diclofop-methyl can be analysed in water by solid phase extraction followed by high performance liquid chromatography with diode array detection (Ozhan *et al*. 2005). The limit of detection for this method is 0.04 µg/L. Diclofop-methyl can also be analysed in environmental samples by gas chromatography–mass spectrometry (Tadeo *et al*. 1996).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for diclofop-methyl is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.25 mg/kg bw/day from a long-term study. The NOEL is based on liver toxicity observed in a 2-year study in mice. The ADI incorporates a safety factor of 100 and was established in 1986.

The previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Diclofop-methyl is readily absorbed via the gastrointestinal tract. It is extensively metabolised and is excreted in the urine and faeces, within 96 hours.

Acute effects: Diclofop-methyl has low oral acute toxicity and moderate acute dermal toxicity. It is a skin sensitiser.

Short-term effects: Medium-term dietary studies in rats and dogs reported increases in liver weight and enlargement of hepatocytes, in addition to changes in blood chemistry at dose levels of 1.5 mg/kg bw/day in rats and at 4 mg/kg bw/day in dogs. Fatty infiltration of the adrenal cortex was reported at high doses in dogs.

Long-term effects: Long-term dietary studies in mice, rats and dogs demonstrated the most sensitive toxic effects to be increased liver, heart and kidney weights in addition to increased serum alkaline phosphatase levels in the mouse, at dose levels of 0.8 mg/kg bw/day. Decreased bodyweight and liver pathology and changes in blood chemistry were observed at high doses in all species. The NOEL of 0.25 mg/kg bw in mice is the basis for the current ADI.

Carcinogenicity: Two-year studies in mice reported an increase in hepatocellular adenomas at 2.5 mg/kg bw/day, considered to be related to liver toxicity. In the absence of positive genotoxicity, these tumours were considered to be a threshold effect.***Genotoxicity:*** Diclofop-methyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rabbits showed no adverse effects on reproduction or development

Poisons Schedule: Diclofop-methyl is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.005 mg/L for diclofop-methyl was determined as follows:

$$0.005 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 200}$$

where:

- 0.25 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise rom the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 200 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation and 2 for uncertainty due to potential for tumour promotion.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Dicofol

(endorsed 2011)

GUIDELINE

Based on human health concerns, dicofol in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Dicofol (CAS 115-32-2) belongs to the organochlorine class of chemicals. Other previously used pesticides in this class include DDT, aldrin, dieldrin, chlordane and heptachlor (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, dicofol would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Dicofol is an acaricide for the control of mites in agricultural, veterinary, and household settings.

There are registered products containing dicofol in Australia. These are intended for professional and home garden use. Use patterns include ground spray onto plants and onto soil for professional use, and by hand-held spray for home garden use. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to dicofol are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of dicofol may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on dicofol in Australian waters. Dicofol has low solubility and a very high sorption coefficient (K_{oc}) and is expected to adsorb rapidly to sediments and suspended matters rather than be present in water, except in exceptional circumstances. For example, dicofol was found at concentrations up to 0.0025 mg/L at Orestimba Creek in the USA following agricultural spraying in the area (Domagalski *et al*. 1996).

TREATMENT OF DRINKING WATER

Dicofol has been shown to be completely removed when water undergoes conventional clarification (with alum), powdered activated carbon dosing, followed by oxidation with ozone (Ormad *et al.* 2008). Adsorption onto powdered activated carbon has been performed with a relatively moderate-high level of removal. Chlorination/ozonation for dicofol removal has also been reported with moderate success.

MEASUREMENT

Dicofol can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for dicofol is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.12 mg/kg bw/day from a 1-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 and was first established in 1990.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Dicofol is rapidly absorbed via the gastrointestinal tract with wide, uniform tissue distribution. It is slowly eliminated, mainly in the faeces, as benzophenone metabolites and de-chlorinated metabolites. Dicofol has a moderate potential for bioaccumulation in body fat.

Acute effects: Dicofol has moderate acute oral toxicity and low dermal toxicity. It is a skin sensitiser in guinea pigs.

Short-term and long-term effects: In short-term and long-term dietary studies in mice, rats and dogs, effects indicative of liver toxicity were reported in all species, and included changes in clinical chemistry parameters, enzyme levels and increased relative liver weight. Rats were the most sensitive species, with effects reported at dose levels of 0.7 mg/kg bw/day and above in a 3-month study and 2.5 mg/kg bw/day and above in a 2-year study. In dogs, pituitary toxicity in the form of cysts was noted at 0.72 mg/kg bw/day and above in a 1-year study. The lowest NOEL was 0.12 mg/kg bw/day and this is the basis of the ADI.

Carcinogenicity: Based on a long-term study in rats, there is no evidence of carcinogenicity for dicofol.

Genotoxicity: Dicofol is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A multigeneration reproduction study in rats and a developmental study in rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Dicofol is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.004 mg/L for dicofol was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.12 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.12 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Diflubenzuron

(endorsed 2011)

GUIDELINE

Based on human health concerns, diflubenzuron in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Diflubenzuron (CAS 35367-38-5) belongs to the benzoylurea class of chemicals. Other pesticides in this class include chlorfluazuron (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, diflubenzuron would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Diflubenzuron is an insecticide and a parasiticide for the control of blowfly and lice in cattle and sheep.

There are registered products that contain diflubenzuron in Australia. These products are intended for professional use and are available as topical solution/suspension formulations to be diluted and applied by dipping or hand jetting, or directly by pour-on along the midline of the back of sheep and cattle. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to diflubenzuron is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The veterinary use of diflubenzuron provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on diflubenzuron occurrence in Australian drinking water supplies were found. Exposure to diflubenzuron through drinking-water is expected to be negligible.

TREATMENT OF DRINKING WATER

No specific data on treatment for diflubenzuron have been found. However, the low aqueous solubility (0.08 mg/L) and relatively high log Kow of 3.7 suggest that it may be amenable to adsorption by activated carbon (WHO 2006). Reverse osmosis is also expected to be effective in removing diflurobenzuron, given its high molecular weight (310 g/mol).

MEASUREMENT

Diflubenzuron can be determined by high-performance liquid chromatography with ultraviolet detector. The method can achieve a limit of quantitation (LOQ) of 0.05 mg/L (Miliadis *et al.* 1999). A high-performance liquid chromatography with atmospheric pressure chemical ionisation and mass spectrometry method can achieve a LOQ of 0.025 mg/L (Barnes *et al.* 1995). Diflubenzuron in drinking water can also be determined by liquid chromatography with electrospray ionization and mass spectrometry, achieving a LOQ of 0.01 µg/L (Li *et al.* 2006). Automated solid-phase extraction and high-performance liquid chromatography with diode-array detection method can achieve a LOQ of 0.1 µg/L for diflubenzuron (Nouri *et al.* 1995). On-line pre-concentration method for the analysis of diflubenzuron in ground water samples using two C18 columns, and fluorescence detection after photochemical induced fluorescence post-column derivatization can achieve a LOQ of 0.01 µg/L (García *et al.* 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for diflubenzuron is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.0 mg/kg bw/day 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 and was established in 1985.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Diflubenzuron is relatively well absorbed from the gastrointestinal tract in rats (up to 50%). The two major metabolic routes are via hydroxylation of the aromatic rings (80%) and via scission of the ureido bridge (20%). Diflubenzuron is rapidly excreted in the urine and faeces, almost completely within 72 hours. There is no accumulation in body tissues.

Acute effects: Diflubenzuron has low acute oral and dermal toxicity. Its skin sensitisation potential has not been tested.

Short-term effects: Medium-term dietary studies were conducted in rats and dogs. In rats, there was an increase in relative adrenal weights and an increase in the incidence of necrotic foci in the liver at 2.5 mg/kg bw/day and above. Haematological changes indicative of anaemia were observed in males at 10 mg/kg bw/day. In dogs, methaemoglobin, sulfaemoglobin and spleen weights were elevated and there was evidence of liver toxicity at 6.6 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in rats and dogs. The 2-year rat study reported elevated methaemoglobin levels at 8 mg/kg bw/day. The 1-year dog study reported increased methaemoglobin and sulfaemoglobin levels, and increased pigmentation in macrophages and Kupffer cells of the liver at 10 mg/kg bw/day. Liver and spleen weights were significantly elevated at 50 and 250 mg/kg bw/day, respectively. The NOEL was 2 mg/kg bw/day in both the rat and dog studies, and is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for diflubenzuron.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: Diflubenzuron was positive in some *in vitro* short-term assays, but negative in all *in vivo* studies. Overall, it is not considered to be genotoxic.

Reproductive and developmental effects: 1-, 2- and 3-generation reproduction studies in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development. Maternotoxicity occurred only at dose levels well in excess of the likely human exposure level.

Poisons Schedule: Diflubenzuron is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for diflubenzuron was determined as follows:

$$0.07 \text{ mg/L} = \frac{2.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.0 mg/kg bw/day is the NOEL based on long-term dietary studies in rats (2-years) and dogs (1-year).
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Dimethoate

(endorsed 2011)

GUIDELINE

Based on human health concerns, dimethoate in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Dimethoate (CAS 60-51-5) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes acephate, chlorpyrifos, diazinon, dichlorvos, fenitrothion, omethoate, profenofos and trichlorfon (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, dimethoate would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Dimethoate is a broad use systemic insecticide and acaricide (miticide) for the control of insects and mites in the home garden and in agricultural crops.

There are registered products that contain dimethoate in Australia. These products are intended for professional and/or home garden use and are available in aerosol formulation or concentrated solutions. Agricultural products for professional use are intended for application as a dilute or concentrated spray using hand-held, ground boom, mist machine or aerial spray equipment, or application as a diluted seed dressing or concentrated pre-planting or post-harvest dip. Home garden products are intended for application as an aerosol spray or concentrated spray using hand-held equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to dimethoate are the use of home garden products and residues in food. Omethoate is an environmental degradant of dimethoate and thus the residue definition for dimethoate is “sum of dimethoate and omethoate, expressed as dimethoate”. Residue levels of dimethoate and omethoate in food produced according to good agricultural practice are generally low.

Agricultural use of dimethoate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on the occurrence of dimethoate in Australian waters could be found. In Canadian waters, dimethoate was not detected in drinking water (<0.6 µg/L) or in surface waters (<0.5 µg/L) (Health Canada 1986). The United States Environmental Protection Agency predicted surface water concentration after application is 0.44 to 33.4 µg/L, depending on use pattern (USEPA 2008).

TREATMENT OF DRINKING WATER

Dimethoate appears to be very well removed by chlorination but is likely to be transformed into omethoate in the process (Ormad *et al.* 2008). Activated carbon is partially effective for the removal of dimethoate (Ormad *et al*. 2008).

MEASUREMENT

Dimethoate can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for dimethoate is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day from a short-term (57-day) human volunteer study. The NOEL is based on cholinesterase inhibition. The ADI incorporates a safety factor of 10 and was established in 1988.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Since omethoate is an environmental degradant of dimethoate, the toxicity of omethoate needs to be considered in the context of the health impact of dimethoate in drinking water. A separate fact sheet is available for omethoate.

Metabolism: Dimethoate is well absorbed via the gastrointestinal tract and distributed rapidly to the tissues, accumulating in the liver and kidneys. It is slowly excreted as metabolites (85-91% of the dose within 5 days), primarily in the urine. The major metabolites were thiophosphate and phosphate esters, and omethoate (1-6%). The parent compound represented 1-2% of the excreted dose.

Acute effects: Dimethoate has moderate acute oral toxicity, and low acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: Short-term dietary studies in rats and dogs reported the main effect to be on the nervous system, with reduced erythrocyte and brain cholinesterase activity from the lowest dose of 2.48 mg/kg bw/day (rats) and 2.2 mg/kg bw/day (dogs). From 40 mg/kg bw/day, severe clinical signs consistent with cholinesterase inhibition were observed. In addition, increased mortality occurred in dogs at high doses.

Short-term (57-day) volunteer studies in humans reported inhibition of cholinesterase in whole blood at doses of 0.4 mg/kg bw/day and above. The NOEL from this study was 0.2 mg/kg bw/day and is the basis for the current ADI.

Long-term effects: Long-term dietary studies in mice, rats and dogs showed the most sensitive effects to be on the nervous system. In mice, erythrocyte cholinesterase inhibition was reported at 3.6 mg/kg bw/day and above. In rats, erythrocyte and brain cholinesterase were inhibited at 0.23 mg/kg bw/day and above. In dogs, brain and erythrocyte cholinesterase were inhibited at 0.125 mg/kg bw/day and above.

NOTE: Important general information is contained in PART II, Chapter 6

At higher dose levels, there were changes in haematological parameters and clinical chemistry, as well as organ weight changes. Clinical neurological signs consistent with cholinesterase inhibition were observed at 50 mg/kg bw/day.

Carcinogenicity: Based on long-term dietary studies in mice, rats and dogs, there was no evidence of carcinogenicity associated with dimethoate.

Genotoxicity: Dimethoate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A two-generation reproduction study in rats and developmental toxicity studies in rats and rabbits did not produce evidence of effects on reproductive parameters or foetal development. A developmental neurotoxicity study in rats reported increased post-natal mortality and cholinesterase inhibition in pups dosed *in utero* and post-natally at 0.5 mg/kg bw/day and above, in the absence of maternal toxicity. The NOEL from this study is 0.1 mg/kg bw/day. The potential effects of dimethoate on foetal development are the subject of a current review.

Poisons Schedule: Dimethoate is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for dimethoate was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a short-term (57-day) human volunteer study.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from human studies. This safety factor incorporates a factor of 10 for intraspecies (human) variation, with an additional safety factor of 10 to account for the uncertainty in the ADI (which is likely to be lower as a result of the current review).

The World Health Organization has a health-based guideline value of 0.006 mg/L for dimethoate (WHO 2004).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Diquat (ion), Diquat dibromide

(endorsed 2011)

GUIDELINE

Based on human health concerns, diquat in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Diquat (CAS 2764-72-9; 85-00-7) is a quaternary ammonium compound and belongs to the bipyridilium class of chemicals. The other pesticide in this class is paraquat (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, diquat would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Diquat is a contact herbicide for the control of aquatic weeds and weeds in agricultural crops. It is also used as a desiccant in seed crops and to clear weeds from bodies of water and sewerage systems.

There are currently products registered in Australia that contain diquat, mostly as diquat dibromide. Diquat products are intended for professional use and are available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to diquat and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The agricultural use of diquat involves direct application into water ways and sewerage systems, which may then enter source water for drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of diquat in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of diquat in drinking water have been identified.

MEASUREMENT

Diquat can be measured in drinking water by solid phase extraction followed by high performance liquid chromatography with mass spectrometry, with a method detection limit of 0.1 µg/L (Grey *et al.* 2002, Nunez *et al.* 2004, Rial-Otero *et al.* 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for diquat is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day from a long-term study. The NOEL is based on cataract formation in a 2-year rat dietary study. The ADI incorporates a safety factor of 100. It was established in 1985 and reaffirmed in 2002.

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 previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Diquat is poorly absorbed via the gastrointestinal tract. The absorbed fraction undergoes minimal metabolism before being rapidly excreted in the urine, almost completely within 48 hours.

Acute effects: Diquat has a high acute oral and dermal toxicity. It is a skin sensitiser in guinea-pigs. Human poisoning incidents indicate the lowest lethal dose to be 6 g. Doses greater than 12 g are usually fatal.

Short-term effects: A 4-week dietary study in rats reported decreased bodyweight gain and food consumption as well as clinical biochemistry changes at doses of 17 mg/kg bw/day.

In a 3-week dermal study, rats were treated with diquat up to 80 mg/kg bw/day. The reported effects were irritation and tissue destruction at the application site at dose levels of 5 mg/kg bw/day. Systemic effects included decreased bodyweight gain, hypothermia and emaciation at the highest dose. Treatment-related increases in mortality were evident at 40 mg/kg bw/day.

Medium-term dietary studies were conducted in rats and dogs. In rats, there was increased inflammation of the tongue and palate and effects on the kidney. Cataract formation was reported at doses above 8.9 mg/kg bw/day. In dogs, the reported dose-related effects were tongue lesions, decreased appetite and decreased bodyweight gain.

Long-term effects: Two-year dietary studies were conducted in mice, rats and dogs. In mice, there was decreased bodyweight gain at doses of 4.2 mg/kg bw/day. In rats, there were effects in the kidney at doses of 10.7 mg/kg bw/day. Cataract formation was increased in both in rats and dogs at doses of 1 mg/kg bw/day and 1.7 mg/kg bw/day, respectively. The NOEL of 0.2 mg/kg bw forms the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for diquat.

Genotoxicity studies: Diquat gave positive results in some *in vitro* short-term assays, but overall, it is not considered to be genotoxic.

NOTE: Important general information is contained in PART II, Chapter 6

Reproduction and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive effects or teratogenicity. There were effects on maternotoxicity and foetal development only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Diquat is included in Schedule 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE VALUE

The health-based guideline value of 0.007 mg/L for diquat was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for diquat based on the available evidence that the chemical is rarely found in drinking water, even though it may be used as an aquatic herbicide. A provisional guideline value of 0.01 mg/L was established based on the practical limit of detection in water (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Dissolved oxygen

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations, it is desirable that the dissolved oxygen concentration in drinking water be greater than 85% saturation.

No health-based guideline value has been set for dissolved oxygen.

GENERAL DESCRIPTION

Drinking water will generally contain an adequate concentration of dissolved oxygen; however, under some circumstances the oxygen concentration may be reduced. This may occur, for instance, where water has been drawn from deep storages, where there is considerable growth of microorganisms in a distribution system, or following prolonged periods of high water temperature.

Low oxygen concentrations or anoxic conditions enable nuisance anaerobic microorganisms to grow, producing by-products that affect the aesthetic quality of the water and increase corrosion of pipes and fittings.

There are a number of such nuisance microorganisms. Manganese-reducing bacteria produce black manganese deposits which can slough off pipes and soil laundry. Sulfate-reducing bacteria can produce hydrogen sulfide, giving drinking water a 'rotten egg' smell. Nitrate-reducing bacteria can produce nitrite. Iron-reducing bacteria can increase the concentration of ferrous ion in solution which will lead to the deposition of insoluble ferric salts when aeration is increased.

Localised pH changes associated with the growth of nuisance microorganisms can cause rapid corrosion in metal pipes.

Water from groundwater sources will generally have low oxygen concentrations and while this may cause no difficulties for most supplies, some supplies may need aeration to improve water quality (e.g. taste and odour).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies the dissolved oxygen concentration is generally greater than 85% saturation. Ground water supplies may have less dissolved oxygen.

TREATMENT OF DRINKING WATER

The dissolved oxygen concentration in drinking water can be increased by aeration or ozonation.

MEASUREMENT

The dissolved oxygen content of drinking water can be determined on site using an oxygen-sensitive membrane electrode (APHA Method 4500-O Part G 1992). Alternatively, the iodometric method (azide modification) can be used (APHA Method 4500-O Part C 1992).

HEALTH CONSIDERATIONS

There have been no direct health effects caused by low oxygen concentrations in drinking water. Indirect effects may result from the corrosion of fittings, which can give rise to higher concentrations of heavy metals such as lead, copper and cadmium, and by the anaerobic generation of hydrogen sulfide and nitrite.

DERIVATION OF GUIDELINE

The guideline value of more than 85% saturation is based on aesthetic considerations for taste, odour and prevention of corrosion of pipes and fittings. If the concentration is lower than 85%, an investigation should be carried out to determine the cause.

REFERENCES

APHA Method 4500-O Part C (1992). Oxygen: Azide modification. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

APHA Method 4500-O Part G (1992). Oxygen: Membrane electrode method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

NOTE: Important general information is contained in PART II, Chapter 6

Disulfoton

(endorsed 2011)

GUIDELINE

Based on human health concerns, disulfoton in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Disulfoton (CAS 298-04-4) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, including fenthion, parathion, profenofos and ethoprophos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, disulfoton would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Disulfoton is an insecticide and acaricide (miticide) for the control of pest infestations in food crops.

There is at currently at least one registered product containing disulfoton in Australia. Disulfoton products are intended for use by professionals and are available as a granular formulation. The use pattern is to apply the granule at or below the soil level to lucerne, cotton, potato, pea, and bean crops in agricultural settings. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to disulfoton is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of disulfoton may potentially lead to contamination of source waters through processes such as run-off or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Information of the presence of disulfoton in Australian waters was not found. In extensive surveys in the USA, disulfoton was not found in surface waters or groundwaters (US-NLM 2009).

TREATMENT OF DRINKING WATER

Disulfoton has been shown to be completely removed when water undergoes advanced oxidation with iron-catalysed ultraviolet irradiation and peroxide (Fenton reaction) (Huston and Pignatello 1999).

MEASUREMENT

Disulfoton is commonly analysed in Australian laboratories after solvent extraction and gas chromatographic determination using a nitrogen-phosphorus detector or mass selective detector. Typical limits of quantitation (LOQ) are 1 µg/L. The use of solid phase microextraction can permit lower LOQs, down to 0.1 µg/L (Queiroz *et al.* 2001).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for disulfoton is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.01 mg/kg bw/day from a 30-day dietary study in humans. This NOEL is based on inhibition of cholinesterase activity. The ADI incorporates a safety factor of 10, and was established in 1988.

The previous ADI set in 1969 was 0.002 mg/kg bw, based on studies reviewed by WHO.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Disulfoton is rapidly absorbed from the gastrointestinal tract, with wide, uniform tissue distribution. It is rapidly eliminated, mainly in the urine as sulfoxide and sulfone metabolites.

Acute effects: Disulfoton has high acute oral toxicity and low acute dermal toxicity. The potential for skin sensitisation is unknown.

Short-term and long-term effects: In a 30-day dietary study in humans, disulfoton administered at a dose of 0.01 mg/kg bw/day did not produce a reduction in cholinesterase activity. This NOEL is the basis for the ADI.

In short- and long-term studies in mice, rats and dogs, all reported reduced cholinesterase activity together with symptoms indicative of nervous system toxicity. In 3-month studies, these effects were observed at 0.65 mg/kg bw/day in mice and 0.12 mg/kg bw/day and above in rats.

In long-term studies in rats and dogs, these effects were observed at 0.12 mg/kg bw/day in rats and 0.06 mg/kg bw/day in dogs.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for disulfoton.

Genotoxicity: Disulfoton is not considered to be genotoxic, on the basis of *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A multigeneration reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or on foetal development. The only effect noted was decreased cholinesterase activity in parental animals at dose levels above 0.1 mg/kg bw/day.

Poisons Schedule: Disulfoton is included in Schedule 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.004 mg/L for disulfoton was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.01 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.01 mg/kg bw/day is the NOEL from a short-term (30-day) dietary study in humans. No cholinesterase inhibition was observed at this dose.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from the human study. The safety factor incorporates a factor of 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

US-NLM (United States National Library of Medicine (2019). Hazardous Substances Database. Available at https://www.nlm.nih.gov/databases/download/hsdb.html

Diuron

(endorsed 2011)

GUIDELINE

Based on human health concerns, diuron in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Diuron (CAS 330-54-1) belongs to the urea class of chemicals. Other pesticides in this class include fluometuron, linuron, methabenzthiazuron, siduron and tebuthiuron (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, diuron would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Diuron is a herbicide used for the control of broad-leaf weeds and grasses on a variety of crops including citrus, pineapple, cereals and sugar cane, as well as around buildings and public rights of way. It is also used as a defoliant on cotton, in marine antifouling paints and in ponds and aquariums to control algae.

There are registered products containing diuron in Australia. These are intended for professional and home garden use and contain diuron alone or in combination with other active ingredients. The products are generally available as suspension concentrates and water dispersible granules to be mixed with water and applied by aerial or ground sprayers. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to diuron are the use of home garden products, entry into treated public areas, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of diuron may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater, or through the discharge of treated aquarium or pond water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of diuron in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Diuron has been shown to be completely removed from water by chlorination when the chlorine dose is adjusted to match chlorine demand (Ormad *et al*. 2008). Ozonation and activated carbon adsorption for diuron removal has also been reported with high-moderate success (Bozkaya-Schrotter *et al*. 2008, Ormad *et al*. 2008). Advanced oxidation using ultraviolet irradiation and peroxide has been demonstrated to achieve a moderate level of diuron removal (Kruithof *et al*. 2002). Conventional coagulation/floculation has been shown to provide a relatively low removal rate (30%).

MEASUREMENT

Diuron can be measured in drinking water by solid phase extraction followed by high performance liquid chromatography with tandem mass spectrometry. The limit of quantitation for this method is typically 0.01 µg/L (QHFSS 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for diuron is 0.007 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.7 mg/kg bw/day 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 and it was established in 2005.

The previous ADI, established in 1987, was 0.006 mg/kg bw based on a NOEL of 0.6 mg/kg bw/day from a 2-year dog study. The NOEL was based on abnormal blood pigments (probably sulfaemoglobin).

The acute reference dose (ARfD) of 0.007 mg/kg bw/day for diuron was established in 2005, based on a NOEL of 0.7 mg/kg bw/day from a 6-month dietary study in rats, as indicated above. The ARfD incorporates a safety factor of 100.

The previous health value was 0.03 mg/L, with a note that this pesticide has either been detected on occasions in Australian drinking water or its likely use would indicate that it may occasionally be detected (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Diuron is rapidly and extensively absorbed from the gastrointestinal tract. It is efficiently metabolised and excreted within the first 24 hours. The main metabolites detected in blood and urine are 3-(3,4-dichlorophenyl)-1-methyl urea, 3-(3,4-dichlorophenyl) urea and 3,4-dichloroaniline.

Acute effects: Diuron has low acute oral and dermal toxicity in rats. It is not a skin sensitiser.

Short-term effects: Short-term dietary studies in rats reported changes to haematological parameters consistent with haemolytic anaemia at dose levels of 1.6 mg/kg bw/day in males and 1.8 mg/kg bw/day in females. Other effects included changes indicative of liver and kidney damage. The NOEL of 0.7 mg/kg bw/day in rats is the basis for the current ADI.

Long-term effects: Long-term dietary studies have been conducted on mice, rats and dogs. These studies reported findings of haemolytic anaemia at 3.1 mg/kg bw/day and above in a 2-year dog study. Other findings included liver enzyme level and organ weight increases and histological changes in liver, spleen and kidney, rats at 1 mg/kg bw/day and dogs at 7.5 mg/kg bw/day and above.

Carcinogenicity: The long-term study in rats reported an increased incidence of tumours in the bladder epitheliu; however, development of these tumours in rats appeared to be related to urinary pH changes as a result of feeding the rats a specific rat diet, rather than to diuron alone, and are therefore not considered to be relevant to humans.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: Diuron is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A reproduction study in rats with diuron reported no changes in reproductive parameters. Developmental toxicity studies in rats and rabbits reported decreased foetal bodyweight only at above maternotoxic dose levels.

Poisons Schedule: Diuron is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for diuron was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.7 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.7 mg/kg bw/day is the NOEL based on a medium-term (6-month) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

Bozkaya-Schrotter B, Daines C, Lescourret A, Bignon A, Breant P, Schrotter J (2008). Treatment of trace organics in membrane concentrates I: pesticide elimination, *Water Science Technology: Water Supply*, 8(2):223-230.

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NOTE: Important general information is contained in PART II, Chapter 6

2,2-DPA

(endorsed 2011)

GUIDELINE

Based on human health concerns, 2,2-DPA in drinking water should not exceed 0.5 mg/L.

RELATED CHEMICALS

2,2-DPA (2,2-dichloropropionic acid)(CAS 127-20-8) belongs to the class of halogenated aliphatic chemicals. Another pesticide in this class is iodomethane (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, 2,2-DPA would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking-water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: 2,2-DPA is a herbicide for the control of grasses and broad-leaf weeds in industrial sites, footpaths, domestic and public areas.

There are registered products that contain 2,2-DPA as its sodium salt in Australia. These products are intended for professional and home garden use. All are soluble powder formulations intended to be diluted and applied by hand spray or backpack spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to 2,2-DPA and its metabolites are the use of home garden products, and exposure from treated public places such as footpaths.

Use of 2,2-DPA in public spaces may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reported occurrences of 2,2-DPA in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No information regarding the effective treatment of 2,2-DPA in drinking water has been identified.

MEASUREMENT

2,2-DPA can be measured in drinking waters by liquid–liquid microextraction, acidic methanol derivatization, and gas chromatography–mass spectrometry. The reported method detection limit is 0.13 μg/L (Xie 2001).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for 2,2-DPA is 0.2 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 15 mg/kg bw/day from a long-term (2-year dietary) study. The NOEL is based on increased kidney weight in rats. The ADI incorporates a safety factor of 100 and it was established in 1989.

The previous health value was 0.5 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: 2,2-DPA is rapidly absorbed from the gastrointestinal tract in humans. Peak levels in blood are reached by 2 to 3 hours, and decrease with a half life of 2-3 days. Metabolism is limited, with the majority of the 2,2-DPA excreted unchanged in urine.

Acute effects: 2,2-DPA has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: Three-month dietary studies were conducted in rats and dogs. In rats, kidney weights were increased at doses of 50 mg/kg bw/day, and at higher doses there were effects on the liver. In dogs, there was no evidence of toxicity at doses up to 1000 mg/kg bw/day, however the study was of a poor quality.

Long-term effects: Long-term dietary studies in mice, rats and dogs reported increased kidney weights at 50 mg/kg bw/day and above. The lowest overall NOEL was 15 mg/kg bw/day in the rat study.

Carcinogenicity: Benign adenomas in lacrimal glands were noted in mice at 200 mg/kg bw/day, however, these tumours were not considered relevant to low-dose human exposure.

Reproductive and developmental effects: A 3-generation reproduction study in rats and a developmental study in rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Genotoxicity: 2,2-DPA is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Poisons Schedule: 2,2-DPA is considered not to require control by scheduling due to its low toxicity and is therefore in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.5 mg/L for 2,2-DPA was determined as follows:

$$0.5 \text{ mg/L} = \frac{15 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 15 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation. An additional safety factor is unnecessary.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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Xie Y (2001). Analyzing haloacetic acids using gas chromatography/mass spectrometry. *Water Research*, 35(6):1599-1602.

Endosulfan

(endorsed 2011)

GUIDELINE

Based on human health concerns, endosulfan in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Endosulfan (CAS 115-29-7) is in the cyclodiene organochlorine class of chemicals. The other pesticide in this class is trinexapac-ethyl (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, endosulfan would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Endosulfan is an insecticide used for the control a range of insects and mites on a broad spectrum of crops, as well as on cotton.

There are registered products containing endosulfan in Australia. The products are for professional use only and are available as emulsifiable concentrates to be diluted before use. Application is by aircraft, boom spray, or hand spray from the ground for crops other than cotton, and by aircraft for cotton crops. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to endosulfan is residues in food. The residue levels in food produced according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

There are few available data on endosulfan concentrations in Australian drinking water. Treated sewage in Australia contains less than 0.5 µg/L (supporting data, NRMMC/EPHC/NHMRC 2008). Internationally, endosulfan contamination does not appear to be widespread in the aquatic environment, but has been found in agricultural run-off and rivers in industrialised areas where it is manufactured or formulated (IPCS 1984). Endosulfan (one or both of its isomers) has been identified in 24 surface water samples and 103 groundwater samples collected from 164 hazardous waste sites in the USA. Surface water samples in the USA generally contain less than 1 µg/L (ATSDR 2000).

TREATMENT OF DRINKING WATER

Like many other pesticides, endosulfan is efficiently removed by activated charcoal (94% removal; Mishra and Patel 2007) and ozonation (94-97%; Yazgan and Kinaci 2003, Yazgan *et al*. 2003).

MEASUREMENT

The method of choice for the determination of endosulfan involves extraction from water with methylene chloride followed by gas chromatography combined with electron capture detection (WHO 2004a). In considering residue levels, the sum of the α- and β-somers plus the endosulfan sulfate metabolite, which is similar in toxicity to the parent compound, have to be considered. Detection limits are 0.015 µg/L for α-endosulfan, 0.024 µg/L for β-endosulfan and 0.015 µg/L for endosulfan sulfate (ATSDR 2000).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for endosulfan is 0.006 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.57 mg/kg bw/day 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 and was established in 1997.

The previous ADI, set in 1968, was 0.007 mg/kg bw, based on a NOEL of 0.7-0.75 mg/kg bw/day established in a 1-year dog dietary study, a 13-week rat dietary study, and rat reproduction and developmental studies, using a 100-fold safety factor.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Endosulfan is readily absorbed via the gastrointestinal tract and widely distributed in the body. It is extensively metabolised to sulfates and has a low potential for bioaccumulation. Excretion occurs mainly in faeces and is complete within 72 hours.

Acute effects: Endosulfan has a high acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In short-term dermal studies in rats, endosulfan produced inhibition of serum and brain acetylcholinesterase and mild liver changes at 9 mg/kg bw/day. In medium-term dietary studies in mice and rats, there was an increase in granular pigment formation in the proximal tubule cells and increased kidney weight at 3.9 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies were conducted in rodents and dogs. A 2-year rat study reported reduced bodyweight, an increased incidence of enlarged kidneys and blood vessel aneurysms, and marked progressive glomerulonephrosis at 2.9 mg/kg bw/day. A 1-year study in dogs reported decreased bodyweight gain at 0.75 mg/kg bw/day. The NOEL of 0.57 in rats and dogs is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for endosulfan.

Genotoxicity: Endosulfan is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A reproduction study in rats and developmental toxicity studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Endosulfan is included in Schedule 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010) depending on concentrations and use patterns. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for endosulfan was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.57 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.57 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variations.

The World Health Organization has not established a guideline value for endosulfan, because it occurs at concentrations well below those at which toxic effects are observed (WHO 2004b).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Endothal

(endorsed 2011)

GUIDELINE

Based on human health concerns, endothal in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Endothal (CAS 145-73-3) belongs to the dicarboxylic-acid class of chemicals. There are currently no other pesticides in this chemical class registered for use (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, endothal would not be a health concern unless the concentration exceeded 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 2-3 times higher than the health-based guideline. Therefore, excursions above this level even for a short period are of concern.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Endothal is a selective contact herbicide used for the control of winter grass in turf crops and lawns.

There are currently products registered in Australia that contain endothal, with both containing endothal as its di-potassium salt. Endothal products are intended for professional use on lawns. Products are liquid concentrates that are applied in diluted form using hand spray or boom spray equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to endothal and its metabolites s residues in foods such as potato and cotton seed oil. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of endothal may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

There are no published reports on endothal occurrence in Australian drinking water supplies.

TREATMENT OF DRINKING WATER

Endothal can be removed from drinking water using granular activated carbon.

MEASUREMENT

Endothal can be detected in drinking water using liquid-solid extraction followed by gas chromatography and electron capture detection, with a limit of detection (LOD) of 11.5 µg/L (EPA Method 548). Endothal has been analysed using derivatisation ion exchange extraction, acidic methanol methylation, and gas chromatography with mass spectrometry (GC/MS), with a LOD of 1.8 µg/L (EPA Method 548.1). Determination can be done using a flame ionisation detector instead of GC/MS, with a reported LOD of 0.7 µg/L (Hodgeson *et al.* 1992).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for endothal is 0.03 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 3.75 mg/kg bw/day from a long-term (1-year) study in dogs. This NOEL is based on liver necrosis and stomach hyperplasia and hyperkeratosis. The ADI incorporates a safety factor of 100 and was established in 1990.

The previous ADI for endothal was 0.1 mg/kg bw/day, established in 1977 and based on a NOEL of 10 mg/kg bw/day in a 2-year study in dogs and a 100-fold safety factor. This study was later found to be inadequate for regulatory purposes, and the ADI was amended in 1990.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Endothal is well absorbed via the gastrointestinal tract and widely distributed. Peak levels in blood are reached at 1 hour after dosing. Metabolism is limited and endothal is excreted unchanged in the urine within 48 hours (99% of total dose). A small amount of unidentified metabolites is excreted in the faeces.

Acute effects: The di-potassium salt of endothal has a moderate acute oral toxicity in rats and endothal itself has a high acute dermal toxicity in rabbits. No studies are available on the skin sensitisation potential of endothal.

Short-term effects: The main toxic effect of endothal in oral short-term toxicity studies was gastrointestinal toxicity. In dogs treated for 6 weeks there was significant gastrointestinal tract erosion at the lowest dose tested, 10 mg/kg bw/day. A NOEL was not obtained for this study. A NOEL of 50 mg/kg bw/day was obtained from a short-term (28-day) dietary study in rat. In this study, high mortality rates associated with gastrointestinal necrosis and overt signs of toxicity were seen at doses of 500 mg/kg bw/day.

Following repeated dermal application of endothal to rabbits, mortality with associated histological changes in skin, liver, and kidney resulted at the lowest dose of 50 mg/kg bw/day.

Long-term effects: In long-term toxicity studies, the main toxic effects are on the stomach and liver. Stomach hyperplasia and hyperkeratosis was seen at 7.5 mg/kg bw/day in rats and 25 mg/kg bw/day in dogs. Liver necrosis was observed at 11 mg/kg bw/day in dogs, and liver hyperplasia/adenoma and ovarian cysts at 15 mg/kg bw/day in rats. The lowest NOEL was 3.75 mg/kg bw/day in a 1-year study in dogs, and this is the basis for the current ADI.

Carcinogenicity: Based on long-term toxicity studies in rats, there is no evidence of carcinogenicity for endothal.

Genotoxicity: Endothal is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and mice did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Poisons Schedule: Endothal is in Schedules 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on the concentration and use pattern. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for endothal was determined as follows:

$$0.1 \text{ mg/L} = \frac{3.75 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 3.75 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dog.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Epichlorohydrin

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of epichlorohydrin in drinking water should not exceed 0.0005 mg/L.

GENERAL DESCRIPTION

Epichlorohydrin is used in the manufacture of glycerine and unmodified epoxy resins, including resins used in water treatment (polyelectrolytes). The United States Environmental Protection Agency has proposed that the maximum residual epichlorohydrin content in flocculating agent shall not exceed 0.01% which, at maximum resin usage rates of 20 mg/L, would lead to an epichlorohydrin concentration in drinking water of less than 0.002 mg/L. No monitoring of epichlorohydrin concentrations in drinking water has been reported. Epichlorohydrin hydrolyses in water and this can cause difficulties in detection.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Epichlorohydrin has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

No published reports are available on water treatment procedures for the removal of epichlorohydrin. Aeration is unlikely to be successful.

MEASUREMENT

Epichlorohydrin can be determined using gas chromatography with electron capture detection (Pesselman and Feit 1988). The limit of determination is approximately 0.05 mg/L.

HEALTH CONSIDERATIONS

In laboratory animals epichlorohydrin is rapidly absorbed after ingestion, inhalation and skin contact, and is distributed to the liver, kidneys and pancreas.

An extensive review and summary of the human and animal toxicity data for epichlorohydrin is available (IPCS 1984).

In humans, skin contact with high concentrations can cause initial redness, itching, or a burning sensation. The initial effects of inhalation are similar, and can be followed by vomiting and severe headache. Long-term exposure can cause kidney and liver damage. Epichlorohydrin has been reported to increase chromosome damage in lymphocytes, and decrease blood cell counts in occupationally exposed workers.

A long-term study where male rats were given epichlorohydrin in their drinking water for 81 weeks reported a decrease in leucocytes and an increase in the incidence of fore-stomach tumours from a dose of 39 mg/kg body weight per day and fore-stomach hyperplasia from 18 mg/kg body weight per day. A 2-year gavage study in rats, using doses of 2 and 10 mg/kg body weight per day, also reported induction of fore-stomach carcinomas. Inhalation studies in rats have reported the appearance of nasal cavity carcinomas.

Epichlorohydrin has been shown to be genotoxic both *in vitro* and *in vivo*. It is an alkylating agent and a direct-acting mutagen.

The International Agency for Research on Cancer has concluded that epichlorohydrin is probably carcinogenic to humans (Group 2A, insufficient evidence in humans, sufficient evidence in animals, and other supportive data) (IARC 1987).

DERIVATION OF GUIDELINE

The assessment of the toxicological data for epichlorohydrin by the World Health Organization (WHO) has been used without review. The guideline value of 0.0005 mg/L was determined as follows:

$$0.0005 \text{ mg/L} = \frac{2 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10{,}000} \times \frac{5}{7}$$

where:

- 2 mg/kg body weight per day is the lowest effect level based on a 2-year gavage study using rats (Wester *et al*. 1985).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 10,000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations, 10 because a lowest effect level was used instead of a no-effect level, and 10 for carcinogenic effects).
- 5/7 is used to convert data based on a 5 day per week feeding study to a 7-day week equivalent.

Although epichlorohydrin is a genotoxic carcinogen, the use of a linear multistage model for estimating cancer risk was considered inappropriate because tumours are seen only at the site of administration where epichlorohydrin is highly irritating.

The limit of determination is approximately 0.05 mg/L; however, concentrations in drinking water can be controlled by product specification.

The WHO guideline value of 0.0004 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

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NOTE: Important general information is contained in PART II, Chapter 6

EPTC

(endorsed 2011)

GUIDELINE

Based on human health concerns, EPTC in drinking water should not exceed 0.3 mg/L.

RELATED CHEMICALS

EPTC (S-ethyl-dipropylthiocarbamate)(CAS 759-94-4) belongs to the thiocarbamate class of chemicals. Other pesticides in this class include pebulate, thiobencarb, and butylate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, EPTC would not be a health concern unless the concentration exceeded 0.3 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: EPTC is a pre-emergent herbicide for the control of certain grasses and broad-leaf weeds in agricultural vegetable crops.

There is at least one registered product containing EPTC in Australia. EPTC products are intended for professional use and are available as a concentrated solution to be diluted and applied directly onto the soil using ground, and hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to EPTC and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of EPTC may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on EPTC occurrence in Australian drinking water supplies were found. In the USA, EPTC was not detected at or above the limit of quantitation (1 µg/L) in any of the 3,873 public water systems sampled (serving a total population of 226 million) (USEPA 2008).

TREATMENT OF DRINKING WATER

There is no evidence that EPTC is substantially removed by conventional treatments, such as coagulation/ flocculation, sedimentation, and inert media filtration (USEPA 2008). Rapid degradation of EPTC has been reported with ultraviolet (UV) light at 254 nm. EPTC-sulfoxide, EPTC-sulfone, propylamine and dipropylamine were detected as photoproducts of EPTC at 254 nm There was negligible degradation of EPTC at 290 nm UV light (Abu-Qare *et al*. 2002). EPTC also shows high reactivity during the ozonation and ozone/hydrogen peroxide advanced oxidation process (Chen *et al*. 2008). Granular activated carbon is also considered a good option for the removal of EPTC from drinking water. Carbamate pesticides can be removed with 85.7% efficiency using a cellulose acetate membrane, 79.6–93% efficiency using a polyamide membrane, and greater than 92.9% efficiency using a thin-film composite membrane. These results indicate that reverse osmosis is effective in removing EPTC from drinking water (USEPA 2008).

MEASUREMENT

A solid-phase microextraction (SPME) method in water samples determined by gas chromatography coupled with flame thermionic detection for the measurement of EPTC can achieve a limit of quantitation (LOQ) of 0.01 µg/L. SPME, gas chromatography and mass spectrometric detection achieved a LOQ of 0.02 µg/L (Lambropoulou *et al*. 2002). EPTC can be detected in drinking water by United States Environmental Protection Agency (USEPA) Methods 507 and 525.2. USEPA Method 507 relies on solvent extraction of EPTC and separation by gas chromatography with a nitrogen-phosphorus detector. The method can achieve a LOQ of 0.08 µg/L. USEPA Method 525.2 uses liquid-solid extraction and capillary column gas chromatography/ mass spectrometry. The method can achieve a LOQ for EPTC in the range of 0.05 to 0.12 µg/L (USEPA 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for EPTC is 0.09 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 9 mg/kg bw/day from a 2-year dietary study in rats. The NOEL is based on hindleg muscle atrophy and sciatic nerve demyelination at at 18 mg/kg bw/day. The ADI incorporates a safety factor of 100, and was established in 1995.

The previous ADI for EPTC of 0.01 mg/kg bw, based on a NOEL of 20 mg/kg bw/day from a long-term dietary study in mice with safety factor of 2000 to allow for the limited database, was set in 1970. The ADI was amended in 1995 after additional studies were submitted, including a long-term dietary study in rats demonstrating a lower overall NOEL.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: EPTC is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, mainly via sulfoxidation and ester hydrolysis. Excretion via the urine was essentially complete by 72 hours.

Acute effects: EPTC has low acute oral and dermal toxicity. It is a weak skin sensitiser in guinea pigs.

Short-term effects: In a 90-day dietary study in rats, there was decreased bodyweight gain and evidence of hepatocyte hypertrophy at the highest dose of 32 mg/kg bw/day. In a 16-week dietary study in dogs, there was hair loss at 22 mg/kg bw/day and decreased brain cholinesterase activity and changes to the gastric mucosa at 44 mg/kg bw/day.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: In a long-term (2-year) dietary study in rats, there was hindleg muscle atrophy, sciatic nerve demyelination, and increased serum AST at 18 mg/kg bw/day. Degenerative cardiomyopathy was seen at doses of 36 mg/kg bw/day and above. The NOEL was 9 mg/kg bw/day, and this is the basis for the current ADI.

Carcinogenicity: Based on a 2-year study in rats, there is no evidence of carcinogenicity for EPTC at doses up to 20 mg/kg/day.

Genotoxicity: EPTC is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study and a developmental toxicity study in rats did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: Hens dosed twice at a 21-day interval with oral doses of 7200 mg/kg bw EPTC did not exhibit any delayed neurotoxicity.

Poisons Schedule: EPTC is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.3 mg/L for EPTC was determined as follows:

$$0.3 \text{ mg/L} = \frac{9 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 9 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Esfenvalerate

(endorsed 2011)

GUIDELINE

Based on human health concerns, esfenvalerate in drinking water should not exceed 0.03 mg/L.

RELATED CHEMICALS

Esfenvalerate (CAS 66230-04-4) belongs to the pyrethroid class of chemicals. This is a large chemical group and includes fenvalerate, cyfluthrin, permethrin and flucythrinate.

There are four optical isomers of esfenvalerate and fenvalerate (SS, SR, RS, RR). The SS isomer is responsible for the insecticidal activity of these compounds. Fenvalerate contains around 20% as the SS form while esfenvalerate is highly enriched in this form. Most of the toxicity of fenvalerate is caused by the RS isomer (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, esfenvalerate would not be a health concern unless the concentration exceeded 0.03 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Esfenvalerate is an insecticide for the control of ants, cockroaches, fleas, spiders and other insect pests in domestic and industrial areas, and in field and pasture crops.

There are registered products that contain esfenvalerate in Australia. These products are intended for professional and domestic use. These products are available for use in domestic and industrial areas as hand and ground sprays; or for use on crops using ground and aerial sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to esfenvalerate are the use of domestic products, and residues in food. Esfenvalerate residues are grouped with those of fenvalerate in the maximum residue limit definition. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of esfenvalerate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Esfenvalerate has been monitored but not detected in Australian drinking water supplies (Muschal 2001). In the Goulburn Murray irrigation area esfenvalerate was detected on one occasion at 65 µg/L in 2005 (Victoria Department of Primary Industries 2006).

TREATMENT OF DRINKING WATER

No specific data on the treatment of esfenvalerate in drinking water have been identified.

MEASUREMENT

Esfenvalerate can be measured by liquid/liquid extraction followed by gas chromatography coupled with an electron capture detector. The method can achieve a limit of detection (LOD) of 0.05 µg/L. High-performance liquid chromatography or gas-liquid chromatography with either electron capture detection or electrolytic conductivity detection has been reported for the quantitation of esfenvalerate (Hengel *et al*. 1997). Solid-phase extraction followed by enzyme linked immunosorbert assay can achieve a LOD of 0.1 µg/L for esfenvalerate in water samples (Shan *et al*. 1999).

Trace levels of esfenvalerate in water can be measured by stir-bar-sorptive extraction followed by liquid desorption and large-volume injection capillary gas chromatography with mass spectrometric detection. This method can achieve a LOD of 2.5 ng/L (Serodio and Nogueira 2005). Gas chromatography/electron capture detector and gas chromatography / nitrogen-phosphorous detector methods can achieve a LOD of esfenvalerate below 2 ng/L (Wang *et al*. 2009).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for esfenvalerate is 0.008 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 7.5 mg/kg bw/day from a medium-term (13-week) dietary study in rats. The NOEL is based on clinical toxicity including abnormal behaviour and parotid salivary gland cell hypertrophy at 35 mg/kg bw/day. The ADI incorporates a safety factor of 1000 and was established in 1993.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Esfenvalerate is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, and is readily excreted in the urine, almost completely within 48 hours.

Acute effects: Esfenvalerate has moderate acute oral and dermal toxicity in rats. It is not a skin sensitiser.

Short-term effects: In a 4-week study in mice, there were signs of neurotoxicity in the form of tremors and excessive salivation at 35 mg/kg bw/day, and convulsions and gait abnormalities at 105 mg/kg bw/day.

In a 90-day feeding study in mice, there was decreased bodyweight gain and haematological changes at 30 mg/kg bw/day, and tremors and convulsions at 100 mg/kg bw/day. In a 13-week feeding study in rats, tremors, unsteady movements and convulsions were observed at 15 mg/kg bw/day. Cellular hypertrophy was observed in the parotid salivary glands and in the pituitary glands at 25 mg/kg bw/day. The lowest NOEL was 7.5 mg/kg bw/day in the rat study. This NOEL is the basis for the current ADI.

Long-term effects: Long-term toxicity studies have not been conducted in rodents with esfenvalerate, and were considered unnecessary given the available data on the closely-related fenvalerate (see the fenvalerate fact sheet).

NOTE: Important general information is contained in PART II, Chapter 6

Carcinogenicity: Esfenvalerate is not considered to be carcinogenic, based on the results of long-term toxicity studies in rodents with fenvalerate.

Genotoxicity: Esfenvalerate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Reproductive and developmental toxicity studies with esfenvalerate have not been conducted. There are no reproductive or developmental concerns based on studies with fenvalerate.

Neurotoxicity: Esfenvalerate did not cause delayed neurotoxicity in special oral dosing studies in rats.

Poisons Schedule: Esfenvalerate is included in Schedule 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010) depending on concentration. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.03 mg/L for esfenvalerate was determined as follows:

$$0.03 \text{ mg/L} = \frac{7.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 7.5 mg/kg bw/day is the NOEL based on a medium-term (13-week) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates factors of 10 for interspecies extrapolation, 10 for intraspecies variation, and an additional 10 for the lack of long-term studies.

Note: This calculated health-based guideline exceeds the normal aqueous solubility of esfenvalerate.

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NOTE: Important general information is contained in PART II, Chapter 6

Ethion

(endorsed 2011)

GUIDELINE

Based on human health concerns, ethion in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Ethion (CAS 563-12-2) is in the organophosphate class of chemicals. There are many other pesticides in this class, including diazinon, dichlorvos, fenthion, parathion and profenofos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, ethion would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Ethion is an insecticide used for the control of cotton worm in agricultural settings, and for controlling mites and fleas in cattle.

There are registered products containing ethion in Australia. These include an emulsifiable concentrate to be diluted and sprayed on cotton, used as ground and aerial sprays; and topical solutions/suspensions used as cattle dips/sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to ethion is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of sources waters through processes such as run-off, spray-drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of ethion in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of ethion in drinking water have been identified.

MEASUREMENT

Ethion can be measured in natural waters using headspace solid-phase microextraction followed by gas chromatography with flame thermionic or mass spectrometric detection. The practical limit of quantitation for this technique is 0.04 µg/L (Lambropoulou and Albanis 2001, Wang *et al*. 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for ethion is 0.0013 mg per kg of bodyweight (mg/kg bw), based on no-observed-effect levels (NOEL) of 0.13 mg/kg bw/day from a 2-year rat dietary study and 0.1 mg/kg bw/day from a 3-generation rat study. In both cases, the NOEL was based on decreased cholinesterase activity. The current ADI incorporates a safety factor of 100 and was established in 1987.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Ethion is rapidly absorbed from the gastrointestinal tract and widely distributed in the body. It is rapidly metabolised to monoxons, dioxons, conjugates and numerous polar compounds, and has low potential for bioaccumulation. It is rapidly eliminated, mainly in the urine and to a minor extent in faeces.

Acute effects: Ethion has high acute oral and dermal toxicity. Symptoms of acute poisoning are indicative of central and peripheral nervous system poisoning and included hyperexcitability, salivation, broncoconstriction, headache, vomiting and other behavioural changes. The effects are dose-related and reversible. Ethion is not a skin sensitiser.

Short-term effects: Short-term and long-term dietary studies in rodents and dogs resulted in symptoms indicative of nervous system toxicity. Decreased cholinesterase activity was observed in serum and brain at dose levels above 0.46 mg/kg bw/day in mice and 1.8 mg/kg bw/day in rats.

Long-term effects: A long-term (2-year) dietary study in rats reported decreased serum cholinesterase. The NOEL was 0.13 mg/kg bw/day, and is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for ethion.

Genotoxicity: Ethion showed no evidence of genotoxicity in *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In reproduction studies in rats and developmental studies in rats and rabbits, there was no evidence of effects on reproductive parameters or on foetal development, but serum cholinesterase was decreased at dose levels above 0.1 mg/kg bw/day.

Poisons Schedule: Ethion is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.004 mg/L for ethion was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.1 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 0.1 mg/kg bw/day is the NOEL based on decreased serum cholinesterase levels in a 3-generation study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies variation and 10 for intraspecies extrapolation.

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NOTE: Important general information is contained in PART II, Chapter 6

Ethoprophos

(endorsed 2011)

GUIDELINE

Based on human health concerns, ethoprophos in drinking water should not exceed 0.001 mg/L.

RELATED CHEMICALS

Ethoprophos (CAS 13194-48-1) belongs to the organothiophosphate class of chemicals. Other pesticides in this class include terbufos, chlorpyrifos, dimethoate, and ethion (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, ethoprophos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Ethoprophos is a nematocide and insecticide for the control of root nematodes in agricultural crops including bananas, cereals and tobacco, and for the control of certain grubs in sugar cane and maize.

There are currently no products registered in Australia that contain ethoprophos, but de-registered compounds may still be detected in water. Previously registered products containing ethoprophos were intended for professional use only. These products were granular formulations applied directly to the soil to control root nematodes or were diluted and applied by hand spray for the control of grubs.

Exposure sources: The main sources of public exposure to ethoprophos and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of ethoprophos in the future may potentially lead to contamination of source waters through processes such as run-off or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of ethoprophos in Australian drinking waters have been identified. It is rarely detected in drinking or environmental waters in overseas countries. When it has occasionally been reported, levels are extremely low; for example, a time-weighted annual concentration in source waters in several USA states of 0.002 ppb and a maximum concentration of 0.012 ppb.

TREATMENT OF DRINKING WATER

No specific data on the treatment of ethoprophos in drinking water have been identified.

MEASUREMENT

Residue determination of ethoprophos is amenable to multiresidue procedures using solvent extraction with dichloromethane followed by gas chromatography with nitrogen-phosphorous detection. Limits of detection are as low as 0.01 µg/L using this technique.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for ethoprophos is 0.0003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.025 mg/kg bw/day from a long-term study. The NOEL is based on decreased erythrocyte cholinesterase activity in a 1-year dietary toxicity study in dogs. The ADI incorporates a safety factor of 100 and was established in 1988.

The previous ADI for ethoprophos was 0.0001 mg/kg bw/day, based on the same NOEL but with a safety factor of 200, due to reporting deficiencies. The ADI was amended after submission of additional information on the study.

The previous health value was 0.001 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Ethoprophos is rapidly absorbed via the gastrointestinal tract and and widely distributed in the tissues of rats. Metabolism is extensive and excretion of phosphorothioic acid and related esters is mainly through urine, but is incomplete by 7 days, with 1.7–3.5% of total dose remaining in tissues

Acute effects: Ethoprophos has high acute oral toxicity and moderate to high acute dermal toxicity. It is a skin sensitiser in guinea-pig tests.

Short-term effects: In both oral and dermal short-term studies from 3 to 6 weeks in rats, rabbits and dogs, the major effect reported was a decrease in chlolinesterase activity at 0.05 mg/kg bw/day and above. In dietary studies from 3-5 months in the rat and dog, there was a decrease in brain, plasma and erythrocyte cholinesterase levels and elevation of adrenal weights (rat) at 0.025 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies in mice, rats, and dogs reported decreases in erythrocyte cholinesterase activity in all species; the lowest dose was 1 mg/kg bw/day in the dog. Decreased brain and plasma cholinesterase activity and reduced haemoglobin levels were seen at higher doses in all species. The lowest overall NOEL was 0.025 mg/kg/day, based on a decrease in erythrocyte cholinesterase activity in dogs. This NOEL is the basis for the current ADI.

Carcinogenicity: Based on an 18-month study in mice and a 2-year study in rats, there is no evidence of carcinogenicity for ethoprophos.

Genotoxicity: Ethoprophos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Poisons Schedule: Ethoprophos is included in Schedule 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.001 mg/L for ethoprophos was determined as follows:

$$0.001 \text{ mg/L} = \frac{0.025 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.025 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Ethylbenzene [CASRN 100-41-4]

(endorsed 2013)

GUIDELINE

Based on aesthetic considerations (taste and odour), the concentration of ethylbenzene in drinking water should not exceed 0.003 mg/L.

Based on health considerations the concentration of ethylbenzene in drinking water should not exceed 0.3 mg/L.

GENERAL DESCRIPTION

Ethylbenzene is a clear colourless liquid, which occurs naturally as a component of crude oil. It constitutes approximately 1-2% of unleaded gasoline by volume.

Ethylbenzene is produced commercially by the alkylation of benzene with ethylene, and by fractionation of petroleum. It is a major component of commercial xylene and is used commercially in paints, insecticides, blends of petrol, and in the production of styrene. It can also be found as a constituent of asphalt and naphtha.

Ethylbenzene has a taste and odour threshold of 0.003 mg/L.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Ethylbenzene has only rarely been identified in Australian drinking waters. Natural concentrations in most water sources are usually very low. Ethylbenzene can occur naturally in groundwater as a result of proximity to, or contact with, coal seams, petroleum and gas deposits, and shales. It may be mobilised by extraction activities (Lesage *et al.*, 1997; Leusch and Bartkow, 2011; Volk *et al*, 2011). However, contamination can occur, usually via exposure to petrochemicals in surface waters or groundwater. Known sources of groundwater contamination include leakage from sub-surface fuel storage tanks (do Rego & Netto, 2007). Emissions of fuel components from boating use is a known source of contamination of multiple-use lakes and reservoirs (Schmidt *et al.*, 2004). Ethylbenzene is generally not detected in groundwater (<0.001 mg/L), but concentrations in contaminated groundwater in the USA were as high as 2 mg/L (IPCS, 1996). Ethylbenzene has been reported at up to 0.000 2 mg/L in municipal drinking water in Croatia (Karaconji *et al.*, 2006), up to 0.011 mg/L in municipal drinking water in Taiwan (Kuo *et al.*, 1997) and is occasionally detected in drinking waters in the USA (Williams *et al.*, 2004) at concentrations up to 0.002 mg/L (ATSDR, 2010). Concentrations in Canadian drinking water ranged from <0.001 - 0.01 mg/L (IPCS, 1996).

TREATMENT OF DRINKING WATER

Volatile organic chemicals such as ethylbenzene are most commonly treated in drinking water by aeration stripping and/or adsorption to granular activated carbon (GAC). A conventional biologically active sand filter has been shown to be highly effective for the removal of ethylbenzene from contaminated water, under suitable conditions (Arvin *et al.*, 2004). Effective bioremediation of highly contaminated groundwaters has also been demonstrated (Sedran *et al.*, 2004; Zein *et al.*, 2006).

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for the analysis of ethylbenzene (APHA, AWWA & WEF, 2012). An inert gas is bubbled through the sample and ethylbenzene is trapped on an adsorbent. The adsorbent is then heated and ethylbenzene analysed using gas chromatography with

mass spectrometric (GC-MS) detection (Method 6200 B) or photoionisation (PI) detection (Method 6200 C) (APHA, AWWA & WEF, 2012). The method detection limit is 32 ng/L for GC-MS and 28 ng/L for GC-PI (APHA, AWWA & WEF, 2012).

HEALTH CONSIDERATIONS

Ethylbenzene is readily absorbed from the human gastrointestinal tract. It can be stored in fat and is metabolised to mandelic and phenylglyoxalic acids and excreted in the urine. It can cross the placenta.

No data are available on the health effects in humans after oral exposure, and inhalation data are limited to short term studies.

A 6 month gavage study using rats reported enlargement of the liver and kidney at high doses (400 mg/kg body weight per day) (Wolf *et al*., 1956). Mellert *et al.* (2007) also reported liver and kidney related impacts in addition to hepatocyte hypertrophy from 4 and 13 week gavage studies using rats at doses above 75 mg/kg bw/day. No longer-term studies are available.

Studies on the mutagenic activity of ethylbenzene to bacteria, insects and mammalian cells have reported negative results.

Ethylbenzene is classified as Group 2B (possibly carcinogenic to humans) by the International Agency for Research on Cancer (IARC, 2000).

DERIVATION OF GUIDELINE

The USEPA (2009) has set a drinking water guideline of 0.7 mg/L for ethylbenzene, while the WHO (2011) proposes a guideline of 0.3 mg/L.

The health-based guideline value for ethylbenzene in drinking water was determined as follows:

$$0.3 \text{ mg/L} = \frac{75 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

Where:

- 75 mg/kg body weight per day is the no effect level based on a 4 and 13 week gavage study using rats (Mellert *et al*. 2007).
- 70 kg is the average weight of an adult
- 0.1 is the proportion of total daily intake attributable to the consumption of water
- 2 L/day is the average amount of water consumed by an adult
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for the limited data and short duration of the study)

This health-based value exceeds the taste and odour threshold of 0.003 mg/L for ethylbenzene in water.

The WHO drinking water guideline value is the same (0.3 mg/L) but is based on a no effect level of 136 mg/kg bw/d for hepatoxicity and nephrotoxicity in a limited 6-month study with rats (WHO, 2011).

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NOTE: Important general information is contained in PART II, Chapter 6

Ethylenediamine tetraacetic acid (EDTA)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of ethylenediamine tetraacetic acid in drinking water (as the free acid) should not exceed 0.25 mg/L.

GENERAL DESCRIPTION

EDTA is a metal-complexing agent and may act to mobilise some heavy metals in the environment. It has occasionally been detected in drinking water supplies overseas at concentrations of up to 0.9 mg/L, but usually less than 0.1 mg/L.

EDTA is used widely in industry and agriculture. It is used in laundry detergents, water softening, electroplating, textile and paper production, as a food additive, and in cosmetics. Most of these uses will result in the release of EDTA to the aquatic environment. It is also used as a drug in chelation therapy, particularly in cases involving lead poisoning.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

EDTA has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

There are no published reports on methods for the removal of EDTA from drinking water, although it may be oxidised by ozone.

MEASUREMENT

EDTA can be analysed by potentiometric stripping analysis (Fayyad *et al*. 1988). The limit of determination is 0.001 mg/L.

HEALTH CONSIDERATIONS

EDTA is poorly absorbed in the gut and does not form any significant metabolites. It does not accumulate in the body.

There is considerable clinical experience in the use of EDTA for the treatment of heavy metal poisoning.

Long-term feeding studies with rats and dogs reported no interference to mineral metabolism. Results from other studies have been affected by the formation of zinc complexes in the gastrointestinal tract, which prevents the zinc from being absorbed.

DERIVATION OF GUIDELINE

The guideline value for EDTA (as the free acid) in drinking water was determined as follows:

$$0.25 \text{ mg/L} = \frac{1.9 \text{ mg/kg body weight per day} \times 13 \text{ kg} \times 0.1}{1 \text{ L/day} \times 10}$$

where:

- 1.9 mg/kg body weight per day is the amount of EDTA that can be consumed from all sources per day without adverse effects (WHO 2003).
- 13 kg is the average weight of a child at 2 years of age (this value was used because of the possibility of complexation of zinc, an essential element for humans, and the need to protect the most sensitive group).
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 1 L/day is the average amount of water consumed by a 2-year-old child.
- 10 is a safety factor to reflect the fact that the data for EDTA are relatively old (the World Health Organization assessment was dated 1974), and concern over zinc complexation.

The World Health Organization guideline value of 0.2 mg/L was based on a child body weight of 10 kg. The difference in guideline values is not significant.

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NOTE: Important general information is contained in PART II, Chapter 6

Etridiazole

(endorsed 2011)

GUIDELINE

Based on human health concerns, etridiazole in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Etridiazole (CAS 2593-15-9) belongs to the thiazole fungicide class of chemicals. Other pesticides in this class include thiabendazole (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, etridiazole would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Etridiazole is a broad-spectrum fungicide used for the control of fungi contamination on seeds, roots and stems in turf crops, non fruit-bearing young trees, cotton and ornamental flower crops.

There are currently products registered in Australia that contain etridiazole. These products are intended for professional use. They are applied by spraying or direct incorporation into soil for cotton, non-food producing trees, turf, or ornamental flower crops. They are available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to etridiazole and its metabolites is through residues on treated non-food crops, such as turf and flowers. Residue levels in crops produced according to good agricultural practice are generally low.

Agricultural use of etridiazole may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on etridiazole occurrence in Australian drinking water supplies were found. Estimated concentrations in groundwater from typical use of etridiazole on golf courses indicate that levels in groundwater are not likely to exceed 0.93 µg/L, and in surface water are not likely to exceed 32.3 µg/L for long-term exposure. Both these estimated concentrations are below guideline values indicating low concern (USEPA 2000).

TREATMENT OF DRINKING WATER

No specific data on the treatment of etridiazole in drinking water have been identified.

MEASUREMENT

Etridiazole can be determined by solid-phase extraction followed by gas chromatography–mass spectrometry (USEPA Method 525.2). Typical limit of quantitation (LOQ) is 0.1 µg/L (Munch 1995). Continuous flow micro-extraction combined with high-performance liquid chromatography and ultraviolet detection can achieve a LOQ of <4 ng/mL (He *et al*. 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for etridiazole is 0.03 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.9 mg/kg bw/day from a long-term (1-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 and it was established in 1991. Before this, no ADI for etridiazole had been set in Australia.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Etridiazole is rapidly absorbed from the gastrointestinal tract, followed by wide tissue distribution, including body fat. It is extensively metabolised, with most of the compound excreted rapidly in urine as metabolites (>90% within 24 hours).

Acute effects: Etridiazole has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea pig tests.

Short-term effects: Dietary studies in rats and dogs resulted in reduced bodyweight gain and increased liver weight, without associated change in histology, at dose levels of 35 mg/kg bw/day (rat) and 33 mg/kg bw/day (dog).

Long-term effects: Long-term dietary studies have been conducted in mice, rats and dogs and effects observed included reduced bodyweight gain, changes in organ weights relative to bodyweight, and effects on both thyroid and liver in the form of carcinomas. The lowest NOEL in these studies was 2.9 mg/kg bw/day in dogs. This NOEL forms the basis for the current ADI.

Carcinogenicity: An increased incidence of liver and thyroid tumours was observed in rats as a result of severe tissue irritation at the high dose (192 mg/kg bw/day). There was a clear threshold dose for this effect, which is not considered relevant at the low levels to which humans are exposed.

Genotoxicity: Etridiazole is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Poisons Schedule: Etridiazole is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for etridiazole remains unchanged from the value established in 2004, and was determined as follows:

$$0.1 \text{ mg/L} = \frac{2.9 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.9 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Fenamiphos

(endorsed 2011)

GUIDELINE

Based on human health concerns, fenamiphos in drinking water should not exceed 0.0005 mg/L.

RELATED CHEMICALS

Fenamiphos (CAS 22224-92-6) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes terbufos, chlorpyrifos, ethion, diazinon, fenitrothion, profenofos, trichlorfon, methidathion and acephate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fenamiphos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fenamiphos is an insecticide used for the control of nematodes and sucking insects (e.g. aphids and thrips) on food and non-food producing crops, and for the control of nematodes in turf.

There are registered products containing fenamiphos in Australia. These products are intended for professional use and are available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to fenamiphos is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of fenamiphos may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Fenamiphos has been found at varying rates in soil (Kookana *et al.* 1997) and in groundwater (Di *et al.* 1995). Point-source fenamiphos pesticide contamination of groundwater from effluent from pest control operators was reported in Perth (Davis *et al.* 1996). Fenamiphos is routinely sampled by drinking water providers but no detections were reported in the literature searched.

TREATMENT OF DRINKING WATER

Reverse osmosis challenger data reduced by more than 99% the initial fenamiphos concentration of 930 µg/L (USEPA 2005). Granular activated carbon is also very efficient in removing trace organic substance including fenamiphos.

MEASUREMENT

Fenamiphos can be extracted from water by liquid/liquid extraction or solid phase extraction. The extract is concentrated and analysed by gas chromatography (GC) coupled with a nitrogen phosphorus detector (NPD) and flame photometric detector. The method can achieve a limit of quantitation (LOQ) of 0.05 µg/L (López-Blanco *et al*. 2006). Solid-phase extraction (SPE) and GC with NPD or mass spectrometry in the selected-ion monitoring mode detection can achieve a LOQ of 0.08–0.60 µg/L, and 0.03–0.13 µg/L, repectively (Psathaki *et al*. 1994). SPE followed by thermospray liquid chromatography–mass spectrometry can achieve a LOQ of 0.012 µg/L (Lacorte *et al*. 1995).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fenamiphos is 0.0001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.014 mg/kg bw/day from a 2-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 acute reference dose (ARfD) of 0.003 mg/kg bw/day for fenamiphos was established in 2005, 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 previous health value was 0.0003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Fenamiphos is extensively and readily absorbed from the gastrointestinal tract, with wide distribution in tissues. Metabolism is extensive, and proceeds via sulfoxidation and phenylation pathways. Excretion is predominantly via the urine and to a lesser extent via the faeces, and is complete within 48 hours.

Acute effects: Fenamiphos has very high acute oral toxicity and high acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 15-22 day dermal toxicity studies in rats and rabbits, plasma cholinesterase activity was decreased at 2.5 mg/kg bw/day in rabbits and at 40 mg/kg bw/day in rats.

In three-month oral toxicity studies in rats and dogs, plasma cholinesterase activity was decreased at 0.8 mg/kg bw/day in rats and at 0.05 mg/kg bw/day in dogs. Red blood cell cholinesterase activity was decreased at 1.6 mg/kg bw/day in rats and at 0.125 mg/kg bw/day in dogs. Clinical symptoms of cholinesterase inhibition were observed at 3.2 mg/kg bw/day in rats and at 0.45 mg/kg bw/day in dogs.

Long-term effects: In long-term dietary studies in mice, rats and dogs, plasma, red blood cell cholinesterase activity was decreased at 0.09 mg/kg bw/day in rats and dogs. In rats, brain cholinesterase activity was decreased and clinical symptoms of cholinesterase inhibition were observed at 2.45 mg/kg bw/day. In dogs, other signs of general toxicity were observed at 0.308 mg/kg bw/day. In mice, bodyweight decrease only was observed at 7.4 mg/kg bw/day. The lowest overall NOEL was 0.014 mg/kg bw/day in dogs. This NOEL is the basis for the current ADI.

NOTE: Important general information is contained in PART II, Chapter 6

Carcinogenicity: Based on a 2-year study in mice and rats, there is no evidence of carcinogenicity for fenamiphos.

Genotoxicity: Fenamiphos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and a developmental toxicity study in rabbits found no evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: A 21-day neurotoxicity study in hens found no evidence for delayed neurotoxicity for fenamiphos.

Poisons Schedule: Fenamiphos is included in Schedule 6 or 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.0005 mg/L for fenamiphos was determined as follows:

$$0.0005 \text{ mg/L} = \frac{0.014 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.014 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for fenamiphos and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Fenarimol

(endorsed 2011)

GUIDELINE

Based on human health concerns, fenarimol in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

Fenarimol (CAS 60168-88-9) belongs to the pyrimidine class of fungicides. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fenarimol would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fenarimol is a fungicide for the control of black spot and powdery mildew in apple and pear agricultural crops.

There is at least one registered product containing fenarimol in Australia. Fenarimol products are intended for professional use and are available as concentrated solutions to be applied in diluted form to foliage of target plants using ground and hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to fenarimol and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of fenarimol may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on occurrence of fenarimol in Australian waters could be found. In the USA, the estimated environmental concentration in surface water was 0.026 mg/L when not in use for residential applications (USEPA 2002).

TREATMENT OF DRINKING WATER

No specific data on the treatment of fenarimol in drinking water have been identified.

MEASUREMENT

Fenarimol can be measured by gas chromatography with alkali flame detector, with a detection limit of 4 µg/L (USEPA Method 633.1).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fenarimol is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1 mg/kg bw/day from a reproduction study and a long-term (2-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, and was established in 1990.

The previous ADI of 0.025 mg/kg bw was established in 1982, based on a NOEL of 2.5 mg/kg bw/day in a long-term dietary study in rats. The ADI was amended to its present level after submission of reproduction and long-term studies demonstrating lower overall NOELs.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Fenarimol was poorly absorbed from the gastrointestinal tract of rats. The absorbed fraction was extensively metabolised (>30 metabolites) with excretion mostly via the faeces within 7 days.

Acute effects: Fenarimol has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: Short-term (2-3 week) dietary studies in rats and mice reported increased P-450 liver enzymes at 20 mg/kg bw/day in mice, and increased relative liver weight and centrilobular hypertrophy at 40 mg/kg bw/day in mice and rats. Similar changes were reported in 3-month dietary studies in mice, rats and dogs.

Long-term effects: Long-term (2-year) dietary studies were conducted in mice and rats. In rats, there were fatty changes in the liver, hepatic nodules, and increased blood glucose at doses of 5 mg/kg bw/day. The lowest NOEL was 1.3 mg/kg bw/day in rats, and this NOEL is partly the basis for the current ADI.

Carcinogenicity: Based on a 2-year study in mice and rats, there is no evidence of carcinogenicity for fenarimol.

Genotoxicity: Fenarimol is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats reported an increased gestation period at doses of 5 mg/kg bw/day, and decreased pregnancy rate and litter size at doses of 13 mg/kg bw/day. The NOEL was 1.07 mg/kg bw/day and this NOEL is partly the basis for the current ADI. In developmental toxicity studies in rats and rabbits, there was no evidence of effects on foetal development.

Poisons Schedule: Fenarimol is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.04 mg/L for fenarimol was determined as follows:

$$0.04 \text{ mg/L} = \frac{1.07 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.07 mg/kg bw/day is the NOEL based on long-term (2-year) dietary studies, and a 3-generation reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Fenchlorphos

(endorsed 2011)

GUIDELINE

The health concerns associated with fenchlorphos have not been fully evaluated and therefore a health-based guideline value for fenchlorphos in drinking water cannot be set.

RELATED CHEMICALS

Fenchlorphos (CAS 299-84-3) belongs to the organophosphate class of chemicals. Other pesticides in this class include dichlorvos, profenofos and acephate (Tomlin 2006).

HUMAN RISK STATEMENT

There are currently insufficient data on which to base a human risk statement.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fenchlorphos is an insecticide formerly used for the control of cockroaches and flies in animal houses, dairies, food storages areas, food containers and packaging, food processing equipment, and for the control of insects in a variety of agricultural crops.

There are no registered products containing fenchlorphos in Australia, but de-registered compounds may still be detected in water. Previously registered products were intended for professional use.

Exposure sources: If used in the future, the main source of public exposure to fenchlorphos would be residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of fenchlorphos in the future may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data on the occurrence of fenchlorphos in Australian waters could be found.

TREATMENT OF DRINKING WATER

No data on the removal efficacy of drinking water treatment for fenchlorphos could be found.

MEASUREMENT

Fenchlorphos can be measured by routine gas chromatography mass spectrometry analysis with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

No acceptable daily intake (ADI) or acute reference dose (ARfD) values have been established for fenchlorphos.

The previous ADI of 0.01 mg/kg bw was set by the World Health Organization in 1968 (IPCS 1968). The basis of this ADI is unknown and it was removed in 2003.

A previous health value of 0.03 mg/L was set in 1996 (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: No studies have been evaluated in Australia.

Short-term/long-term effects: No studies have been evaluated in Australia.

Carcinogenicity: No studies have been evaluated in Australia.

Genotoxicity: No studies have been evaluated in Australia.

Reproductive and developmental effects: No studies have been evaluated in Australia.

Poisons Schedule: Fenchlorphos is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

There are currently insufficient data on which to establish a health-based guideline for fenchlorphos in drinking water in Australia.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Fenitrothion

(endorsed 2011)

GUIDELINE

Based on human health concerns, fenitrothion in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Fenitrothion (CAS 122-14-5) belongs to the organophosphate class of chemicals. There are many other pesticides in this class including fenthion, parathion, profenofos and ethoprophos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fenitrothion would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fenitrothion is an insecticide for the control of a variety of pests (grasshoppers, locusts, beetles, weevils) on crops, fruits, vegetables and pastures. It is also used to treat flour mills, grain storage facilities (prior to storage) and broiler poultry houses (before restocking).

There are registered products containing fenitrothion in Australia, all of which are intended for professional use. All products are liquid concentrates which are diluted and then sprayed. Ground spraying can be done using air-assisted, misting, electrostatic and boom sprayers. Aerial applications are also used, particularly for large scale locust control, where ultra-low volume (ULV) application is common. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to fenitrothion is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of fenitrothion may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on fenitrothion in Australian drinking waters. In the 1981 spruce budworm spray program in Canada, the concentrations of fenitrothion residues detected in water were low (maximum 1.30 µg/L), and post-spray samples did not contain detectable concentrations (<0.01 µg/L) (Mallett and Cassista 1984, cited in WHO 2004a).

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of fenitrothion in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Fenitrothion can be measured by routine gas chromatography with mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fenitrothion is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day from a 1-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 was 0.003 mg/kg bw/day based on a NOEL of 0.3 mg/kg bw/day from a 92-week rat study.

The acute reference dose (ARfD) of 0.03 mg/kg bw/day for fenitrothion was established in 2000, 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).

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Following oral administration, fenitrothion is readily absorbed from the gastrointestinal tract in all species. It is initially metabolised in the liver to fenitrooxon, then to other metabolites, which are excreted mainly via the urine. The main metabolites are desmethylfenitrothion, desmethylfenitrooxon and 3-methyl-4-nitrophenol (both free and conjugated with sulfate or βglucuronic acid).

Acute effects: Fenitrothion has low to moderate acute oral and dermal toxicity. It does not cause skin sensitisation.

Short-term effects: Short-term studies in rats reported decreased plasma, brain and red blood cell (RBC) cholinesterase activity and symptoms indicative of nervous system toxicity. A decrease in RBC cholinesterase was observed in a 4-week study at dose levels above 1 mg/kg bw/day.

Long-term effects: Long-term dietary studies in rodents, dogs and monkeys also showed the main effect to be on the nervous system, measured as inhibition of cholinesterase activity. A 1-year dietary study in dogs reported a decrease in plasma cholinesterase inhibition at 0.3 mg/kg bw/day and above. The NOEL of 0.2 mg/kg bw/day in this study is the basis for the current ADI.

Carcinogenicity: Based on long-term dietary studies, there is no evidence of carcinogenicity for fenitrothion.

Genotoxicity: Fenitrothion is not considered to be genotoxic, based on short-term *in vitro* and *in vivo* studies (JMPR 2000).

Reproductive and developmental effects: Reproduction studies in rats and developmental studies in rats, rabbits and mice reported no evidence of effects on reproduction, no developmental delays and no evidence of teratogenicity due to fenitrothion.

Neurotoxicity: There was no evidence of delayed neurotoxicity in hens.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Fenitrothion is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for fenitrothion was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for fenitrothion and it is included in the list of agricultural chemicals for which a guideline value has not been established because it "occurs in drinking water at concentrations well below those at which toxic effects may occur" (WHO 2004b).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Fenthion

(endorsed 2011)

GUIDELINE

Based on human health concerns, fenthion in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Fenthion (CAS 55-38-9) is in the organophosphate chemical class. There are many pesticides in this group, including chlorpyrifos, diazinon, dichlorvos, ethion, parathion and profenofos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fenthion would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fenthion is an insecticide used for pre- and post-harvest treatment of various fruits and vegetables. It is also used as a commercial and domestic insecticide and as an ectoparasiticide in cattle and dogs.

There are registered products containing fenthion in Australia. These products include a spot-on treatment for cattle, an insecticide dust and spray, as well as paint, paste and gels for control of pest birds. Some products are available for use in the home garden and as household insecticides.
Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to fenthion and its metabolites are use of household insecticide products, and residues in food. Residue levels in crops grown according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data for fenthion in Australian drinking water are available. The highest predicted surface water concentration in the USA was 1.3 µg/L (USEPA 2001). The highest concentration reported in surface water in Japan was 0.27 µg/L (Tsuda *et al.* 1998). Fenthion concentration in Australian treated sewage was less than 2.4 µg/L (supporting data, NRMMC/EPHC/NHMRC, 2008).

TREATMENT OF DRINKING WATER

Although no empirical data is currently available, it is likely that activated carbon would provide efficient removal for this chemical based on its chemical structure.

MEASUREMENT

Fenthion residues in water can be analaysed by solid-phase extraction–liquid chromatography with electrospray tandem mass spectrometry, with a detection limit of 0.021 µg/L (Hernandez *et al*, 2001); or by solid-phase extraction–gas chromatography–mass spectrometry, with a detection limit of 0.13 µg/L (Psathaki *et al*, 1994).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fenthion is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.02 mg/kg bw/day from a 28-day human study showing cholinesterase inhibition. The ADI incorporates a safety factor of 10 and was established in 2004.

The acute reference dose (ARfD) of 0.007 mg/kg bw/day for fenthion was established in 2000, 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.

A health value has not been previously established by NHMRC for fenthion.

HEALTH CONSIDERATIONS

Metabolism: Fenthion is rapidly absorbed from the gastrointestinal tract and broadly distributed in tissues, particularly in lipid stores. Metabolism is extensive and elimination is almost complete after 48 hours (90% in the urine). There are 3 major urinary metabolites – the oxygen analogue of fenthion and its sulfoxide and sulfone derivatives.

Acute effects: Fenthion has moderate acute oral and dermal toxicity. Symptoms of acute poisoning were indicative of central and peripheral nervous system poisoning and included hyperexcitability, salivation, broncoconstriction, headache, vomiting and other behavioural changes. It is not a skin sensitiser.

Short-term and long-term effects: In short-term and long-term studies in rodents, monkeys and dogs, the main effect was the inhibition of cholinesterase (plasma, brain and red blood cell) at dose levels of 0.04 mg/kg bw/day (mouse) 0.07mg/kg bw/day (monkey), 0.32 mg/kg bw/day (dog) and above.

In a 4-week human volunteer study, there was a dose-related inhibition of plasma cholinesterase at 0.07 mg/kg bw/day. There was no inhibition of red blood cell cholinesterase. The NOEL of 0.02 mg/kg bw/day is the basis for the ADI.

Carcinogenicity: Based on long-term studies in rodents, there is no evidence of carcinogenicity for fenthion.

Genotoxicity: Fenthion is not considered to be genotoxic, based on *in vitro* or *in vivo* short-term studies.

Reproductive and developmental effects: In a reproduction study in rats, there was decreased fertility, decreased litter sizes and increased neonatal deaths at high doses. Similarly, developmental studies in rats and rabbits showed increased resorptions and delayed skeletal development as a result of high dose maternotoxicity. In both cases, this was the result of central nervous system effects and well above the likely levels of human exposure.

Neurotoxicity: There was no evidence of delayed neurotoxicity in hen, rat and dog studies.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Fenthion is included in Schedule 5, 6 or 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on the concentration and the use of the product. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.007 mg/L for fenthion was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.02 \text{ mg/kg bodyweight /day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.02 mg/kg bw/day is the NOEL based on a short-term (28-day) study in human volunteers.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is a safety factor applied to the NOEL derived a human study to account for variation within the human population (intraspecies variation).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Fenvalerate

(endorsed 2011)

GUIDELINE

Based on human health concerns, fenvalerate in drinking water should not exceed 0.06 mg/L.

RELATED CHEMICALS

Fenvalerate (CAS 51630-58-1) belongs to the pyrethroid class of chemicals. This is a large chemical group and includes the closely related esfenvalerate (esterified form), cyfluthrin, permethrin, and flucythrinate.

There are four optical isomers of fenvalerate and esfenvalerate (SS, SR, RS, RR). The SS isomer is responsible for the insecticidal activity of these compounds. Fenvalerate contains around 20% as the SS form, while esfenvalerate is highly enriched in this form. Most of the toxicity of fenvalerate is caused by the RS isomer (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fenvalerate would not be a health concern unless the concentration exceeded 0.06 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fenvalerate is an insecticide used for the control of buffalo fly and *Culicoides* midge on cattle and horses.

There is at least one registered product containing fenvalerate in Australia. Fenvalerate products are intended for professional use, to be diluted and applied by handspray to the backline of cattle and horses.

Exposure sources: The main source of public exposure to fenvalerate and its metabolites is residues in meat. Residue levels in food produced according to good agricultural practice are generally low.

The veterinary use of fenvalerate provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Esfenvalerate, a sterified form of fenvalerate, has been detected in 2004-2006 in passive samples and spot water samples from the Goulburn Murray Water irrigation supply channels in Victoria. In October 2005 the Torrumbarry Irrigation Area Kerang Town Channel reported an esfenvalerate concentration of 65 µg/L (Rose and Kibria 2006).

TREATMENT OF DRINKING WATER

No specific data on the treatment of fenvalerate in drinking water have been identified.

MEASUREMENT

After extraction with n-hexane or dichloromethane, fenvalerate can be analysed by gas chromatography equipped with an electron capture detector (ECD) or with a mass selective detector (MSD). A limit of quantitation (LOQ) of 0.05 µg/L using the ECD and 0.1 µg/L using the MSD have been reported (California Department of Food and Agriculture 2000, Xue *et al.* 2005). Fenvalerate can also be extracted and pre-concentrated by micro liquid–liquid extraction and analysed by gas chromatography–mass spectrometry (GC-MS) with selected ion monitoring, with a reported LOQ in the ng/L concentrations (Fernández-Gutiérrez *et al.* 1998). A modification of the EPA method 8270: GC-MS electron ionisation, using a narrow range selected ion scan to analyse pyrethroids, can achieve a LOQ of 5 ng/L in water (Heines and Halpin 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fenvalerate is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.7 mg/kg bw/day from a 2-year dietary mouse study. The NOEL is based on micro-nodular inflammation in the liver, lymph nodes, and spleen. The ADI incorporates a safety factor of 100 and was established in 1987.

The previous ADI of 0.04 mg/kg bw was set in 1985 based on a NOEL of 3.5 mg/kg bw/day from a 20-month dietary study in mice. The ADI was updated after submission of an additional long-term study demonstrating a lower overall NOEL.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Fenvalerate is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, and is rapidly excreted in the urine, almost completely within 48 hours.

Acute effects: Fenvalerate has moderate acute oral toxicity and low dermal toxicity. It is not a skin sensitiser.

Short-term effects: A 90-day and a 15-month dietary study in rats reported decreased bodyweight gain and decreased haemoglobin levels at 7.5 mg/kg bw/day and above. A 6-month dietary study in dogs reported behavioural effects including tremors and lack of coordination at 6.25 mg/kg bw/day.

Long-term effects: Long-term (2-year) dietary studies in mice and rats reported micro-nodular inflammatory changes in the liver, lymph nodes, and spleen of mice at doses of 9 mg/kg bw/day, and decreased bodyweight gain and decreased haemoglobin levels in rats at higher doses. The lowest overall NOEL was 1.7 mg/kg bw/day in mice. This NOEL is the basis for the current ADI.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for fenvalerate. The micro-nodular changes noted in mouse tissues were considered evidence of localised tissue inflammation rather than cancer.

Genotoxicity: Fenvalerate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal developmental.

Neurotoxicity: Fenvalerate has some potential for neurotoxicity, but only at levels much greater than likely human exposures. A single oral dose of 500 mg/kg bw in rats caused axonal and myelin lesions, with a NOEL of 200 mg/kg bw/day. In a 15-month dietary study in rats, the NOEL was 75 mg/kg bw/day based on sciatic nerve damage at higher doses. Doses up to 1 g/kg bw did not caused delayed neurotoxicity in hens.

Poisons Schedule: Fenvalerate is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.06 mg/L for fenvalerate was determined as follows:

$$0.06 \text{ mg/L} = \frac{1.7 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.7 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

Note: This calculated health-based guideline exceeds the normal aqueous solubility of fenvalerate.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Fipronil

(endorsed 2011)

GUIDELINE

Based on human health concerns, fipronil in drinking water should not exceed 0.0007 mg/L.

RELATED CHEMICALS

Fipronil (CAS 120068-37-3) belongs to the phenylpyrazole class of chemicals. Another pesticide in this class is ethiprole (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fipronil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fipronil is a broad-spectrum insecticide that has a range of agricultural uses, including seed dressings, control of pests in bananas, cotton, sorghum, vegetables and turf. Fipronil is also included in insect baits for household and commercial uses, and in home veterinary products for cats and dogs.

There are registered products containing fipronil in Australia. The products are intended for agricultural, professional, home garden, and household pet use. They are available as sprays, baits, dusts, and gels for control of cockroaches, fruit flies, ants and termites; as concentrated granular formulations for control of insect pests in turf; spot on and spray insecticide treatments for pets; and as liquid concentrates and/or wettable granules for application to seeds, and vegetable and other crops, to be applied in diluted form by ground and aerial sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to fipronil and its metabolites are residues in food.

Agricultural and veterinary use of fipronil may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of fipronil in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific literature on the removal of fipronil has been identified. Jar testing to identify the effectiveness of various removal methods in specific waters is recommended if fipronil is detected.

MEASUREMENT

The practical limit of quantification (LOQ) for fipronil in water is 0.001 mg/L using liquid chromatography with tandem mass spectrometry (Alder *et al*. 2006). This LOQ is slightly above the guideline value.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fipronil is 0.0002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.02 mg/kg bw/day from a 2-year rat dietary study for effects on the nervous system, thyroids and kidneys. The ADI includes a safety factor of 100 and it was initially established in 1994 and reconfirmed in 2006.

The current acute reference dose (ARfD) is 0.02 mg/kg bw, set in 2006 and 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 ARfD was 0.003 mg/kg bw.

The ADI and ARfD values are a group value covering the parent compound and its main metabolites.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Fipronil is completely absorbed via the gastrointestinal tract and extensively metabolised. Excretion is slow (more than 8 days) via the faeces. Dermal absorption is low.

Acute effects: Fipronil has moderate oral toxicity and low to moderate dermal toxicity. It is not a skin sensitiser in guinea pigs.

Short-term effects: In 4-6 week studies in mice, rats and dogs, effects were observed on the nervous system (muscular incoordination, convulsions and hyperactivity in mice at 6.5 mg/kg bw/day and head nodding in dogs at 10 mg/kg bw/day), and on the liver (at 2.4 mg/kg bw/day and above in mice, and 3.4 mg/kg bw/day in rats) and thyroid (at 3.4 mg/kg bw/day in rats).

In 3-month dietary studies in rats and dogs, there was increased liver and thyroid weight, and associated follicular cell hypertrophy and hyperplasia in rats, and decreased body weight gain in dogs at doses of 2 mg/kg bw/day. Symptoms of nervous system toxicity in dogs (convulsions, tremors, in-coordination) were seen at higher doses.

Long-term effects: In long-term studies in mice, rats and dogs, effects on the nervous system (irritability, hyperactivity and vocalisation) were observed in rats at 0.06 mg/kg bw/day and in dogs (convulsions, facial twitching, and disorientation) at 2 mg/kg bw/day. Nephropathy and increased liver and thyroid weight associated with hypertrophy and hyperplasia were observed in all species. The lowest NOEL was 0.02 mg/kg bw/day in the 2-year rat study, and is the basis for the current ADI.

Carcinogenicity: Based on a 2-year study in rats, there is no evidence of carcinogenicity for fipronil.

Genotoxicity: Fipronil is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproduction and developmental effects: Reproduction studies in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

NOTE: Important general information is contained in PART II, Chapter 6

Neurotoxicity: In a single oral dosing study in rats, there was decreased hind leg splay at 5 mg/kg bw/day. In a 6-day oral dosing study in rats, there was decreased levels of serotonin in the brain at 5 mg/kg bw/day. In a 13-week dietary study in rats, there was an increased incidence in "startled" responses and decreased forelimb strength at 7.2 mg/kg bw/day.

Poisons Schedule: Fipronil is either exempt from scheduling or is included in Schedule 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard) (DoHA 2010)., depending on concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.0007 mg/L for fipronil was determined as follows:

$$0.0007 \text{ mg/L} = \frac{0.02 \text{ mg/kg bodyweight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.02 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from a study conducted in rats. The safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Flamprop-methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, flamprop-methyl in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Flamprop-methyl and its isomer, flamprop-m-methyl (CAS 52756-25-9) belong to the arylaminopropionic acid class of chemicals. There are no other pesticides in this class registered for use in Australia (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, flamprop-methyl would not be a health concern unless the concentration exceeded 0.004 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Flamprop-methyl is a herbicide for the control of wild-oat weeds in wheat and triticale crops.

There are currently products registered in Australia that contain flamprop-methyl, all as the m-methyl isomer. Flamprop-methyl products are intended for professional use. Products are emuslifiable concentrate and liquid formulations intended to be sprayed in diluted form onto crops by aerial, boom spray, and hand-held spray equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to flamprop-methyl and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of flamprop-methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on flamprop-methyl occurrence in Australian drinking water supplies have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of flamprop-methyl in drinking water have been identified.

MEASUREMENT

Flamprop-methyl in drinking water can be determined by gas chromatography (GC) or gas-liquid chromatography after abstraction followed by electron capture detection. Determination by GC or GC with mass spectrometry can achieve limits of detection of 0.1 mg/L (Hirahara *et al.* 2005). Flamprop-methyl can also be analysed by high-performance liquid chromatography with ultraviolet detection.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for flamprop-methyl is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.125 mg/kg bw/day from a long-term study. The NOEL is based on liver hypertrophy and increased liver weight in a 2-year dietary study. The ADI incorporates a safety factor of 100. It was established in 1980 and reaffirmed in 1991.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: In rats, flamprop-methyl is readily absorbed and extensively metabolised, and completely excreted (>95-97%) within 48 hours of dosing. Excretion is mostly via faeces.

Acute effects: Flamprop-methyl and its m-isomer have low oral and dermal acute toxicity. Flamprop-methyl is not a skin sensitiser in guinea-pig tests.

Short-term effects: In a 5-week dietary study in rats, increased liver weight was reported at 2.5 mg/kg bw/day and above, and increased caecum weight at 25 mg/kg bw/day. In a 6-week dietary study in dogs, increased liver weights and associated increases in liver enzymes were seen at 125 mg/kg bw/day. The lowest overall NOEL was 0.25 mg/kg bw/day based on increased liver weights in rats.

In 90-day dietary studies in rats and dogs, liver changes were observed at 50 mg/kg bw/day in rats, and 2.5 mg/kg bw/day in dogs.

Long-term effects: In 2-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.

Carcinogenicity: Based on a 2-year study in rats, there is no evidence of carcinogenicity for flamprop-methyl.

Genotoxicity: Flamprop-methyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and a developmental study in rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Poisons Schedule: Flamprop-methyl and flamprop-m-methyl are included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 0.004 mg/L for flamprop-methyl was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.125 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.125 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Hirahara Y, Kimura M, Inoue T, Uchikawa S, Otani S, Haganuma A, Matsumoto N, Hirata A, Maruyama S, Iizuka T, Ukyo M, Ota M, Hirose H, Suzuki S, Uchida Y (2005). Validation of multiresidue methods for the determination of 186 pesticides in 11 agricultural products using gas chromatography. *Journal of Health Science,* 51(5):617-27.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

Fluometuron

(endorsed 2011)

GUIDELINE

Based on human health concerns, fluometuron in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Fluometuron (CAS 2164-17-2) belongs to the phenylurea class of chemicals. Other pesticides in this class include linuron and diuron (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, fluometuron would not be a health concern unless the concentration exceeded 0.07 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Fluometuron is a herbicide for the control of broad-leaf weeds and grasses in cotton, cereal, citrus and sugar cane crops.

There are currently products registered in Australia that contain fluometuron. Fluometuron products are intended for professional use. They are water-soluble granules, wettable powders, or liquid formulations intended to be diluted and applied by ground spray or aerial spray directly onto soil for pre-emergent treatment, and by hand spray directly at weeds for post-emergent treatment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to fluometuron and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of fluometuron may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on fluometuron occurrence in Australian drinking water supplies were found. In the USA, fluometuron was the most detected pesticide in surface water of the Mississippi river (mean = 2.1 µg/L, median = 0.40 µg/L, maximum = 50 µg/L) (Thurman *et al.* 1998).

TREATMENT OF DRINKING WATER

No specific data on the treatment of fluometuron in drinking water have been identified.

MEASUREMENT

Fluometuron in drinking water can be analysed by solid phase extraction followed by high performance liquid chromatography (HPLC) with diode array detector or post-column photolysis and derivatisation detection. Typical limits of reporting (LOR) with DAD range from ranged from 4 to 40 ng/L (Ruberu *et al*. 2000). HPLC method and measurement with ultraviolet detector can achieve a LOR of 11 µg/L. Photo-induced chemiluminescence has been used for the determination of fluometuron in a quick and continuous procedure (Sa *et al*. 2007). Fluometuron can also be analysed by direct injection onto a liquid chromatography mass spectrometer (LC-MS) instrument in multiple reaction monitoring mode, with a LOR of 10 µg/L.

In addition to the standard approach of gas chromatography with mass spectrometry (GC-MS) or LC-MS for the evaluation of fluometuron in water, the enzyme-linked immunosorbent assay (ELISA) can be. ELISA is portable and there is a good correlation between the test and GC-MS (Thurman *et al*. 1998).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for fluometuron is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2 mg/kg bw/day from a long-term study. The NOEL is based on a 2-year dietary study in mice in which conjunctivitis and decreased bodyweight gain were observed. The ADI incorporates a safety factor of 100 and was established in 1989.

The previous ADI of 0.01 mg/kg bw/day was based on a NOEL of 1 mg/kg bw/day from a reproductive toxicity study in rats for decreased body weight gain and haematological disturbances.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Fluometuron is rapidly absorbed from the gastrointestinal tract (65-80%) and extensively metabolised. Excretion is rapid, being almost complete by 72 hours, and is mainly through urine.

Acute effects: Fluometuron has low acute oral and dermal toxicity. It was not a skin sensitiser in guinea-pig tests.

Short-term effects: In a 21-day dermal study in rabbits, no toxicity was observed at 1000 mg/kg bw/day.

In 90-day dietary studies in rats, mice, and dogs, red blood cell haemolysis and increased spleen weights were reported at 12.5 mg/kg bw/day, and decreased bodyweight gain and congested liver, spleen, and kidney at higher dose levels.

Long-term effects: In long-term dietary studies in rats, mice and dogs, anaemia, increased spleen size, and haemosiderin deposition in spleen and liver were reported at doses of 63 mg/kg bw/day. Decreased food consumption and bodyweight gain were seen at doses of 100 mg/kg bw/day. The lowest overall NOEL was 2 mg/kg bw/day in the mouse study, and this is the basis for the current ADI.

Carcinogenicity: Based on long-term dietary studies in mice and rats, there is no evidence of carcinogenicity for fluometuron.

Genotoxicity: Fluometuron is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Fluometuron is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for fluometuron was determined as follows:

$$0.07 \text{ mg/L} = \frac{2.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.0 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Ruberu SR, WM Draper, Perera SK (2000). Multiresidue HPLC methods for phenyl urea herbicides in water. *Journal of Agricultural and Food Chemistry,* 48(9):4109-4115.

Sa F, Lopez Malo D, Martinez Calatayud J (2007). Determination of the herbicide fluometuron by photo-induced chemiluminescence in a continuous-flow multicommutation assembly. *Analytical Letters,* 40(13-15):2872-2885.

Thurman EM, Zimmerman LR, Scribner EA, Coupe RH (1998). Occurrence of cotton pesticides in surface water of the mississippi embayment. US Department of the Interior, US Geological Survey.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

Fluoride

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of fluoride in drinking water should not exceed 1.5 mg/L.

GENERAL DESCRIPTION

Fluoride occurs naturally in seawater (1.4 mg/L), soil (up to 300 parts per million) and air (from volcanic gases and industrial pollution). Naturally occurring fluoride concentrations in drinking water depend on the type of soil and rock through which the water drains. Generally, concentrations in surface water are relatively low (<0.1–0.5 mg/L), while water from deeper wells may have quite high concentrations (1–10 mg/L) if the rock formations are fluoride-rich.

Inorganic fluorine compounds are used in aluminium production, as a flux in the steel and glass fibre industries, and in phosphate fertilisers, bricks, tiles and ceramics.

Virtually all foodstuffs contain traces of fluoride. In particular, high amounts can be found in dried tea leaves because of natural concentration by the tea plant. Total daily intake from all sources varies considerably, but has been estimated at 0.46 mg to 5.4 mg, with about 10% coming from unfluoridated drinking water.

Fluoride is used to protect teeth against dental caries. It is present in most brands of toothpaste, and it is often added to drinking water supplies.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In unfluoridated supplies, fluoride concentrations are typically less than 0.1 mg/L, but can range from less than 0.05 mg/L up to 1.5 mg/L, with the higher values reported from groundwater sources.

In fluoridated supplies, the target fluoride concentration is between 0.7 and 1 mg/L, with the lower concentrations applying where the climate is hot, to allow for a higher average consumption of water.

TREATMENT OF DRINKING WATER

Fluoride concentrations in drinking water can be reduced by dilution with other sources, or by using activated alumina or bone char. Conventional coagulation with alum is much less effective.

MEASUREMENT

The fluoride concentration in drinking water can be determined using an ion-specific electrode (APHA Method 4500-F^- Part C 1992). The limit of determination is 0.1 mg/L.

HEALTH CONSIDERATIONS

Because fluoride is widely dispersed in the environment, all living organisms are exposed to it and all tolerate modest amounts. It has been claimed that fluoride is an essential trace element for humans, but this is difficult to establish conclusively, and no data are available on the minimum amount needed. Fluoride is absorbed quickly following ingestion. It is not metabolised, but diffuses passively into all body compartments. About 40% is excreted in urine within 9 hours, and about 50% over 24 hours. Fluoride has an affinity for mineralising tissues of the body: in young people, bone and teeth; in older people, bone. Thus excretion is somewhat greater in adults because they have proportionately less mineralising tissue than children.

Fluoride has been shown to prevent dental caries very effectively, and knowledge of its anti-caries effect came from the observed association of low caries prevalences with naturally occurring fluoride in drinking water (at about 1 mg/L). The NHMRC has extensively reviewed health aspects of fluoride and its prevention of dental disease. Many health authorities around the world recommend fluoridation of public water supplies as an important public health measure.

Concentrations above 1.5 mg/L may disturb tooth mineralisation in children up to about 6 to 8 years, leading to dental fluorosis, a mottling of the teeth which can occasionally occur to an unsightly degree.

Skeletal fluorosis, characterised by hypermineralisation and thus brittle bones, has occurred in association with high fluoride concentrations in drinking water, and also with occupational exposure to fluoride-containing dust. It generally occurs after prolonged exposure (several years) and is reversible: if the exposure is removed, the fluoride levels in bones gradually decline.

Regular consumption of water with fluoride concentrations above about 4 mg/L involves progressively increasing risks of skeletal fluorosis. The United States Environmental Protection Agency has set this level as the maximum acceptable for drinking water: above it, communities are required to lower the fluoride concentration by treatment to remove it, or by dilution.

People with kidney impairment have a lower margin of safety for fluoride intake. Limited data indicate that their fluoride retention may be up to three times normal.

There is no substantiated epidemiological evidence that fluoride or fluoridation causes cancer. One animal study showed an increased incidence of bone tumours in some male rats that were exposed to very high concentrations of fluoride in water, but female rats and mice were not affected.

Tests for mutagenicity with strains of bacteria have been negative. Chromosome aberrations have been reported in tests with mammalian cells but only at extremely high fluoride concentrations.

The International Agency for Research on Cancer has concluded that fluoride is not classifiable as to its carcinogenicity in humans (Group 3, inadequate evidence in humans and in animals) (IARC 1987).

DERIVATION OF GUIDELINE

It was recognised in setting the guideline value of 1.5 mg/L that there is a narrow margin between concentrations producing beneficial effects to teeth and those producing objectionable fluorosis.

The minimum concentration required for a protective effect against dental caries is about 0.5 mg/L, and concentrations around 1 mg/L in temperate climates are optimal for caries prevention. At concentrations between 1.5 and 2 mg/L, mottling of teeth due to dental fluorosis may occur, sometimes to an objectionable degree.

The guideline value of 1.5 mg/L has been set to protect children from the risk of dental fluorosis. If this value is exceeded in circumstances where it is not practical to defluoridate, then parents should be advised to use rainwater or bottled water for children up to about 6 years to limit or prevent dental fluorosis.

The guideline value should not be regarded as a recommended value for fluoridation of water supplies.

REFERENCES

APHA Method 4500-F^- Part C (1992). Fluoride: Ion-selective electrode method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

NHMRC (1991). The effectiveness of water fluoridation. National Health and Medical Research Council, and Department of Health, Housing and Community Services, Canberra.

NOTE: Important general information is contained in PART II, Chapter 6

Flupropanate

(endorsed 2011)

GUIDELINE

Based on human health concerns, flupropanate in drinking water should not exceed 0.009 mg/L.

RELATED CHEMICALS

Flupropanate (CAS 756-09-2) belongs to the halogenated alkanoic acid class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, flupropanate would not be a health concern unless the concentration exceeded 0.009 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Users: Flupropanate is a herbicide used to control the growth of grass weeds in industrial or pasture land.

There are registered products containing flupropanate in Australia. These are available as concentrated solutions applied as a dilute spray by aerial, ground boom or hand spray techniques. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The potential sources of public exposure to flupropanate and its metabolites are residues in food and drinking water. Flupropanate is not registered for use on food crops and the maximum residue limits are set at the level of detection.

Agricultural use of flupropanate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of flupropanate in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of flupropanate in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

No suitable analytical techniques have been identified, but the use of high performance liquid chromatography with tandem mass spectrometry is expected to be suitable for residue levels of this pesticide in water.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for flupropanate is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day from a 90-day dietary rat study. The NOEL is based on effects on the liver. The ADI incorporates a safety factor of 2000 and it was established in 1987.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: No data are available on the absorption, distribution, metabolism or excretion of flupropanate.

Acute effects: Flupropanate has low acute oral and dermal toxicity. Its skin sensitisation potential is unknown.

Short-term effects: A 90-day dietary study in rats reported changes in liver weight at 15 mg/kg bw/day and changes in kidney weight at 50 mg/kg bw/day. The NOEL from the rat study was 5 mg/kg bw/day, and this is the basis of the ADI.

Long-term effects: A 1-year dietary study in mice reported kidney weight changes at 15 mg/kg bw/day and changes in bodyweight gain and liver weight, together with evidence of liver toxicity, at 30 mg/kg bw/day. The study was of poor quality and the NOEL of 7 mg/kg bw/day was not used to establish the ADI.

Carcinogenicity: There are no studies available to assess the potential carcinogenicity of flupropanate.

Genotoxicity: Only short-term bacterial *in vitro* studies were available, and based on these, flupropanate is not considered to be genotoxic; however, no *in vitro* mammalian studies or *in vivo* studies were available.

Reproductive and developmental effects: There were no data available on the reproductive effects of flupropanate. Developmental studies in mice and rats did not show any evidence of effects on foetal development; however, both studies were considered to be of poor quality.

Poisons Schedule: Flupropanate is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.009 mg/L for flupropanate was determined as follows:

$$0.009 \text{ mg/L} = \frac{5 \text{ mg/kg bodyweight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 2000}$$

where:

- 5 mg/kg bw/day is the NOEL based on a medium-term (90-day) dietary study in rats.
- 70 kg is taken as the average weight of an adult.

NOTE: Important general information is contained in PART II, Chapter 6

- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 2000 is a safety factor applied to the NOEL derived from animal studies. The safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variations, and an additional factor of 20 for using a NOEL derived from a medium-term study.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

Formaldehyde

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of formaldehyde in drinking water should not exceed 0.5 mg/L.

GENERAL DESCRIPTION

Formaldehyde may be present in drinking water through ozonation of naturally occurring humic material, contamination by accidental spills, or deposition from the atmosphere. Typical concentrations in air are probably in the low parts-per-billion range. Overseas, formaldehyde has been detected in ozonated drinking water at concentrations up to 0.03 mg/L.

Formaldehyde is used industrially in the wood, paper and textile industries. It is also used in the production of a number of chemicals and for the preservation of biological material. It is occasionally used as a disinfectant, sometimes to disinfect water filters. Other sources of exposure include cigarette smoke and food. Formaldehyde is present in almost all common foods, and adult dietary intake is estimated at 11 mg/day. Drinking water would contribute less than 10% of total intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on the concentrations of formaldehyde in Australian drinking waters.

TREATMENT OF DRINKING WATER

There are no published reports on methods for the removal of formaldehyde from drinking water.

MEASUREMENT

Formaldehyde can be determined by formation of the 2,4-dinitro-phenylhydrazone derivative followed by analysis with high performance liquid chromatography with UV detection (Whittle and Rennie 1988). The limit of determination is 0.006 mg/L.

HEALTH CONSIDERATIONS

Formaldehyde is readily absorbed from the gastrointestinal tract and is rapidly metabolised to formic acid and subsequently to carbon dioxide and water.

An extensive review and summary of the human and animal toxicity data for formaldehyde is available (IPCS 1989).

Most human health data are from inhalation studies, where formaldehyde causes irritation of the respiratory tract, and dermal studies, where it causes skin irritation. Formaldehyde has been linked to outbreaks of haemolytic anaemia in patients using improperly serviced dialysis units, where formaldehyde was used to disinfect the units and residual amounts remained in the water filter.

A number of epidemiological studies have looked at the effects of inhalation of formaldehyde. No effects could be directly attributed to long-term occupational exposure, but studies among exposed workers have reported elevated incidences of a number of cancers including nasal, buccal, nasopharyngeal, skin, prostate and colon cancers. The available human evidence indicates that formaldehyde does not have a high carcinogenic potential (IPCS 1989).

In a 2-year drinking water study using rats, severe damage to gastric mucosa was reported only at the highest doses (over 80 mg/kg body weight per day), but no tumours were observed, either in the stomach or at other sites. Other studies have shown similar pathological changes to the stomach, but again only at the highest doses.

There was no evidence of tumour-promoting activity when formaldehyde was applied to mouse skin, but rats inhaling formaldehyde exhibited a markedly increased incidence of cancer of the nasal cavity. Formaldehyde has demonstrated mutagenic activity when applied to cells *in vitro* but not when applied *in vivo*.

The International Agency for Research on Cancer has concluded that formaldehyde is probably carcinogenic to humans (Group 2A, limited human evidence, sufficient animal evidence, based on inhalation studies) (IARC 1987). The weight of evidence indicates that formaldehyde is not carcinogenic by the oral route.

DERIVATION OF GUIDELINE

The guideline value for formaldehyde in drinking water was determined as follows:

$$0.5 \text{ mg/L} = \frac{15 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 15 mg/kg body weight per day is the no-effect level based on a 2-year drinking water study in rats (Til *et al*. 1989).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 100 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations and 10 for intraspecies variations). The use of this safety factor was recommended by the NHMRC Standing Committee on Toxicity.

The World Health Organization derived a guideline value of 0.9 mg/L based on a 20% allocation of total daily intake to drinking water. In determining the Australian guideline value, it was felt that sufficient data were available to indicate that 10% was a more realistic figure.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

IPCS (International Programme on Chemical Safety) (1989). Formaldehyde. Environmental Health Criteria, 89. World Health Organization, IPCS.

Til HP, Woutersen RA, Feron VJ, Hollanders VHM, Falke HE, Clary JJ (1989). Two-year drinking water study of formaldehyde in rats. *Food and Chemical Toxicology*, 27:77–87.

Whittle PJ, Rennie PJ (1988). Determination of formaldehyde in river water by high-performance liquid chromatography. *Analyst*, 113:665–666.

NOTE: Important general information is contained in PART II, Chapter 6

Glyphosate

(updated 2011)

GUIDELINE

Based on human health concerns, glyphosate in drinking water should not exceed 1 mg/L.

RELATED CHEMICALS

Glyphosate (CAS 1071-83-6) is an aminophosphonic analogue of the natural amino acid glycine. It is available in a variety of salts, but is not chemically related to other pesticides (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population to glyphosate is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, glyphosate would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Glyphosate is a non-selective post-emergence herbicide used in the control of weeds in agriculture industry, forestry and public service areas including the aquatic environment.

There are many registered products containing glyphosate salts in Australia. Glyphosate products are intended for professional and home garden use, and are available as concentrated or ready-to-use solutions to be applied using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to glyphosate and its metabolites are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of glyphosate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Glyphosate is generally not reported in analysis of Australian waters. It is strongly sorbed to soils but overseas studies show that there is potential for it to be present in waters as a result of over-spray or run-off from agricultural drainage ditches. For example, Netherlands surface waters were shown to contain up to 0.001 mg/L, and pond water in the USA was shown to contain up to 1.7 mg/L (IPCS 1994), demonstrating the high levels of contamination possible with some applications.

TREATMENT OF DRINKING WATER

Glyphosate has been shown to be completely removed by ozonation (Bozkaya-Schrotter *et al*, 2008). Moderate removal can be achieved using powdered activated carbon adsorption.

MEASUREMENT

Glyphosate in Australian laboratories in commonly analysed by high performance liquid chromatography (HPLC) followed by post-column derivitisation using orthophthaldehyde and subsequent fluorescent detection (Eaglesham, personal communication). Some of the best equipped Australian laboratories are now using HPLC–tandem mass spectrometry for rapid and sensitive analysis without the need for derivitisation. Sensitivities for both procedures allow for low microgram per litre levels to be determined (Eaglesham, personal communication). The National Measurement Institute notes a limit of reporting of 0.01 mg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for glyphosate is 0.3 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 30 mg/kg bw/day from a long-term (3-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 and was established in 1985.

The previous health value was 1.0 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Glyphosate has low absorption from the gastrointestinal tract (30-36%) in rats and rabbits. Dermal absorption is less than 5% in monkeys. It is essentially not metabolised, with 99% excreted in the urine as unchanged glyphosate.

Acute effects: Glyphosate has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: Three-month dietary studies in mice and dogs reported decreased bodyweight and food consumption at dose of 7500 mg/kg bw/day (mice) and 500 mg/kg bw/day (dogs).

Long-term effects: Long-term dietary studies in mice reported decreased bodyweight, hepatotoxicity, and changes in the urinary bladder and in the kidney at 814 mg/kg bw/day.

A long-term dietary study in dogs reported no significant toxicological effects up to the dose level of 45 mg/kg bw/day.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for glyphosate.

Genotoxicity: Glyphosate is not considered genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity at the dose levels up to 30 mg/kg bw/day. The ADI was based on the NOEL from this study, which was the highest dose tested (30 mg/kg bw/day).

A single-generation reproduction study in rats at doses up to 10 mg/kg bw/day reported no significant reproductive effects.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Glyphosate is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF HEALTH-BASED GUIDELINE

The health-based guideline of 1 mg/L for glyphosate was determined as follows:

$$1 \text{ mg/L} = \frac{30 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 30 mg/kg bw/day is the NOEL based on a 3-generation reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for glyphosate and it is excluded from the list of agricultural chemicals guideline value derivation because "its health-based value is orders of magnitude higher than concentrations normally found in drinking-water" (WHO 2006).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

Bozkaya-Schrotter B, Daines C, Lescourret A, Bignon A, Breant P, Schrotter J (2008). Treatment of trace organics in membrane concentrates I: pesticide elimination, *Water Science & Technology. Water Supply*, 8(2):223-230.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Eaglesham G (2009). Queensland Health Scientific Services, personal communication.

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NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

WHO (World Health Organization) (2006). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Haloacetonitriles
dichloroacetonitrile
trichloroacetonitrile
dibromoacetonitrile
bromochloroacetonitrile

(endorsed 2011)

GUIDELINE

Data are inadequate to set guideline values for haloacetonitriles in drinking water

GENERAL DESCRIPTION

Haloacetonitriles are formed from organic precursors during chlorination or chloramination of drinking water. Concentrations of dihaloacetonitriles reported overseas range up to 0.04 mg/L but are typically less than 0.003 mg/L. Concentrations of trichloroacetonitrile are less than 0.001 mg/L.

Trichloroacetonitrile has been used as an insecticide. No data are available on uses for the other haloacetonitriles.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on concentrations of haloacetonitriles in Australian drinking waters.

LIMITING FORMATION IN DRINKING WATER

The presence of haloacetonitriles in drinking water can be minimised by removing naturally occurring organic matter from the source water, reducing the amount of chlorine added, or using alternative disinfectants

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of haloacetonitriles (USEPA Method 551.1 1995). A salting agent is added to the sample and the haloacetonitriles extracted using methyl tert-butyl ether or pentane. The extracts are then analysed using gas chromatography with an electron capture detector. Limits of determination are less than 0.0001 mg/L.

HEALTH CONSIDERATIONS

Haloacetonitriles are rapidly absorbed from the gastrointestinal tract and metabolised to single carbon compounds, including cyanide. Insufficient data are available to indicate whether haloacetonitriles can accumulate in specific organs.

No data are available on the health effects of haloacetonitriles in humans.

Dichloroacetonitrile and dibromoacetonitrile caused decreased body weights in 90-day feeding studies with rats, but specific target organs were not identified. Dibromoacetonitrile and bromochloroacetonitrile caused an increase in the incidence of squamous cell carcinomas when applied to the skin of mice in the presence of agents that promote tumour growth. No significant increase was observed for dichloroacetonitrile or trichloroacetonitrile.

Dichloroacetonitrile and bromochloroacetonitrile were direct-acting mutagens in tests on bacteria, whereas tests with dibromoacetonitrile and trichloroacetonitrile were negative. All four compounds

induced DNA damage (sister chromatid exchange and DNA strand breaks) in mammalian cells.

Studies with rats indicate that dichloroacetonitrile and trichloroacetonitrile can cause foetal deformities. A short-term reproductive and developmental toxicity study of dibromoacetonitrile in male and female rats found no evidence of reproductive toxicity at dose levels up to 150 mg/L.

A two-year study of dibromoacetonitrile in drinking water conducted recently by the US National Toxicology Program (2008) is reported to have shown clear evidence of carcinogenicity in male rats, and some evidence of carcinogenic activity in female rats, as well as clear evidence of carcinogenic activity in male and female mice, however the final report from this study is not yet available.

The NHMRC Standing Committee on Toxicity reviewed the available data for haloacetonitriles in 1991, and concluded that data were insufficient to set no-effect levels for these compounds. This finding was supported by a review by the NHMRC Water Quality Advisory Committee in 2009, but will be reassessed when the National Toxicology Program report on dibromoacetonitrile becomes available.

DERIVATION OF GUIDELINE

The World Health Organization (WHO 2004) has set a provisional guideline value for dichloroacetonitrile (0.02 mg/L) based on a 90-day study which found increased liver weight in male and female rats. This calculation involved a high uncertainty value. The WHO guideline value for dibromoacetonitrile (0.07 mg/L) is derived from the no-observed-adverse-effects level in a 13-week study of increased body weight in male rats.

These data were not considered to be sufficient to set an Australian guideline value for dichloroacetonitrile. It was also considered not appropriate to set a guideline for dibromoacetonitrile in view of the pending National Toxicology Report report on carcinogenicity for this compound.

REFERENCES

National Toxicology Program (2008) TR-544 Toxicology and carcinogenesis studies of dibromoacetonitrile (CAS No. 3252-43-5) in F344/N Rats and B6C3F1 mice (Drinking water studies) Draft abstract.

USEPA Method 551.1 (1995). Determination of chlorination disinfection by-products and chlorinated solvents in drinking water by liquid-liquid extraction and gas chromatography with electron capture detection. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

WHO (World Health Organization) (2004). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

Haloxyfop

(endorsed 2011)

GUIDELINE

Based on human health concerns, haloxyfop in drinking water should not exceed 0.001 mg/L.

RELATED CHEMICALS

Haloxyfop (CAS 69806-34-4)(Haloxyfop-methyl (CAS 69806-40-2), Haloxyfop-P-methyl (CAS 72619-32-0) belongs to the aryloxyphenoxypropionate class of chemicals. Haloxyfop is a racemic mixture while haloxyfop-R is the resolved R-enantiomer (also known as haloxyfop-P) and has the greater herbicidal activity. It is used as the methyl ester. Other pesticides in this class include diclofop-methyl and diclofop-P-methyl (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, haloxyfop would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Haloxyfop is a post-emergence herbicide for the control of a wide range of annual and perennial grass weeds in a range of agricultural crops, including pasture and fruits as well as in forests.

There are registered products that contain haloxyfop in Australia. The products are intended for professional use and are available as concentrated solutions or wettable granules to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to haloxyfop are residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of haloxyfop may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on the occurrence of haloxyfop in Australian waters were found.

TREATMENT OF DRINKING WATER

No data on drinking water treatment removal efficiency were found for haloxyfop.

MEASUREMENT

Haloxyfop can be measured by routine liquid chromatography–mass spectrometry analysis, with a limit of reporting of 0.01 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for haloxyfop is 0.0003 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.03 mg/kg bw/day from a long-term (2-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 and was established in 1987.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Haloxyfop is rapidly absorbed via the gastrointestinal tract. In mice, male rats and dogs, the major excretion route is faeces, while in female rats, monkeys and humans, it is urine. Haloxyfop is not extensively metabolised and its half life varies from 24 hours in monkeys, to 1.8 days in mice, 6.3 days in humans, and 10 days in rats.

Acute effects: Haloxyfop has a low acute oral and dermal toxicity. It is not a skin sensitiser in guinea-pigs.

Short-term effects: Short-term studies have been performed in mice, rats, dogs and monkeys and indicate that the main target organ is the liver.

In a 4-day study in mice, haloxyfop caused liver enlargement from 10 mg/kg bw/day, and in a 14-day study in rats, there were hepatocellular hypertrophy and cytoplasmic changes at 30 mg/kg bw/day. Peroxisome proliferation in the liver was measured in 4-week dietary studies in mice and rats at 0.5 mg/kg bw/day and above. Liver effects were not noted in a 5-week dietary study in dogs, where haematological changes and increase in kidney weight were observed at 45 mg/kg bw/day.

A 13-week study in monkeys resulted in a dose-related increase in liver and kidney weights and decrease in thyroid weight from 10 mg/kg bw/day to 30 mg/kg/day.

Long-term effects: In a 2-year dietary study in mice, liver changes (increased liver weight and cytoplasmic alterations in both sexes, and increased alkaline phosphatase in males) were observed from 0.6 mg/kg bw/day. Liver tumours were noted from 0.065 mg/kg bw/day. The NOEL was 0.03 mg/kg bw/day, and this study is the basis for the ADI. In a 2-year dietary study in rats, changes in the liver (increased liver weight and clinical chemistry) were observed at 0.065 mg/kg bw/day. Kidney discolouration (increased pigment in the proximal convoluted tubules) and a decrease in haematological parameters were observed at 0.1 mg/kg bw/day at 6 months. Haematological parameters and liver weight were normal at the end of the study. A 1-year study in dogs showed decreased haematological values in males from 0.5 mg/kg bw/day.

Carcinogenicity: A 2-year dietary study in mice resulted in an increased incidence of liver adenomas and carcinomas from 0.065 mg/kg bw/day. Tumours were not noted in long-term studies in rats. The carcinogenic risk to humans is considered low, as the mice liver tumours are considered to be species-specific.

Genotoxicity: Only short-term *in vitro* studies are available, and based on these, haloxyfop is not considered to be genotoxic. There are no *in vivo* studies available.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 2- and 3-generation reproduction study and developmental study in rats did not produce any evidence of effects on reproductive parameters or foetal development. In rabbits, there was a marginal increase in abnormalities and delayed development at maternotoxic dose levels that were well in excess of the likely level of human exposure.

Poisons Schedule: Haloxyfop is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.001 mg/L for haloxyfop was determined as follows:

$$0.001 \text{ mg/L} = \frac{0.03 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.03 mg/kg bw/day is the NOEL based on a long-term (2-year) study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Queensland Health (2007). Organochlorine, organophosphorous and synthetic pyrethroid pesticide, urea and triazine herbicides and PCBs in water. QHFSS SOP 16315.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Hardness (as calcium carbonate)

(endorsed 1996)

GUIDELINE

To minimise undesirable build-up of scale in hot water systems, total hardness (as calcium carbonate) in drinking water should not exceed 200 mg/L.

GENERAL DESCRIPTION

Hard water requires more soap than soft water to obtain a lather. It can also cause scale to form on hot water pipes and fittings. Hardness is caused primarily by the presence of calcium and magnesium ions, although other cations such as strontium, iron, manganese and barium can also contribute.

Total hardness is the sum of the concentrations of calcium and magnesium ions expressed as a calcium carbonate equivalent. Hardness may also be classified as carbonate (temporary) or noncarbonate (permanent) hardness. Carbonate hardness is the total alkalinity expressed as calcium carbonate, where alkalinity is the sum of the carbonate, bicarbonate and hydroxide content. Noncarbonate hardness is the difference between the total and carbonate hardness.

Degrees of hardness can be described as follows:

<60 mg/L $CaCO_3$	soft but possibly corrosive
60–200 mg/L $CaCO_3$	good quality
200–500 mg/L $CaCO_3$	increasing scaling problems
>500 mg/L $CaCO_3$	severe scaling

Public acceptance of hardness can vary considerably among communities and is generally related to the hardness that the consumer has come to expect, which in turn is due to the source of the water.

Soft water may lead to greater corrosion of pipes, although this will depend on other factors such as pH, alkalinity and dissolved oxygen concentration. Total hardness above 200 mg/L may lead to excessive scaling of pipes and fittings, and cause blockage of safety relief valves in hot water systems.

High total hardness may be a problem for supplies reliant on groundwater. Surface waters can generally be expected to have acceptable values.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Total hardness in major Australian reticulated supplies ranges between about 5 mg/L and about 380 mg/L.

MEASUREMENT

Hardness can be determined by titration of calcium and magnesium with EDTA (APHA Method 2340C 1992).

TREATMENT OF DRINKING WATER

Carbonate (temporary) hardness can be readily reduced by treatment, for example using lime softening; however, this is rarely practised for Australian drinking water. Sodium hexametaphosphate has been used to reduce scale build-up, but does not affect hardness.

HEALTH CONSIDERATIONS

Some epidemiological studies have found that hard water may have a beneficial effect on health, particularly on some types of cardiovascular disease (NAS 1977), but the data are inadequate to conclude that the association is causal.

There is some indication that soft water, with a hardness of less than about 75 mg/L, may adversely affect mineral balance.

DERIVATION OF GUIDELINE

The guideline value is based on two considerations:

- difficulty in obtaining a lather with soap;
- water with a total hardness (as calcium carbonate) above 200 mg/L can cause a rapid build-up of undesirable deposits, or scale, in hot water pipes and fittings. Removal of these deposits can be costly.

GUIDELINES IN OTHER COUNTRIES

The 1984 World Health Organization (WHO) Guideline value for total hardness is 500 mg/L. The 1993 WHO Guidelines do not provide a specific value for hardness.

The Canadian Guidelines rate over 500 mg/L as unacceptable, over 200 mg/L as poor, and 80–100 mg/L as acceptable.

The EEC standards do not include a maximum concentration for hardness, but consider a minimum concentration of at least 60 mg/L to be desirable.

REFERENCES

APHA Method 2340C (1992). Hardness: EDTA titrimetric method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

NAS (National Academy of Sciences) (1977). Drinking water and health. National Academy of Sciences, Washington DC.

NOTE: Important general information is contained in PART II, Chapter 6

Heptachlor and heptachlor epoxide

(endorsed 1996)

GUIDELINE

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).

GENERAL DESCRIPTION

Heptachlor is a broad spectrum insecticide 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. Heptachlor epoxide, an oxidation product of heptachlor, is not commercially available.

Heptachlor is moderately persistent in soil. It is transformed slowly to the epoxide, which is very resistant to further chemical or biological degradation.

Heptachlor has been detected at low nanogram per litre concentrations in water supplies in Europe and the United States. It has been found in a number of foods including human milk. The daily adult intake for heptachlor and the epoxide in the United States has been estimated at about 0.000007 mg/day (7 ng/day) and 0.0002 mg/day respectively. The 1990 Australian Market Basket Survey did not find heptachlor or the epoxide in any of the foods tested (NHMRC and NFA 1991).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Heptachlor has not been detected in major Australian drinking water supplies.

TREATMENT OF DRINKING WATER

No published reports are available on methods for the removal of heptachlor from drinking water supplies. Granular activated carbon would probably be effective.

MEASUREMENT

Heptachlor can be extracted from water using a nonpolar solvent such as pentane, and analysed using gas chromatography with electron capture detection (APHA Method 6630 Part B 1992). The limit of determination is 0.00005 mg/L (50 ng/L).

HEALTH CONSIDERATIONS

Heptachlor is absorbed rapidly from the gastrointestinal tract of rats and distributed throughout the body. It is metabolised to the epoxide and excreted in faeces.

Extensive reviews and summaries of the human and animal toxicology of heptachlor are available (IPCS 1984, JMPR 1991, IARC 1991, NHMRC 1992).

Heptachlor is acutely neurotoxic in animals and humans at high doses, and is hepatotoxic in animals. It caused liver tumours in mice, and in one study, thyroid follicular cell carcinoma in rats. At high exposure levels, heptachlor can affect the viability of the offspring of rodents and dogs.

Heptachlor has not been reported to be genotoxic or teratogenic in animals.

The International Agency for Research on Cancer has concluded that heptachlor is possibly carcinogenic to humans (Group 2B, inadequate evidence in humans, sufficient evidence in experimental animals) (IARC 1991).

DERIVATION OF GUIDELINE

The health-based guideline value of 0.0003 mg/L for heptachlor and heptachlor epoxide was determined as follows:

$$0.0003 \text{ mg/L} = \frac{0.0001 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day}}$$

where:

- 0.0001 mg/kg body weight per day is the maximum acceptable daily intake (ADI) based on a no-effect level of 0.025 mg/kg body weight per day from two studies using dogs (JMPR 1991).
- 70 kg is the average weight of an adult.
- 0.1 gives a guideline value based on 10% of the ADI.
- 2 L/day is the average amount of water consumed by an adult.

The maximum ADI value includes a safety factor of 200 (10 for interspecies variations, 10 for intraspecies variations and 2 for the inadequacy of the data base). No additional safety factors are necessary.

The World Health Organization guideline value of 0.00003 mg/L (30 ng/L) was determined using 1% of the ADI to allow for increased exposure from other sources. Such a low percentage of the ADI was considered inappropriate for Australia.

REFERENCES

APHA Method 6630 Part B (1992). Organochlorine pesticides: Liquid–liquid extraction, gas chromatographic method I. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

IARC (International Agency for Research on Cancer) (1991). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Occupational Exposures in Insecticide Application, and Some Pesticides. World Health Organization, IARC, 53.

IPCS (International Programme on Chemical Safety) (1984). Heptachlor. Environmental Health Criteria, 38. World Health Organization, I{CS.

JMPR (1991). Pesticide Residues in Food — 1991. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues. Food and Agricultural Organization of the United Nations, FAO Plant Production and Protection Paper III, Rome.

NHMRC (National Health and Medical Research Council) (1992). Cyclodiene Insecticide Use in Australia. NHMRC, AGPS, Canberra.

NHMRC and NFA (National Health and Medical Research Council and National Food Authority) (1991). The 1990 Australian Market Basket Survey. NHMRC and NFA, AGPS, Canberra.

NOTE: Important general information is contained in PART II, Chapter 6

Hexachlorobutadiene

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of hexachlorobutadiene in drinking water should not exceed 0.0007 mg/L.

GENERAL DESCRIPTION

Hexachlorobutadiene has occasionally been detected in drinking water supplies in the United States and some European countries at concentrations less than 0.005 mg/L.

Hexachlorobutadiene is used as a solvent in chlorine gas production, an intermediate in the manufacture of rubber compounds, a lubricant, a pesticide and a fumigant.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Hexachlorobutadiene has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

Granular activated carbon has proved effective in trials for the removal of hexachlorobutadiene from drinking water.

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for analysis (USEPA Draft Method 502.1 1986). An inert gas is bubbled through the sample and hexachlorobutadiene trapped on an adsorbent. The adsorbent is then heated and hexachlorobutadiene analysed using gas chromatography with electron capture detection. The limit of determination is approximately 0.0004 mg/L.

HEALTH CONSIDERATIONS

Experiments in laboratory animals have revealed that approximately 95% of the ingested dose of hexachlorobutadiene is absorbed. It has been found in the blood, liver, brain, spleen, kidney and mesentery. Hexachlorobutadiene is metabolised in the gastrointestinal tract and kidney to a number of water soluble metabolites, and excreted in the urine.

Long-term intermittent human exposure has been reported to cause higher incidences of hypotension, myocardial dystrophy, nervous system and liver disorders, and respiratory tract lesions.

In studies using rats, hexachlorobutadiene caused multiple toxicologic effects, with the kidney being the organ most affected. Kidney tumours have been induced at doses of 20 mg/kg body weight per day.

Tests for mutagenicity with different strains of bacteria have reported both positive and negative results. Some metabolites have given positive results.

The International Agency for Research on Cancer has concluded that hexachlorobutadiene is not classifiable as to its carcinogenicity to humans (Group 3, no adequate evidence in humans and limited evidence in animals) (IARC 1987).

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF GUIDELINE

The assessment of the toxicological data for hexachlorobutadiene by the World Health Organization (WHO) has been used without review. The guideline value of 0.0007 mg/L was determined as follows:

$$0.0007 \text{ mg/L} = \frac{0.2 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 0.2 mg/kg body weight per day is the no-effect level based on a 2-year feeding study using rats (Kociba 1977).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for possible carcinogenic effects and genotoxicity of some metabolites).

The WHO guideline value of 0.0006 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

Kociba RJ, Keyes DG, Jersey GC, Ballard JJ, Dittenber DA, Quast JF, Wade CE, Humiston CG, Schwetz BA (1977). Results of a two-year toxicity study with hexachlorobutadiene in rats. *American Industrial Hygiene Association Journal*, 38:589–602.

USEPA Draft Method 502.1 (1986). Volatile halogenated organic compounds in water by purge and trap gas chromatography. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Hexazinone

(endorsed 2011)

GUIDELINE

Based on human health concerns, hexazinone in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Hexazinone (CAS 51235-04-2) belongs to the triazinone class of chemicals. Another pesticide in this class is metribuzin. This class of chemicals is structurally similar to the triazine class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, hexazinone would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Hexazinone is a herbicide used for the control of annual and perennial weeds in pine forest plantations, and annual and perennial grasses, broad-leaf weeds, and vines in industrial areas and sugar cane crops.

There are registered products that contain hexazinone in Australia. The products are intended for professional use and all are available as soluble concentrates intended to be diluted and applied by handspray when used in public areas, and by groundspray and aerial spray when used in other areas. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to hexazinone is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of hexazinone may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on the occurrence of hexazinone in Australian waters could be found. Groundwater contamination has been reported in the USA up to 0.034 mg/L, and the concentration of hexazinone in surface waters can be as high as 0.14 mg/L up to 6 months after application (USEPA 1994).

TREATMENT OF DRINKING WATER

No data on drinking water treatment removal efficiency could be found for hexazinone.

MEASUREMENT

Hexazinone can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 0.01 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for hexazinone is 0.1 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 10 mg/kg bw/day from a long-term (2-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 and was first established in 1978.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Hexazinone is readily absorbed from the gastrointestinal tract. It is extensively metabolised by hydroxylation of the cyclohexyl ring, and monodemethylation of the diethylamino group. Excretion is almost complete by 24 hours, mostly as metabolites in urine and to a lesser extent in faeces.

Acute effects: Hexazinone has low acute oral toxicity and low dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 90-day oral studies in rats and dogs, there was decreased bodyweight gain at doses of 100 mg/kg bw/day in rats and at 300 mg/kg bw/day in dogs.

Long-term effects: In long-term (2-year) dietary studies in mice and rats, effects were confined to decreased bodyweight gain in rats at doses of 30 mg/kg bw/day, and hepatocellular hypertrophy and increased relative liver weight at doses of 125 mg/kg bw/day in mice. The lowest overall NOEL was 10 mg/kg bw/day in rats. This NOEL is the basis for the current ADI.

Carcinogenicity: Based on a 2-year studies in mice and rats, there is no evidence of carcinogenicity for hexazinone.

Genotoxicity: Hexazinone is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: No reproduction studies have been conducted. Developmental toxicity studies in rats and rabbits did not produce any evidence of effects on foetal development.

Poisons Schedule: Hexazinone is in Schedules 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for hexazinone was determined as follows:

$$0.4 \text{ mg/L} = \frac{10 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 10 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Queensland Health (2007). Organochlorine, organophosphorous and synthetic pyrethroid pesticide, urea and triazine herbicides and PCBs in water. QHFSS SOP 16315.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th edition, British Crop Production Council, UK.

USEPA (United States Environmental Protection Agency) (1994). Reregistration eligibility decision (RED) for hexazinone. USEPA.

NOTE: Important general information is contained in PART II, Chapter 6

Hydrogen sulfide

Sulfide

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations, the concentration of hydrogen sulfide in drinking water should not exceed 0.05 mg/L.

No health-based guideline value has been set for hydrogen sulfide, or sulfide, as the aesthetic guideline is considerably below the concentration that would cause health problems.

GENERAL DESCRIPTION

Hydrogen sulfide is formed in drinking water by the hydrolysis of soluble sulfides, or through the reduction of sulfate by the action of microorganisms. Both processes require anoxic conditions. In well-oxygenated water, sulfide will be chemically or biologically oxidised to sulfate or elemental sulfur, and concentrations are extremely low. Higher concentrations can occur in anoxic water drawn from deep storages.

In water, hydrogen sulfide will be in equilibrium with the sulfide and hydrosulfide ions. The ratio will depend on pH, temperature and salinity. At pH 7.4, about a third will be present in undissociated form, with the remainder present as hydrosulfide. Above pH 10, the sulfide ion will be the dominant form; below pH 5, undissociated hydrogen sulfide will predominate.

Hydrogen sulfide has an obnoxious 'rotten egg' gas odour, with a taste and odour threshold of 0.05 mg/L. High concentrations in air can have a deceptively sweet smell and cause 'olfactory fatigue' (a deadening of the sense of smell).

Hydrogen sulfide is used industrially in the production of sulfur, sulfuric acid, inorganic sulfides, thiophenes and other organic compounds. It occurs as a by-product in a number of processes including petrol refining, coke ovens, paper mills, iron smelters, food processing and tanneries. It is present in sewers and is a major component of sewage odour.

Data on the concentration of hydrogen sulfide in food are scarce, although a number of foods and drinks are known to contain sulfides.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for hydrogen sulfide, or sulfide.

TREATMENT OF DRINKING WATER

Hydrogen sulfide can be removed from drinking water by keeping the water well oxygenated.

MEASUREMENT

The sulfide concentration of drinking water can be determined using the methylene blue colorimetric method (APHA Method 4500-S^{2-} Part D 1992). The limit of determination is 0.02 mg/L.

HEALTH CONSIDERATIONS

Soluble sulfides are absorbed rapidly from the gastrointestinal tract, although hydrogen sulfide is absorbed principally by the lung. Animal studies have indicated that after absorption, hydrogen sulfide is distributed to the brain, liver, kidneys, pancreas and small intestine.

An extensive review and summary of the human and animal toxicity data for hydrogen sulfide is available (IPCS 1981).

There are no data on the human health effects of ingesting water that contains hydrogen sulfide. Ingestion of sulfides has been known to cause nausea, vomiting and irritation of the mucous membranes. Inhalation of hydrogen sulfide is known to be extremely toxic to humans, with exposure to amounts as low as 5 ppm for 30 minutes or more producing headaches, dizziness, nausea, gastrointestinal disorders and breathing problems. Inhalation of concentrations above 500 ppm can cause cardiac failure and death.

Animal data are mainly from short-term inhalation studies. Effects include neurotoxic activity and distortions in cardiac rhythm.

No long-term carcinogenicity bioassays have been undertaken on hydrogen sulfide. Sodium sulfide did not induce cancers in experimental animals. Hydrogen sulfide was not found to be mutagenic in tests with different strains of bacteria.

DERIVATION OF GUIDELINE

The guideline value of 0.05 mg/L is based on the aesthetic considerations of taste and odour. Insufficient data are available to determine a guideline value based on health considerations. The guideline value is, however, considerably lower than the concentration likely to have a harmful effect and it is therefore unlikely that a person would consume a harmful dose.

REFERENCES

APHA Method 4500-S^{2-} Part D (1992). Sulfide: Methylene blue method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

IPCS (International Programme on Chemical Safety) (1981). Hydrogen Sulfide. Environmental Health Criteria, 19. World Health Organization, IPCS.

NOTE: Important general information is contained in PART II, Chapter 6

Imazapyr

(endorsed 2011)

GUIDELINE

Based on human health concerns, imazapyr in drinking water should not exceed 9 mg/L.

RELATED CHEMICALS

Imazapyr (CAS 81334-34-1) belongs to the imidazolinone class of chemicals. Other pesticides in this class include imazamox and imazethapyr (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, imazapyr would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Imazapyr is a broad spectrum herbicide for the pre- and post-emergence control of certain annual grass and broad-leaf weeds in agricultural crops

There are registered products that contain imazapyr, or its isopropylamine or ammonium salt, in Australia. The products are intended for professional use and are available as soluble concentrates or water-dispersible granule formulations which are diluted and applied using ground boom sprayers. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to imazapyr is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of imazapyr may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for imazapyr in Australian waters were found. In the USA, the modelled estimated surface and groundwater concentration were 0.34–79 µg/L and 39 µg/L, respectively (USEPA 2006).

TREATMENT OF DRINKING WATER

No data on drinking water treatment removal efficiency were found for imazapyr.

MEASUREMENT

Imazapyr can be measured in water by liquid chromatography–mass spectrometry with an electrospray interface, with a limit of detection of 0.004 µg/L (D'Ascenzo *et al.* 1998).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for imazapyr is 2.5 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 250 mg/kg bw/day from a 1-year dietary study in dogs. 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.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Imazapyr is readily and extensively absorbed via the gastrointestinal tract in rats. It was rapidly excreted in the urine and faeces (within 2 days).

Acute effects: Imazapyr and its isopropylamine salt have low acute oral toxicity and low dermal toxicity. Neither imazapyr nor its isopropylamine salt is a skin sensitiser.

Short-term effects: In a 13-week dietary study in rats, no treatment-related effects were observed at the highest dose tested (879 mg/kg bw/day).

Long-term effects: In an 18-month dietary study in mice, there was no evidence of treatment-related toxicity at the highest dose tested (1639 mg/kg bw/day). In 1-year dietary studies in rats and dogs, there was no evidence of treatment-related toxicity at the highest dose tested (639 and 250 mg/kg bw/day in rats and dogs respectively). The NOEL of 250 mg/kg bw/day in dogs is the basis of the current ADI.

Carcinogenicity: There was no evidence of carcinogenicity, based on an 18-month dietary study in mice and a 2-year dietary study in rats.

Genotoxicity*:* Imazapyr is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive or developmental effects.

Poisons Schedule: Imazapyr is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 9 mg/L for imazapyr was determined as follows:

$$9\ \text{mg/L} = \frac{250\ \text{mg/kg bodyweight/day} \times 70\ \text{kg} \times 0.1}{2\ \text{L/day} \times 100}$$

where:

- 250 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.

NOTE: Important general information is contained in PART II, Chapter 6

- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

D'Ascenzo G, Gentili A, Marchese S, Perret D (1998). Development of a method based on liquid chromatography-electrospray mass spectrometry for analyzing imidazolinone herbicides in environmental water at part-per-trillion levels. *Journal of Chromatrography A*, 800(1):109-119.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

USEPA (United States Environmental Protection Agency) (2006). Reregistration Eligibility Decision for Imazapyr. EPA 738-R-06-007, OPP-2005-0495.

NOTE: Important general information is contained in PART II, Chapter 6

Iodine, Iodide

(endorsed 2011)

GUIDELINE

Iodide: Based on health considerations, the concentration of iodide in drinking water should not exceed 0.5 mg/L.

Iodine: No guideline value has been set for molecular iodine.

GENERAL DESCRIPTION

The element iodine is present naturally in seawater, nitrate minerals and seaweed, mostly in the form of iodide salts. It may be present in water due to leaching from salt and mineral deposits. Iodide can be oxidised to molecular iodine with strong disinfectants such as chlorine.

Molecular iodine solutions are used as antiseptics and as sanitising agents in hospitals and laboratories. Iodine is occasionally used for the emergency disinfection of water for field use but is not used for disinfecting larger drinking water supplies. Iodide is used in pharmaceutical and photographic materials.

Iodine has a taste threshold in water of about 0.15 mg/L.

Iodide occurs in cows' milk and seafood. Some countries add iodide to table salt to compensate for iodide-deficient diets.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Concentrations of iodide in Australian source or treated water ranges from 0.005 to 2.9 mg/L (median 0.03 mg/L, mean 0.1 mg/L).

TREATMENT OF DRINKING WATER

It is unlikely that the concentration of iodine or iodide in drinking water would ever be high enough to justify water treatment.

MEASUREMENT

The iodine or iodide concentration in drinking water can be determined using the Leuco crystal violet method (APHA 4500-I-, Part B 1992). The limit of determination is approximately 0.01 mg/L.

A test for iodide alone may not determine all the iodide present at the time of sampling (given the equilibrium between iodine species in water – molecular iodine, iodide, iodate, and hypoiodite). A screening test for total iodine may be carried out by inductively coupled plasma mass spectrometry. If total iodine is found to be elevated, then analysis for iodide may be carried out by ion selective electrode, with further investigation and sampling if necessary.

HEALTH CONSIDERATIONS

Iodine is an essential trace element for humans and is used in the synthesis of thyroid hormones. Tolerable upper intake levels for iodine in children and adults recommended by Food Standards Australia and New Zealand (FSANZ 2008) are 0.2 and 1.1 mg/day respectively.

Iodine is efficiently absorbed by the gastrointestinal tract and deposited in the thyroid gland, the eye, and muscle tissue. More than 70% is found in the thyroid gland.

High oral doses (more than 30 mg/kg bodyweight) of iodine can be lethal. Lower doses (3.3 mg/kg bodyweight) have been used to treat asthmatic patients without adverse effects.

Chronic exposure to high amounts of iodide in the diet (over 2 mg/day) can result in a condition known as iodism. Symptoms resemble those of a sinus cold. Long-term consumption of iodinated drinking water has not been associated with adverse health effects in humans. Prisoners drinking water containing up to 1 mg/L iodine for five years showed no signs of iodism or hypothyroidism, but some changes in uptake of iodine by the thyroid gland were observed.

Animal studies using chickens susceptible to autoimmune thyroiditis reported an increase in the incidence of the disease when they were given high doses of iodide in their drinking water (200 mg/L). Excessive iodide consumption may increase the incidence of this disease in humans.

Iodide has not been shown to increase the incidence of cancer of the thyroid in laboratory animals. No data are available on the mutagenic activity of iodine.

DERIVATION OF GUIDELINE

In healthy adults, sub-clinical hypothyroidism is associated with intakes of 1.7 to 1.8 mg/day, and for children with intakes of 1.15 mg/day (EFSA 2006, FSANZ 2008). Chronic iodine intakes of approximately 1 mg/day, however, appear to be well tolerated by healthy adults. This is consistent with the provisional maxium tolerated daily intake of 1 mg/day established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA 1989), and the nutrient reference value and tolerable upper intake level of 1.1 mg/day respectively recommended by the NHMRC (2006) and Food Standards Australia New Zealand (FSANZ 2008) for iodine intake by adults in Australia and New Zealand.

The majority of iodine is taken in via the diet. Food Standards Australia New Zealand noted that Australian and New Zealand dietary intakes of iodine were the same (FSANZ 2008). The daily dietary intake of New Zealanders 5 years old and over is 0.1 mg/person (FSANZ 2008). It has been proposed that table salt and salt used in bread be mandatorily fortified with iodine; if this occurs, intake would rise to 0.2 mg/person.

Applying the method of International Program on Chemical Safety (IPCS 2002) for essential trace elements, a drinking water guideline of 0.5 mg/L (rounded up) can be calculated:

$$0.45 \text{ mg/L} = \frac{1.1 \text{ mg/person} - 0.2 \text{ mg/person}}{2 \text{ L/day}}$$

Where:

- 1.1 mg/person is the tolerable daily intake for iodine.
- 0.2 mg/person is the background dietary intake assuming mandatory salt fortification.
- 2 L/day is the estimated maximum amount of water consumed by an adult.

Recent data from studies on rats indicate that the effects of molecular iodine in drinking water on thyroid hormone concentrations in the blood differ from those of iodide. The guideline value therefore applies only to iodide. No guideline value can be established for molecular iodine.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

APHA Method 4500-I-Part B (1992). Iodide: Leuco crystal violet method. *Standard Methods for the Examination of Water and Wastewater*, 18th edition. American Public Health Association, Washington.

EFSA (European Food Safety Authority (2006). Tolerable upper intake levels for vitamins and minerals. EFSA.

FSANZ (Food Standards Australia New Zealand) (2008). Final Assessment Report: Proposal P230. Consideration of mandatory fortification with iodine for New Zealand. FSANZ.

IPCS (International Programme on Chemical Safety) (2002). Principles and methods for the assessment of risk from essential trace elements. Environmental Health Criteria 228. World Health Organization, IPCS, Geneva, Switzerland.

JECFA (Joint FAO/WHO Expert Committee on Food Additives) (1989). Toxicological evaluation of certain food additives and contaminants: Iodine. World Health Organization Food Additive Series, 24, 267-294. The 33rd meeting of the Joint FAO/WHO Expert Committee on Food Additives, Geneva, Switzerland.

NHMRC (National Health and Medical Research Council) (2006). *Nutrient Reference Values for Australia and New Zealand including Recommended Dietary Intakes*. NHMRC, Commonwealth of Australia, Canberra. Available at https://www.nhmrc.gov.au/about-us/publications/nutrient-reference-values-australia-and-new-zealand-including-recommended-dietary-intakes

NOTE: Important general information is contained in PART II, Chapter 6

Iprodione

(endorsed 2011)

GUIDELINE

Based on human health concerns, iprodione in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Iprodione (CAS 36734-19-7) belongs to the dicarboximide class of chemicals. Another pesticide in this class is procymidone (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, iprodione would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Iprodione is a fungicide for the control of disease in a wide range of agricultural crops.

There are registered products that contain iprodione in Australia. The products are intended for professional use and are available as a suspension concentrate, suspoemulsion or wettable granule formulation. They are applied as either a dilute or concentrated spray to crops and turf, or as a liquid seed dressing. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to iprodione is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of iprodione may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of iprodione in Australian drinking waters were found.

TREATMENT OF DRINKING WATER

No reports of the treatment of iprodione in drinking water were found. However, research indicates that ultraviolet photolysis and advanced oxidation are likely to be effective treatment processes (Garbin *et al.* 2007).

MEASUREMENT

Iprodione can be measured in water by solid phase extraction followed by high performance liquid chromatography with diode array detection (D'Archivio *et al*. 2007). The reported limit of quantitation for the technique in groundwater is 0.05 µg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for iprodione is 0.04 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 4 mg/kg bw/day from a 1-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 and it was established in 1986.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Iprodione is extensively metabolised and excreted in the urine and faeces, almost completely within 96 hours.

Acute effects: Iprodione has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: Short-term studies in mice and dogs identified the liver as the major target organ. In short-term dietary studies in mice, reduced bodyweight gain and histopathological changes in the liver, testes, kidney and urinary bladder were seen at 900 mg/kg bw/day. In a 5-month dietary study in rats, no treatment-related adverse effects were reported at the highest dose tested of 50 mg/kg bw/day. In a 3-month dietary study in dogs, there was slight liver hypertrophy and changes in clinical chemistry at 180 mg/kg bw/day.

Long-term effects: In 1- and 2-year dietary studies in mice and rats, there were changes in spleen and kidney histopathology in rats at 12 mg/kg bw/day, testicular interstitial cell hyperplasia in both mice and rats at 115 mg/kg bw/day, changes in liver histopathology in mice at 115 mg/kg bw/day, and increased organ weights in mice at 575 mg/kg bw/day.

In a 1-year dietary study in dogs, changes in liver and prostate weights and histological changes within the adrenal glands, kidneys, liver and urinary bladder were observed at 25 mg/kg/bw/day. At 151 mg/kg bw/day, there were also changes in haematological and clinical chemistry parameters. The NOEL was 4 mg/kg bw/day and this is the basis for the current ADI.

Carcinogenicity: In mice, there was an increased incidence of benign and malignant liver cell tumours and ovarian luteomas at 575 mg/kg bw/day. In rats, there was an increased incidence of benign testicular tumours (interstitial cell tumours and bilateral interstitial cell tumours) at 65 mg/kg bw/day. These effects were noted at dose levels well in excess of the likely level of human exposure in drinking water.

Genotoxicity: Iprodione is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a 3-generation reproduction study in rats, there was no effect on reproductive parameters at the highest dose tested (119 mg/kg bw/day), however, the litter size and pup bodyweights were reduced in the third generation at the high dose in the absence of maternal toxicity. In a separate 2-generation study in rats, there were no effects on reproductive parameters or on pups. In developmental studies in rats and rabbits, there was no evidence of effects on foetal development at doses that did not result in maternotoxicity.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Iprodione is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for iprodione was determined as follows:

$$0.1 \text{ mg/L} = \frac{4 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 4 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

D'Archivio AA, Fanelli M, Mazzeo P, Ruggieri F (2007) Comparison of different sorbents for multiresidue solid-phase extraction of 16 pesticides from groundwater coupled with high-performance liquid chromatography. *Talanta,* 71(1):25-30.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Garbin JR, Milori D, Simoes ML, da Silva WTL, Neto LM (2007) Influence of humic substances on the photolysis of aqueous pesticide residues. *Chemosphere,* 66(9):1692-1698.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Iron

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (precipitation of iron from solution and taste), the concentration of iron in drinking water should not exceed 0.3 mg/L.

No health-based guideline value has been set for iron.

GENERAL DESCRIPTION

Iron occurs commonly in soil and rocks as the oxide, sulfide and carbonate minerals. In water, it is present in oxidised forms as ferric (Fe(III)) or ferrous (Fe(II)) compounds.

Iron has many domestic and industrial applications, ranging from iron and steel products and pigments in paints to food colours and preparations for preventing iron deficiency in humans. Iron sulfate (hydroxylated ferrous sulfate) is used as a flocculant in water treatment.

In aerated surface waters, iron is often complexed with organic matter such as humic material, or adsorbed onto suspended matter. Iron concentrations in uncontaminated surface waters are usually less than 1 mg/L; however, water supplied through rusting iron pipes can have concentrations of 5 mg/L or higher.

In oxygen-depleted ground water, iron concentrations of up to 100 mg/L have been recorded.

Iron has a taste threshold of about 0.3 mg/L in water, and becomes objectionable above 3 mg/L. High iron concentrations give water an undesirable rust-brown appearance and can cause staining of laundry and plumbing fittings, fouling of ion-exchange softeners, and blockages in irrigation systems. Growths of iron bacteria, which concentrate iron, may cause taste and odour problems and lead to pipe restrictions, blockages and corrosion.

Food is the major source of iron intake, and iron is a natural constituent in plants and animals. Fish, green vegetables and tomatoes have high iron content.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, total iron concentrations range up to 4 mg/L, with typical concentrations around 0.1 mg/L.

TREATMENT OF DRINKING WATER

Iron salts can be effectively removed by the standard water treatment processes of coagulation followed by filtration. Groundwater supplies with a high iron content can be treated to form iron precipitates using aeration, oxidation with chlorine, pH adjustment or lime softening.

MEASUREMENT

The iron concentration in drinking water can be determined using inductively coupled plasma emission spectroscopy or graphite furnace atomic absorption spectroscopy (APHA Method 3500-Fe Parts B or C 1992). The limits of determination are 0.01 mg/L and 0.005 mg/L respectively. Alternatively the phenanthroline colorimetric method (APHA 3500-Fe Part D 1992), which has a limit of determination of 0.01 mg/L, can be used. Flame atomic absorption spectroscopy is not sufficiently sensitive.

HEALTH CONSIDERATIONS

Iron is an essential trace element for humans. Minimum daily requirement varies with age and sex. For example, women aged 11–50 years need about 14 mg per day but this requirement doubles for pregnant women, while men require about 7 mg per day. Iron deficiency is common and affects people throughout the world.

The amount of iron absorbed from food by the gastrointestinal tract varies from 1% to 20%, according to individual requirements and the source of iron. It is used in the production of haemoglobin, myoglobin and a number of enzymes, and is stored in the spleen, liver, bone marrow and muscle.

Numerous cases of iron poisoning have been reported, mainly among young children who ingest medicinal iron supplements formulated for adults. Physiological regulation of iron absorption confers a high degree of protection against iron toxicity and there are a number of reports of people, particularly adults, taking high doses of iron with no adverse effects.

Studies with animals over long periods have reported only very mild adverse effects associated with a high iron intake.

There is no evidence that iron induces cancer in laboratory animals. Most iron salts have been inactive in tests for mutagenicity and do not induce chromosome aberrations in human cells.

DERIVATION OF GUIDELINE

Insufficient data are available to determine a health-based guideline value for iron in drinking water. The guideline value is based on the taste threshold of 0.3 mg/L, which is similar to the concentration that would result in iron precipitating out of solution. Sufficient human data exist to indicate that iron in drinking water would not become a health concern unless the concentration was above 3 mg/L, well in excess of the concentration that would cause water to taste objectionable, and it is unlikely that such water would be consumed.

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NOTE: Important general information is contained in PART II, Chapter 6

Lanthanum

(endorsed 2017)

GUIDELINE

Based on human health considerations, the concentration of lanthanum in drinking water should not exceed 0.002 mg/L.

GENERAL DESCRIPTION

Lanthanum is an element in the rare earth group (also known as lanthanides group) that can enter water via run-off from agricultural soil where it has been used as fertiliser, from the weathering of rock, from specific discharges or use as a phosphate binder, and from leaching from the tailings of rare earth mining.

In water, lanthanum's oxidation state is primarily trivalent and it may be present in varying amounts as dissolved lanthanum or as insoluble forms associated with particulates. The concentration of total lanthanum in raw drinking water sources in the Netherlands was reported to range between 0.0005 to 0.013 mg/L, although concentrations in surface waters within rare earth mining areas or downstream of some industrial activities may be much higher (de Boer *et al* 1996, Protano and Riccobono 2002, Kulaksiz and Bau 2011).

An assessment estimating the total daily intake of lanthanum in humans was not available.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for lanthanum. Limited analytical results from a small number of water sources in Australia indicate levels orders of magnitude lower than when lanthanum is applied for phosphate control.

The National Industrial Chemical Notification and Assessment Scheme (NICNAS) recommends regular monitoring of Australian drinking water reservoirs if they have been subject to the addition of a lanthanum-based water treatment product (NICNAS 2014). In this circumstance, as part of a drinking water supply system assessment, consideration should be given to the possibility of accumulation of lanthanum in the water or sediment following multiple applications of a lanthanum-based product.

TREATMENT OF DRINKING WATER

It is expected that lanthanum levels in water will be reduced by the processes used to prepare water for drinking (e.g. coagulation, flocculation, sedimentation, filtration, pH correction, anti-scaling, or a combination of these) (NICNAS 2014).

MEASUREMENT

The concentration of lanthanum in water samples can be determined by inductively coupled plasma mass spectroscopy (ICP-MS) with a limit of reporting of less than 0.001 mg/L. The guideline value is for total lanthanum, so an analytical method should be used which measures both soluble and insoluble lanthanum.

HEALTH CONSIDERATIONS

In Australia, NICNAS reviewed the literature on lanthanum in its Secondary Notification Assessment for Phoslock™ (NICNAS 2014).

The health information for lanthanum is based on the data for soluble and insoluble lanthanum salts.

All lanthanum salts have very low oral bioavailability. The absorption and kinetics of lanthanum from lanthanum carbonate (a relatively insoluble salt) have been reasonably well studied in humans; it has an oral bioavailability of 0.00015–0.02%, but with a terminal half-life of 15–37 hours and only 1.7% of the absorbed dose excreted in urine (NICNAS 2014). The oral bioavailability of soluble forms of lanthanum may be one or two orders of magnitude higher than that of lanthanum carbonate (Pennick *et al* 2006, He *et al* 2007).

Several studies on the effects of human exposure to lanthanum carbonate, approved for medical use in non-pregnant adults with end-stage renal failure to prevent absorption of dietary phosphate, indicate that no adverse systemic effects were seen and the most frequently reported local effect following ingestion of the chemical is gastrointestinal in nature (Health Canada 2007, US FDA 2008, Swedish MPA 2006).

There is very little epidemiological data on lanthanum. The available published studies are poorly documented and inconclusive for determination of effects of lanthanum exposure due to the absence of direct exposure measurements and potential confounding factors, for example co-exposure to other chemicals in the environment (NICNAS 2014).

Lanthanum toxicity is caused by the free cation, with adverse systemic effects being observed in experimental animals from exposure to soluble lanthanum compounds. A number of oral repeat dose studies with lanthanum carbonate in a variety of animal species show no systemic toxicity relevant to humans; the observed local effect is gastric irritation due to high doses precipitating in the rodent stomach (NICNAS 2014). Repeated oral exposures of rodents to lanthanum chloride caused adverse systemic effects in the liver, and local irritation effects in the stomach (Cheng *et al* 2012, Cheng *et al* 2014, NICNAS 2014).

Studies in rodents of up to six months' exposure to lanthanum chloride have reported that it can cause histopathological neurotoxicity, learning deficiency, small but measurable increases of lanthanum in the brain after high doses, and various changes in brain biochemistry (Briner *et al* 2000, Feng *et al* 2006a, Feng *et al* 2006b, He *et al* 2008, NICNAS 2014). The no-observed-adverse-effect-level (NOAEL) for lanthanum chloride established from the critical studies is 0.1 mg/kg bw/day, based on neurotoxicity (decreased numbers of brain cells) and learning decrements (NICNAS 2014). The equivalent amount of lanthanum ion is 0.06 mg La^{3+}/kg bw/day.

There is no firm evidence that lanthanum is carcinogenic. The weight of evidence indicates that lanthanum is not mutagenic in tests with bacteria and that it does not damage DNA (NICNAS 2014).

DERIVATION OF GUIDELINE

The guideline value for lanthanum in drinking water was derived as follows:

$$0.002 \text{ mg/L} = \frac{0.06 \text{ mg/kg bw/day} \times 70 \text{ kg} \times 0.1}{100 \times 2 \text{ L/day}}$$

where:

- 0.06 mg/kg bw/day is the La^{3+} NOAEL for neurotoxic and neurobehavioural effects in rats.
- 70 kg is the average weight of an adult.

NOTE: Important general information is contained in PART II, Chapter 6

- 0.1 is a proportionality factor based on the assumption that 10% of daily intake is attributable to drinking water.
- 100 is the uncertainty factor to account for intra- and inter-species variations.
- 2 L/day is the estimated maximum amount of water consumed by an adult.

Factors for 'less than lifetime' exposure and/or uncertainty in the 'toxicological database' are not recommended because a comprehensive database for lanthanum carbonate, consisting of many repeat oral dose investigations in different species, including lifetime carcinogenicity studies, indicates only local effects at the site of application (stomach) and a NOAEL of 100 mg/kg bw/day. These toxicological studies have been performed using an insoluble lanthanum salt and such insoluble forms may be in drinking water sources to variable extents, and included in the total lanthanum analytical measurement. That is, some of the measured lanthanum may be in a form that has much less toxicity than the soluble lanthanum chloride upon which the drinking water guideline is based.

This guideline value is based on the effects of lanthanum from chronic exposure. As such, occasional detections of lanthanum above the guideline value would not normally be a human health concern.

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NOTE: Important general information is contained in PART II, Chapter 6

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Lead

(endorsed 1996)

GUIDELINE

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

GENERAL DESCRIPTION

Lead can be present in drinking water as a result of dissolution from natural sources, or from household plumbing systems containing lead. These may include lead in pipes, or in solder used to seal joints. The amount of lead dissolved will depend on a number of factors including pH, water hardness and the standing time of the water.

Lead is the most common of the heavy metals and is mined widely throughout the world. It is used in the production of lead acid batteries, solder, alloys, cable sheathing, paint pigments, rust inhibitors, ammunition, glazes and plastic stabilisers. The organo-lead compounds tetramethyl and tetraethyl lead are used extensively as anti-knock and lubricating compounds in gasoline.

Drinking water concentrations of lead reported overseas are usually less than 0.002 mg/L, but concentrations of 0.1 mg/L have been reported in Scotland where lead pipes and soft, acidic water are contributing factors.

Approximately 80% of the daily intake of lead is from the ingestion of food, dirt and dust. Food contains small but significant quantities of lead, which can increase when acidic food is stored in lead-glazed ceramic pottery or lead-soldered cans. The use of lead-free solders is becoming more widespread in the food processing industry. The average Australian adult dietary intake of lead is approximately 0.1 mg per day.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, total lead concentrations range up to 0.01 mg/L, with typical concentrations less than 0.005 mg/L.

TREATMENT OF DRINKING WATER

Lead concentrations in drinking water can be reduced by conventional methods of water treatment using coagulants or lime softening.

MEASUREMENT

The concentration of lead in drinking water can be determined by graphite furnace atomic absorption spectroscopy (APHA Method 3500-Pb Part B 1992). The limit of determination is 0.005 mg/L.

HEALTH CONSIDERATIONS

Lead can be absorbed by the body through inhalation, ingestion or placental transfer. In adults, approximately 10% of ingested lead is absorbed but in children this figure can be 4 to 5 times higher. After absorption, the lead is distributed in soft tissue such as the kidney, liver, and bone marrow where it has a biological half-life in adults of less than 40 days, and in skeletal bone where it can persist for 20 to 30 years.

In humans, lead is a cumulative poison that can severely affect the central nervous system. Infants, fetuses and pregnant women are most susceptible. Placental transfer of lead occurs in humans as early as the 12th week of gestation and continues throughout development.

Many epidemiological studies have been carried out on the effects of lead exposure on the intellectual development of children. Although there are some conflicting results, on balance the studies demonstrate that exposure to lead can adversely affect intelligence.

These results are supported by experiments using young primates, where exposure to lead causes significant behavioural and learning difficulties of the same type as those observed in children.

Other adverse effects associated with exposure to high amounts of lead include kidney damage, interference with the production of red blood cells, and interference with the metabolism of calcium needed for bone formation.

Epidemiological studies have found no association between lead and tumour incidence. Kidney tumours, however, have been reported in rats, mice and hamsters fed lead salts in their diet, but only at doses above 27 mg/kg body weight per day. Gliomas (brain tumours) have also been reported in rats. In addition, lead salts given orally to rats have increased the carcinogenic activity of known carcinogens.

Tests for mutagenicity using strains of bacteria have largely been negative. Tests using mammalian cells have been inconclusive, with some studies reporting negative results and some reporting chromosome damage.

The International Agency for Research on Cancer has concluded that lead is possibly carcinogenic to humans (Group 2B, inadequate human data but sufficient evidence in animals for inorganic lead compounds) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline value for lead in drinking water is based on a World Health Organization assessment and was determined by the need to protect young children, infants and pregnant women, the groups most at risk. The value was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.0035 \text{ mg/kg body weight per day} \times 13 \text{ kg} \times 0.2}{1 \text{ L/day}}$$

where:

- 0.0035 mg/kg body weight per day is the lead intake which, based on metabolic studies with infants, does not result in an increase in lead retention (Ziegler *et al.* 1978, Ryu *et al.* 1983).
- 13 kg is the average weight of a child at 2 years of age.
- 0.2 is the proportion of total lead intake attributable to water consumption. Sufficient data are available to indicate that 80% of intake is from food, dirt and dust.
- 1 L/day is the average amount of water consumed by a young child.

The NHMRC in 1993 established guidelines for lead in Australians, which provide the basis for establishing acceptable levels of lead in air, food, soil and water. Pending an assessment of the impact of this review on the guideline value for lead, the guideline should be regarded as an interim value.

NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Lindane

(endorsed 2011)

GUIDELINE

Based on human health concerns, lindane in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Lindane (CAS 58-89-9) belongs to the cyclodiene organochlorine class of chemicals. Another pesticide in this class is endosulfan. Lindane exists in a number of isomeric forms – lindane technical is the gamma stereoisomer; however it contains 0.5% as the alpha, beta, and delta isomers (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, lindane would not be a health concern unless the concentration exceeded 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 3-month dietary study.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Lindane is an insecticide for the control of grubs and symphylids in pineapple plantations.

There is at least one registered product containing lindane in Australia. Lindane products are intended for professional use and are available as a pre- and post-emergent insecticide on pineapple crops. They are to be diluted and applied to soil using ground or aerial spray, or by soil fumigation. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to lindane and its metabolites is residues in pineapples. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of lindane may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Lindane has been occasionally reported in Australian drinking waters in concentrations of less than 1 µg/L. Lindane has been detected indrinking water at similar concentrations in many other parts of the world (Aydin and Yurdun 1999, Badach *et al.* 2000, Na *et al.* 2006, Badach *et al.* 2007, Thacker *et al.* 2008).

TREATMENT OF DRINKING WATER

No specific data on the treatment of lindane in drinking water have been identified.

MEASUREMENT

Lindane may be measured in drinking waters by gas chromatography–mass spectrometry, with a limit of detection 0.01 µg/L (WHO 2004, Van Hoof *et al*. 2001). Alternatively, extraction from water may be undertaken using solid phase micro-extraction (Arrebola *et al*. 2004).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for lindane is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.31 mg/kg bw/day from a short-term (3-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, and was established in 1986.

The previous ADI of 0.01 mg/kg bw was established in 1975, based on a NOEL of 1.25 mg/kg bw/day from a long-term study in rats. The ADI was amended after submission of a three-month dietary study in rats that demonstrated a lower overall NOEL.

The previous health value was 0.02 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Lindane is rapidly absorbed from the gastrointestinal tract of rats, with wide distribution to tissues and moderate accumulation in fats. Metabolism is extensive, with hydroxylation and conjugation being the main pathways in humans and other mammals. Excretion is mostly through urine.

Acute effects: Lindane has high acute oral toxicity and moderate dermal toxicity. It is not a skin sensitiser in humans or guinea pigs.

Short-term effects: A 3-month oral study in rats reported kidney tubule distension, nephritis, increased liver weight and centrilobular hypertrophy at 1.6 mg/kg bw/day. Liver lesions were fully recovered and kidney lesions partially recovered after 6 weeks. The overall NOEL was 0.31 mg/kg bw/day and this NOEL is the basis for the current ADI.

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. No adverse effects were reported in mice up to 10 mg/kg bw/day. Liver toxicity in the form of hepatocyte hypertrophy, fatty infiltration, and necrosis was reported in rats at doses of 2 mg/kg bw/day, and cerebellar vacuolisation, nephritis and glomerular fibrosis at 6 mg/kg bw/day. Fibrosis in liver and kidney tissue was reported at doses of 3.75 mg/kg bw/day and increased liver weight at 15 mg/kg bw/day in dogs.

Carcinogenicity: The liver tumours noted at high dose levels in mice were not considered relevant to humans at the normal levels of exposure. There was no evidence of carcinogenicity for lindane based on a 2-year dietary study in rats.

Genotoxicity: Lindane is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats, mice and rabbits did not produce any evidence for effects on reproductive parameters or foetal development.

Poisons Schedule: Lindane is included in Schedule 2, 4, 5, and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for lindane was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.31 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.31 mg/kg bw/day is the NOEL based on a medium-term (3-month) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a health-based guideline value of 0.002 mg/L for lindane (WHO 2004).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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Maldison (Malathion)

(endorsed 2011)

GUIDELINE

Based on human health concerns, maldison in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Maldison (malathion)(CAS 121-75-5) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, including fenthion, parathion, profenofos and ethoprophos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, maldison would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Maldison is an insecticide and parasiticide for the control of various insect pests such as fruit fly and locusts on various crops, and in grain storage facilities. It is also used on dogs and cats and in aviaries for treatment of lice, brown dog tick and mange.

There are registered products containing maldison in Australia. The products are intended for both professional and home garden/veterinary use. Products are formulated as liquid concentrates (to be diluted and sprayed), dusts, lures/traps and insecticidal washes. Aerial ultra-low volume (ULV) application is permitted, as well as ground-based ULV application. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to maldison and its metabolites are the use of home garden and home veterinary products, and residues in food. Residue levels in food produced according to good agricultural practice are anticipated to be generally low.

Agricultural use of maldison may potentially lead to contamination of source waters through processes such as run-off, spray drift (especially from aerial and ULV application) or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on maldison in Australian waters. Maldison was not detected in surveys of municipal and private drinking-water supplies conducted in Canada between 1971 and 1986 (Health Canada 1989). It was detected in 4 of 949 stream samples in southern Ontario agricultural watersheds at concentrations of 0.24 to 1.8 µg/L (Health Canada 1989). In the USA, maldison has been reported in surface water at levels up to 0.18 µg/L and in drinking-water at 0.1 µg/L (ATSDR 2000, WHO 2004a).

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of maldison in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective. Maldison has been shown to have relatively high removal rates when water undergoes advanced oxidation with iron-catalysed ultraviolet irradiation and peroxide (Fenton reaction) (Huston and Pignatello 1999).

MEASUREMENT

Maldison can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 0.1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for maldison is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2 mg/kg bw/day from a 2-year dietary study in rats. This NOEL is based on inhibition of red blood cell cholinesterase. The ADI incorporates a safety factor of 100 and it was established in 2005.

The previous ADI was 0.02 mg/kg bw/day, based on a NOEL of 0.26 mg/kg bw/day for inhibition of red blood cell and plasma cholinesterase in a human study and a safety factor of 10. The NOEL in this study was not maintained due to the absence of information regarding the purity of the material tested.

The acute reference dose (ARfD) of 1.5 mg/kg bw/day for maldison was established in 2005, 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 previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Maldison is rapidly and extensively absorbed from the gastrointestinal tract. Metabolism is extensive, with oxidation to malaoxon, and further hydroxylation to another six to eight metabolites. Maldison has a low potential for accumulation, with <1% of the dose present in blood and tissues after 72 hours.

Acute effects: Maldison has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea pigs, although there is some evidence of skin sensitisation in humans.

Short-term and long-term effects: Short-term and long-term dietary studies in rats report cholinesterase inhibition as the main toxicological effect. In a 3-month study, cholinesterase inhibition occurred at 34 mg/kg bw/day and above. In a 2-year study, inhibition of red blood cell cholinesterase occurred at 29 mg/kg bw/day and above. The NOEL of 2 mg/kg bw/day in this rat study is the basis for the current ADI.

A 56-day human study reported inhibition of red blood cell cholinesterase at a dose of 0.4 mg/kg bw/day.

Carcinogenicity: Adenomas were reported in the liver in mice and rats and in the thyroid in rats at high dose levels, but these were considered rodent-specific. There was no other evidence of carcinogenicity for maldison.

Genotoxicity: Maldison is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits reported no evidence of effect on reproductive parameters or foetal development.

Neurotoxicity: Maldison did not cause delayed neurotoxicity in hens.

Poisons Schedule: Maldison (Malathion) is included in Schedule 3, 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for maldison was determined as follows:

$$0.07 \text{ mg/L} = \frac{2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for malathion and it is excluded from the list of agricultural chemicals guideline value derivation because it "occurs in drinking-water at concentrations well below those at which toxic effects may occur" (WHO 2004b).

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Mancozeb

(endorsed 2011)

GUIDELINE

Mancozeb degrades in the environment to ethylene thiourea (ETU), hence the health-based guideline for mancozeb has been based on the toxicity of ETU. Based on human health concerns, ETU in drinking water should not exceed 0.009 mg/L.

RELATED CHEMICALS

Mancozeb (CAS 8018-01-7; Ethylene thiourea CAS 96-45-7) belongs to the ethylenebis-dithiocarbamate class of chemicals. Other pesticides in this class include metiram and zineb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, the environmental degradant of mancozeb, ethylene thiourea (ETU), would not be a health concern unless the concentration exceeded 0.009 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Mancozeb is a broad spectrum fungicide for the control of fungal diseases in tree fruits, vegetable crops, field crops, and grapes, sod crops (lawns), ornamental plants and harvested seed.

There are registered products that contain mancozeb in Australia. The products are intended for professional use and are available as concentrated solutions to be applied in diluted form using ground and aerial spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: Mancozeb hydrolyses rapidly in the environment to ETU and carbon disulfide (CS_2), both of which have higher toxicity than mancozeb. It is considered highly unlikely that residues of mancozeb or its degradants will be present in food. Mancozeb residues are grouped with other dithiocarbamates (mancozeb, metham, metiram, propineb, thiram, zineb and ziram) in the maximum residue limit definition.

Agricultural use of mancozeb may potentially lead to contamination of source waters by both mancozeb and ETU through adsorption into soil and subsequent entry into ground water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for mancozeb or ETU in Australian waters were found. In the USA, the predicted surface and groundwater concentrations for ETU were 0.1–25.2 µg/L and 0.21 µg/L, respectively (USEPA 2005). The parent compound is short-lived in soil and water and is not expected to reach water used for human consumption (USEPA 2005).

TREATMENT OF DRINKING WATER

Chlorine dioxide and ozonation appear moderately effective at removing mancozeb and ETU from water, however these processes produce as-yet undefined degradation products (Hwang *et al.* 2003).

MEASUREMENT

Mancozeb can be measured in water by liquid chromatography mass spectrometry with an electrospray interface, with a limit of detection of 0.04 µg/L (Hanada *et al.* 2002). ETU can be measured by gas chromatrography with nitrogen-phosphorous detector, with a limit of detection of 2.7 µg/L (USEPA 1992).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for mancozeb is 0.006 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.6 mg/kg bw/day from a long-term (1-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 and was first established in 1993. There is currently no ADI for ETU.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Mancozeb is rapidly and extensively absorbed from the gastrointestinal tract of rats and widely distributed in tissues, particularly the thyroid. A small percentage (3–6%) is metabolised to ETU. Excretion is rapid, mainly as unchanged compound in faeces and urine, and is almost complete by 5 days. ETU is also excreted in the urine.

Acute effects: Mancozeb is of low acute oral and dermal toxicity in mammals. It is a skin sensitiser in humans, based on reports from occupational exposure. ETU has low acute oral toxicity.

Short-term effects: Short-term dietary studies with mancozeb were conducted in mice, rats and dogs. Thyroid hyperplasia was observed in rats at 7.5 mg/kg bw/day. Histopathological changes were also observed in other organs at 30 mg/kg bw/day and above in dogs and mice. In rats, organ weight and histopathological changes were observed in several organs at 60 mg/kg bw/day, as well as decreased serum thyroxine levels. In dogs, decreased bodyweight gain and serum thyroxine levels, as well as clinical chemistry changes were seen at 150 mg/kg bw/day.

In short-term studies with ETU, the thyroid was the target organ. In a dietary study in rats over 14 days, histological changes including thyroid hyperplasia, bone marrow depletion, and lymphatic lesions occurred from 25 mg/kg bw/day. When administered in the drinking water of rats over 28 days, decreased levels of thyroxine and serum triiodothyronine, increased levels of thyroid stimulating hormone in serum, and thyroid follicular necrosis were seen at doses from 10.6 mg/kg bw/day. Other effects seen at 17.6 mg/kg bw/day and above include proximal tubule kidney cell hypertrophy and vacuolisation.

In 3- and 4-month dietary studies in rats and mice with ETU, effects in rats included follicular cell hypertrophy and thyroid hyperplasia from 3 mg/kg bw/day and above. At higher doses there was also increased relative thyroid weight and decreased iodine uptake into the thyroid at 8 mg/kg

NOTE: Important general information is contained in PART II, Chapter 6

bw/day; decreased levels of thyroxine and increased levels of thyroid stimulating hormone in serum, and increased absolute thyroid weights at 10 mg/kg bw/day; and thyroid adenomas at 12.5 mg/kg bw/day. In mice, thyroid adenomas and pituicyte vacuolisation occurred from 12.5 mg/kg bw/day, hepatocellular hypertrophy from 37.5 mg/kg bw/day, and thyroid hyperplasia from 75 mg/kg bw/day. The lowest overall NOEL was 2 mg/kg bw/day (rats) in these studies.

Long-term effects: Long-term dietary studies with mancozeb were conducted in mice, rats and dogs. Decreased iodine uptake into the thyroid was reported at 2.4 mg/kg bw/day in dogs and thyroid hyperplasia at 3 mg/kg bw/day in rats. In mice, effects were confined to decreased bodyweight gain at 150 mg/kg bw/day. The lowest overall NOEL was 0.6 mg/kg bw/day in dogs. This NOEL is the basis for the current ADI.

In a 1-year rat study with ETU, there was increased thyroid vascularisation and thyroid acinar cell papillation at the lowest dose tested of 0.025 mg/kg bw/day. At 1.25 mg/kg bw/day, there was decreased bodyweight gain. Increased relative thyroid weight occurred at 7 mg/kg bw/day and thyroid tumours at 15 mg/kg bw/day.

In a 2-year rat study with ETU, thyroid hyperplasia, elevated TSH and decreased triiodothyronine and thyroxine were seen at the lowest dose of 0.25 mg/kg bw/day. Thyroid carcinomas were observed at 8.7 mg/kg bw/day. In a 2-year mouse study with ETU, decreased bodyweight gain, increased TSH, thyroid cell hypertrophy and hyperplasia and thyroid adenomas and carcinomas were observed at the lowest dose tested of 16 mg/kg bw/day.

Carcinogenicity: Based on long-term studies in rats with both mancozeb and ETU, there was evidence of an increased incidence of tumours (adenomas and carcinomas) in the thyroid at high dose levels only, which are well in excess of the likely level of human exposure. In mice, ETU produced thyroid follicular-cell tumours and tumours of the liver and anterior pituitary gland. However, due to its nongenotoxicity and disturbance of thyroid function, ETU would not be expected to produce thyroid cancer in humans exposed to concentrations that do not alter thyroid hormone homeostasis.

Genotoxicity: Mancozeb is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies. ETU was positive in some *in vitro* short-term assays, but overall, it is not considered to be genotoxic.

Reproductive and developmental effects: Two and three-generation reproduction studies in rats and developmental studies in mice, rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development. Developmental studies in rats and rabbits with ETU caused effects on development only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Mancozeb is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.009 mg/L for the degradant of mancozeb, ETU, was determined as follows:

$$0.009 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 1}{2 \text{ L/day} \times 1000}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 0.25 mg/kg bw/day is the LOEL based on a long-term (2-year) dietary study in rats on ETU.
- 70 kg is taken as the average weight of an adult.
- The proportionality factor is 1 since mancozeb has no residues in food and is degraded to ETU in the environment. It is assumed, therefore, that 100% of the ADI (nominal in this case) for ETU will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the LOEL for ETU derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation, and an additional factor of 10 because a LOEL was used to derive the guideline.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Manganese

(endorsed 2011)

GUIDELINE

Based on aesthetic considerations, the concentration of manganese in drinking water should not exceed 0.1 mg/L, measured at the customer's tap.

Manganese would not be a health consideration unless the concentration exceeded 0.5 mg/L.

GENERAL DESCRIPTION

Manganese is present in the environment in the divalent (Mn(II)), tetravalent (Mn(IV)), and heptavalent (Mn(VII)) states. Most of the divalent compounds are soluble in water. The most common tetravalent compound, manganese dioxide, is insoluble; however, the heptavalent permanganate is soluble.

Manganese is principally used in the manufacture of iron, steel and alloys.

Uncontaminated rivers and streams generally have low concentrations of manganese, ranging from 0.001 mg/L to 0.6 mg/L. High concentrations may occur in polluted rivers or under anoxic conditions such as at the bottom of deep reservoirs or lakes, or in groundwater.

At concentrations exceeding 0.1 mg/L, manganese imparts an undesirable taste to water and stains plumbing fixtures and laundry. Even at concentrations of 0.02 mg/L, manganese will form a coating on pipes that can slough off as a black ooze. Some nuisance microorganisms can concentrate manganese and give rise to taste, odour and turbidity problems in distribution systems. A discretionary target of 0.01 mg/L is suggested at the treatment plant.

Manganese interferes with the commonly used DPD method for determining chlorine residual, resulting in an overestimation of the residual so that chlorine appears to be present when it may not be.

Concentrations of manganese in food can vary considerably. The highest concentrations have been reported in grains, nuts and vegetables, while tea leaves can have extremely high concentrations.

It has been estimated that the average dietary intake of manganese is 2–4 mg per day.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, manganese concentrations can range up to 1.41 mg/L, with typical concentrations less than 0.01 mg/L. For regional NSW, for example, a median value of 0.005 mg/L was found over a nine-year period.

TREATMENT OF DRINKING WATER

Manganese concentrations in drinking water can be lowered by converting soluble forms to insoluble precipitates, followed by filtration. Manganese levels below 0.02 mg/L can be achieved with a well operated and optimised potassium permanganate system. Achieving <0.01 mg/L manganese in treated water is not possible with potassium permanganate alone, so high pH coagulation processes or a two-stage filtration process are employed at several plants; however, this process will not be suitable for all waters. Pre-filtration chlorination can help to achieve a target of 0.01 mg/L.

MEASUREMENT

The manganese concentration in drinking water can be determined using inductively coupled plasma emission spectroscopy or graphite furnace atomic absorption spectroscopy (APHA Method 3500-Mn Parts B or C, 1992). The limits of determination are 0.005 mg/L and 0.001 mg/L respectively.

HEALTH CONSIDERATIONS

Manganese is an essential element and is required by mammals and birds for normal growth. Manganese deficiency affects bone, the brain and reproduction in a number of animal species. Although no specific symptoms have been described in humans, it has been suggested that manganese deficiency may be associated with anaemia and, in children, with bone disorders.

Owing to the low solubility of manganese in gastric juices, only 3-8% of ingested manganese is absorbed by the gastrointestinal tract. After absorption, it is concentrated in the liver and eventually excreted in faeces. In humans it has a relatively short biological half-life of 13 to 37 days.

An extensive review and summary of the human and animal toxicity data for manganese is available (IPCS 1981).

In humans, manganese toxicity has occurred mainly as a result of inhalation of manganese dust over long periods. By the oral route, manganese is regarded as one of the least toxic elements.

In one case involving heavy consumption of highly contaminated well water, resulting symptoms included lethargy, increased muscle tone, tremor and mental disturbances. Concentrations of manganese were over 14 mg/L; however, concentrations of other metals were also high and the reported effects may not have been due solely to manganese.

Experiments with laboratory animals have shown no adverse effects other than a change in appetite and a reduction in the metabolism of iron in haemoglobin synthesis.

There is no firm evidence that manganese is carcinogenic. Some studies indicate that it may, in fact, have an anticarcinogenic effect. Some *in vitro* studies using mammalian and bacterial cells have reported that manganese acts as a mutagen.

DERIVATION OF GUIDELINES

The aesthetic guideline of 0.1 mg/L at the customer's tap is based on practical experience and has been reported by utilities to be acceptable to customers. The discretionary target of 0.01 mg/L at the treatment plant is also based on experience; that although manganese accumulates in distribution systems, a plant producing 0.01 mg/L generally does not generate customer complaints, while a concentration of 0.02 mg/L or more tends to lead to various problems.

The health-based guideline value for manganese in drinking water can be derived as follows:

$$0.5 \text{ mg/L} = \frac{10 \text{ mg/day} \times 0.1}{2 \text{ L/day}}$$

where:

- 10 mg/day is the amount of manganese that can be safely consumed from all sources (WHO 1973).
- 0.1 is a proportionality factor based on the assumption that 10% of daily intake is attributable to the consumption of water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.

The maximum tolerable daily intake value includes adequate safety factors, so no additional safety factors are necessary. This value exceeds the concentration at which manganese can cause taste and odour problems.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

MCPA

(endorsed 2011)

GUIDELINE

Based on human health concerns, MCPA in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

2-methyl-4-chlorophenoxyacetic acid (MCPA)(CAS 94-74-6) belongs to the phenoxycarboxylic acid class of chemicals. Other pesticides in this class include 2,4-D, 2,4-DB, dichlorprop, dichlorprop-P, MCPB and mecoprop (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, MCPA would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: MCPA is a herbicide for the control of various broad-leaf weeds in crops, pastures and turf.

There are many registered products that contain MCPA or its salt/variants in Australia. The products are intended for professional and home garden use and are generally available as emulsifiable concentrates, aqueous concentrates and liquids to be applied using ground boom, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to MCPA are the use of home garden products and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of MCPA may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for MCPA in Australian waters could be found, however it has occasionally been measured in some Australian drinking-water supplies at concentrations generally less than 1 µg/L. In the USA, MCPA was detected up to 0.54 µg/L in surface waters and up to 5.5 µg/L in groundwater (WHO 2003).

TREATMENT OF DRINKING WATER

No data on drinking water treatment removal efficacy could be found for MCPA, although activated carbon is expected to be quite effective, based on its structure.

MEASUREMENT

MCPA can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 0.01 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for MCPA is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.1 mg/kg bw/day from a 2-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, and was established in 1994.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: MCPA is readily absorbed via the gastrointestinal tract. It is not extensively metabolised, and is rapidly excreted, mainly unchanged, in the urine.

Acute effects: MCPA has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 13-week dietary studies in rats and dogs, there was evidence of kidney and liver damage. In rats, increased kidney weights were reported at 7.5 mg/kg bw/day and increased creatinine and decreased calcium at 22.5 mg/kg bw/day. In dogs, increased serum glutamic pyruvic transaminase, blood urea nitrogen and creatinine levels were reported at 3 mg/kg bw/day. Decreased bodyweight gain and bile duct proliferation were reported at 12 mg/kg bw/day, and gross pathological changes in the liver and microscopic changes in both the liver and kidney at 48 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice and rats. A 2-year mouse study reported pathological changes in the kidney at 71.4 mg/kg bw/day. A 2-year rat study reported an increase in serum glutamic pyruvic transaminase levels at 4 mg/kg bw/day. At 16 mg/kg bw/day there was a slight decrease in bodyweight gain, haemosiderosis in the spleen, and an increase in absolute kidney weight in males, accompanied by evidence of chronic nephropathy. The NOEL of 1.1 mg/kg bw/day in the rat study is the basis for the current ADI.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for MCPA.

Genotoxicity: MCPA is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats reported reduced pup bodyweight gain at 15 mg/kg bw/day and above. Developmental studies in rats and rabbits reported decreased bodyweight gain and increased post-implantation loss at 75 mg/kg bw/day. There were no effects at lower dose levels on reproductive parameters or foetal development.

Poisons Schedule: MCPA is included in Schedule 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.04 mg/L for MCPA was determined as follows:

$$0.04 \text{ mg/L} = \frac{1.1 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.1 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a health-based guideline value of 0.002 mg/L for MCPA (WHO 2004).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Mercury

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of total mercury in drinking water should not exceed 0.001 mg/L.

GENERAL DESCRIPTION

Natural release of mercury into drinking water is extremely low, but contamination can result from industrial emission or spills. Mercury compounds fall into two categories: inorganic mercury salts, many of which are very insoluble in water; and organic mercury compounds, the most notable being methyl mercury. Inorganic mercury can be converted into methyl mercury, possibly by the action of bacteria in sediments, and can then readily enter the food chain.

Mercury is used widely in electrical components including cells, lamps, arc rectifiers and switches. It is also used in dental amalgams, fungicides, antiseptics, preservatives and pharmaceuticals.

Concentrations of total mercury in natural water are generally so low that accurate analysis is difficult. Studies overseas have reported concentrations of less than 0.0005 mg/L, with some sources less than 0.00003 mg/L (30 ng/L). The highest value was 0.0055 mg/L from some wells in Japan.

Food is the main route of exposure, with highest concentrations found in fish and fish products. The average Australian adult dietary intake of mercury is approximately 0.004 mg per day. Drinking water is likely to constitute only a small fraction of total intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, the concentrations of total mercury range up to 0.001 mg/L, with typical concentrations usually less than 0.0001 mg/L.

TREATMENT OF DRINKING WATER

Coagulation is moderately effective in reducing the concentration of inorganic mercury in drinking water. Granular activated carbon is effective in removing both inorganic and organic mercury from water.

MEASUREMENT

The concentration of total mercury in drinking water can be determined by the cold vapour atomic absorption method (APHA 3500-Hg Part B 1992). The limit of determination is 0.0001 mg/L.

HEALTH CONSIDERATIONS

Inorganic mercury

Less than 15% of inorganic mercury in drinking water is absorbed by the gastrointestinal tract. Inorganic mercury compounds accumulate in the kidney and have a long biological half-life, probably many years.

An extensive review and summary of the human and animal toxicity data for inorganic mercury is available (IPCS 1991).

Many studies have looked at groups of workers occupationally exposed to mercury, and have reported health effects including tremors, mental disturbances and gingivitis (inflammation of the mucous membrane surrounding the teeth). The main toxic effects are to the kidney, leading to kidney failure.

In animal studies, the principal target organs of mercury toxicity are the kidney and the central nervous system. Some disruption to ovulation in female rats has also been reported.

Various reports indicate that inorganic mercury binds to, and damages, mammalian DNA. Some evidence of carcinogenicity in rats has been reported.

Organic mercury

Organic mercury compounds are unlikely to be found in uncontaminated drinking water; however, the toxic effects are more severe than those of inorganic mercury.

An extensive review and summary of the human and animal toxicity data for methyl mercury is available (IPCS 1990).

Methyl mercury compounds are almost completely absorbed by the gastrointestinal tract. Methyl mercury has greater lipid solubility than inorganic mercury and can cross biological membranes, especially in the brain, spinal cord, peripheral nerves and placenta.

The main effects of methyl mercury poisoning are severe irreversible neurological disorder and mental disability.

In Japan, two major epidemics of methyl mercury poisoning, known as Minamata disease, were caused by the industrial release into Minamata Bay of methyl mercury and other mercury compounds. The compounds accumulated in fish, which were subsequently eaten by humans. Other countries have reported cases of poisoning caused by mercury contamination of bread and cereal.

Animal studies with rats, cats, monkeys and squirrels have shown similar results, with the main effects of long-term exposure being behavioural changes, neurological disturbances and disturbances to the movement of legs and tails.

Data are insufficient to determine the carcinogenic effects of methyl mercury; however, it is active in inducing chromosomal aberrations *in vivo*.

DERIVATION OF GUIDELINE

The guideline value for mercury in drinking water was derived as follows:

$$0.001 \text{ mg/L} = \frac{0.00047 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day}}$$

where:

- 0.00047 mg/kg body weight per day is the maximum tolerable daily intake to ensure that adverse effects will not occur (WHO 1988).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.

The maximum tolerable daily intake value includes adequate safety factors. No additional safety factors are necessary.

The guideline value was set on the basis of the toxicity of methyl mercury, as this is the most toxic form. It is likely that methyl mercury would be less than 10% of the total mercury concentration.

NOTE: Important general information is contained in PART II, Chapter 6

The guideline value should be sufficient to protect pregnant women and nursing mothers, who are at greatest risk from the adverse effects of methyl mercury. Data are insufficient to determine a separate value for this group.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Metaldehyde

(endorsed 2011)

GUIDELINE

Based on human health concerns, metaldehyde in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Metaldehyde (CAS 108-62-3) belongs to aldehyde class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, metaldehyde would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Users: Metaldehyde is used to control snails and slugs in food crops.

There are registered products containing metaldehyde in Australia. The products are for professional and home garden use and are available in bait or pellet form, as powders, and in granular formations. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to metaldehyde is the use of home garden products.

Agricultural and home garden use of metaldehyde may potentially lead to contamination of source waters through processes such as run-off or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of metaldehyde in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of metaldehyde in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

No suitable analytical techniques have been identified for analysis of metaldehyde in drinking water. However, if a need to monitor for metaldehyde is identified, it is expected that gas chromatography–mass spectroscopy should be suitable, since this technique has been used for monitoring metaldehyde in human and animal blood serum.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for metaldehyde is 0.005 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day in a rat study and applying a safety factor of 1000. The NOEL was based on neurological effects in rats and was established in 1986.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Metaldehyde is readily absorbed from the gastrointestinal tract. Only a small percentage of the parent compound is excreted in the urine.

Acute effects: Metaldehyde has a moderate acute oral toxicity and low dermal toxicity. Clinical symptoms of toxicity reported in human poisoning cases included salivation, restlessness, muscle cramps and increased heart rate, indicative of mild neurotoxicity. Similar symptoms were observed in animal studies.

Short-term effects: No short-term studies have been evaluated.

Long-term effects: A 2-year dietary study in rats reported liver enzyme changes and increased liver weight at 12 mg/kg bw/day; however, the study was poorly reported.

Carcinogenicity: Based on a long-term study in rats, there is no evidence of carcinogenicity for metaldehyde; however, the study was poorly reported.

Genotoxicity: Only short-term *in vitro* studies are available; these report no evidence that metaldehyde is mutagenic.

Reproductive and developmental effects: A 3-generation reproduction study in rats produced effects on reproductive parameters at extremely high dose levels only. No developmental toxicity studies have been evaluated.

Poisons Schedule: Metaldehyde is included in Schedule 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on the concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for metaldehyde was determined as follows:

$$0.02 \text{ mg/L} = \frac{5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 5 mg/kg bw/day is the NOEL based on a a long-term (1-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.

NOTE: Important general information is contained in PART II, Chapter 6

- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation and an additional factor of 10 because of the poor quality of the data.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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Metham

(endorsed 2011)

GUIDELINE

Metham rapidly degrades to methylisothiocyanate (MITC) in the environment, hence the health-based guideline for metham has been based on the toxicity of MITC. Based on human health concerns, MITC in drinking water should not exceed 0.001 mg/L.

RELATED CHEMICALS

Metham (CAS 144-5-54-7) belongs to the n-methyl-dithiocarbamate class of chemicals. There are no other pesticides in this class. A closely related class of chemicals is ethylenebis-dithiocarbamates, which includes mancozeb, metiram, and zineb. The insecticidal and fungicidal activity of metham sodium is due to degradation to methylisothiocyanate (MITC) in the environment. MITC is also a degradant of the pesticide dazomet (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, the degradation products of metham would not be a health concern unless the concentration exceeded 0.001 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Metham is a herbicide and insecticide for the control of tree roots, and soil-borne pests in ornamental, food and tobacco crops.

There are currently registered fumigant products that contain metham as its sodium salt. The products are for professional use only and are available as various liquids, suspensions or aqueous concentrates. Most products are for use as pre-plant soil fumigants and are applied by soil injection, rotary tiller, spot treatment, and trickle irrigation systems. Some products are for direct addition into pipes in sewage and wastewater collection systems. Methylisothiocyanate was formerly used as a soil fumigant in Australia. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: Metham is highly unstable in the environment and spontaneously hydrolyses to MITC. It is considered highly unlikely that residues of metham itself will be present in food, although it is possible there may be residues of MITC in food.

Agricultural use of metham may potentially lead to contamination of source waters by MITC through absorption into the soil moisture and subsequent leaching into groundwater. Some metham products are also added directly to sewer or wastewater pipes.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on metham occurrence in Australian drinking water supplies were found. Based on the registered use patterns for metham, exposure from drinking water is not expected and no dietary risk mitigation is warranted (USEPA 2009).

TREATMENT OF DRINKING WATER

Powdered activated carbon filtration, granulated activated carbon filtration, and reverse osmosis have been demonstrated to be highly effective processes at removing certain pesticides including dithiocarbamates (USEPA 2001a). Metham has a hydrolysis half-live of less than 1 day in alkaline (pH 9) water and can be removed during lime-soda softening (pH 10~11) by alkaline hydrolysis (USEPA 2001b).

MEASUREMENT

Metham sodium and methyl isothiocyanate (MITC) can be analysed in water by high-performance liquid chromatography (Mullins and Kirkbright 1987, Dhoot *et al.* 1993). These methods can achieve a limit of quantitation (LOQ) of 1 µg/L for MITC and 70 µg/L for metham. Direct immersion solid phase microextraction followed by gas chromatography electron capture detector or gas chromatography nitrogen phosphorus detector analysis can achieve a LOQ of 0.5 µg/L for methyl isothiocyanate in water (Fuster *et al.* 2005).

HISTORY OF THE HEALTH VALUES

An acceptable daily intake (ADI) has not been set for metham since ADIs are required only for pesticides with residues in food.

The current ADI for the degradant MITC is 0.0004 mg per kg body weight (mg/kg bw) based on a no-observed-effect level (NOEL) of 0.04 mg/kg bw/day from a 3-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.

An acute reference dose (ARfD) has not been set for metham since ARfDs are required only for pesticides with residues in food.

The current ARfD for the degradant MITC is 0.0005 mg/kg bw/day 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.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Metham sodium is readily and extensively absorbed via the gastrointestinal tract in rats. It is spontaneously hydrolysed to MITC and other alkyl isothiocyanates and isothiocarbamates including 1,3,-dimethylthiourea, ethylenethiourea (ETU), and carbon disulfide by passive chemical processes, and is rapidly excreted in the urine as mercapturic acid derivatives, and in the breath as carbon disulfide, almost completely within 48 hours.

Acute effects: Metham sodium has high acute oral toxicity in mice and moderate acute oral and dermal toxicity in rats. Metham sodium and its breakdown product MITC are skin sensitisers in humans. The breakdown product, MITC, has a similar acute oral and dermal toxicity to metham.

NOTE: Important general information is contained in PART II, Chapter 6

Short-term effects: In a 3-month oral study in dogs with the degradant MITC, an increased incidence and severity of periportal hepatocyte vacuolation and lipid deposition was seen at doses of 0.4 mg/kg bw/day and above, and decreased testis weights and increased pancreas weight at doses of 2 mg/kg bw/day. The NOEL in this study was 0.04 mg/kg bw/day and this is the basis for the current ADI for MITC.

Long-term effects: No long-term studies are available for metham (including metham sodium). In studies where the degradant MITC was added to the drinking water of rats at doses up to 2.7 mg/kg bw/day and in mice up to 27 mg/kg bw/day, the major toxicological findings were decreased food consumption and decreased bodyweight gain at doses of 2.5 mg/kg bw/day in rats, and at 14 mg/kg bw/day in mice.

Carcinogenicity: There are no carcinogenicity studies available for metham. Based on a 2-year study in mice and rats, there is no evidence of carcinogenicity for the degradant MITC.

Genotoxicity: Metham sodium and the degradant MITC were positive in some *in vitro* short-term assays, but based on the weight of evidence, neither is considered to be genotoxic.

Reproductive and developmental effects: There are no studies available on reproductive toxicity of metham sodium. A reproduction study in rats with the degradant MITC did not provide any evidence of reproductive toxicity at doses up to 10 mg/kg bw/day. In developmental toxicity studies with metham sodium, there were effects on reproduction and development, but only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Metham and MITC are both included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.001 mg/L for the degradant of metham, MITC, was determined as follows:

$$0.001 \text{ mg/L} = \frac{0.04 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.04 mg/kg bw/day is the NOEL for MITC based on a short-term (3-month) oral study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is the proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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USEPA (United States Environmental Protection Agency) (2009) Amended Reregistration Eligibility Decision (RED) for the Methyldithiocarbamate Salts (Metamsodium, Metam-potassium) and Methyl Isothiocyanate (MITC), EPA 738-R-09-310, Prevention, Pesticides and Toxic Substances.

NOTE: Important general information is contained in PART II, Chapter 6

Methidathion

(endorsed 2011)

GUIDELINE

Based on human health concerns, methidathion in drinking water should not exceed 0.006 mg/L.

RELATED CHEMICALS

Methidathion (CAS 950-37-8) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes terbufos, ethion, fenamiphos, and acephate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, methidathion would not be a health concern unless the concentration exceeded 0.006 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Methidathion is an insecticide for the control of insect pests in orchards, sub-tropical, vegetable, cereal, pasture, cotton, and sunflower agricultural crops.

There are registered products containing methidathion in Australia. The products are intended for professional use, and are available in concentrated solutions, which are diluted and applied to infested areas by ground or aerial spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to methidathion is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of methidathion may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Methidathion was not detected in the Mt Lofty Ranges, the main catchment area for Adelaide's drinking water supply (Oliver *et al*. 2005). No other published reports on methidation occurrence in Australian drinking water supplies were found. Methidathion exposures from water are expected to be non-significant, based on pesticide tolerances (USEPA 2002) and drinking water risk assessment reports (Lewis 2001).

TREATMENT OF DRINKING WATER

Water treatment processes such as granular activated carbon and membranes are capable of removing methidation (USEPA 2000). During chlorination in water treatment plants, methidathion can be oxidised forming oxons and/or other oxidation analogues (Kamel *et al*. 2009).

MEASUREMENT

Methidathion can be extracted from water by liquid/liquid and analysed by gas chromatography coupled with a nitrogen phosphorus detector and flame photometric detector. The method can achieve a limit quantitation (LOQ) of 0.05 µg/L. Methidathion can also be extracted by polypropylene hollow fiber liquid phase microextraction and analysed by gas chromatography with flame thermionic detection. The method can achieve a LOQ of 3 ng/L (Lambropoulou and Albanis 2005). Methidathion can also be accurately quantified by solid-phase extraction (SPE) and liquid chromatography (LOQ 0.01 µg/L) (Wang *et al*. 2007). SPE with multiwalled carbon nanotubes, without the need for chromatographic separation, can achieve a LOQ of 3 µg/L for methidathion (Al-Degs *et al*. 2009). SPE with liquid chromatography and tandem mass spectrometry reported a LOQ of 2.3 µg/L for methidathion (Rodrigues *et al*. 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for methidathion is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.16 mg/kg bw/day from a 90-day dietary study in dogs. The NOEL is based on increased liver cholesterol and decreased red blood cell cholinesterase activity at doses of 1.96 mg/kg bw/day and above. The ADI incorporates a safety factor of 100 and was established in 2004.

The acute reference dose (ARfD) of 0.01 mg/kg bw/day for methidathion was established in 2004, based on a NOEL of 1 mg/kg bw/day from an acute neurotoxicity study based on inhibition of red blood cell and brain cholinesterase activity in rats. The ARfD incorporates a safety factor of 100.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Methidathion is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised via hydrolysis and oxidation to sulfoxides, sulfones, and oxons. Excretion is via the urine and is almost complete within 24 hours.

Acute effects: Methidathion has a moderate to high acute oral toxicity in dogs, rats and mice, and a moderate acute dermal toxicity in rats. It is not a skin sensitiser.

Short-term effects: In a 21-day dermal toxicity study in rabbits, there was decreased red blood cell and brain cholinesterase activity at 10 mg/kg bw/day. In a 4-week oral toxicity study in rats, there was decreased red blood cell cholinesterase activity at 0.83 mg/kg bw/day. In 90-day oral toxicity studies in rats and dogs, there was decreased red blood cell cholinesterase activity and increased levels of cholesterol in the liver at 2 mg/kg bw/day. The lowest overall NOEL was 0.16 mg/kg bw/day in dogs. This is the basis for the current ADI.

In a 6-week oral toxicity study in humans, there was no effect on cholinesterase activity and no clinical signs of toxicity at 0.11 mg/kg bw/day.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: In a 2-year oral toxicity study in mice, there was no evidence of toxicity apart from clinical signs of cholinesterase inhibition at 7 mg/kg bw/day. In 2-year oral toxicity studies in rats and monkeys, there was decreased plasma and red blood cell cholinesterase activity at 1.7 mg/kg bw/day in rats and at 1.0 mg/kg bw/day in monkeys. In a 1-year oral toxicity study in dogs, there were decreases in red blood cell cholinesterase activity and evidence of liver toxicity at 1.3 mg/kg bw/day.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for methidathion.

Genotoxicity: Methidathion is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Two- and 3-generation reproduction studies in rats, and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: In a 21-day neurotoxicity study in hens, there was no evidence of delayed neurotoxicity.

Poisons Schedule: Methidathion is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.006 mg/L for methidathion was determined as follows:

$$0.006 \text{ mg/L} = \frac{0.16 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.16 mg/kg bw/day is the NOEL based on a medium-term (90-day) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Methiocarb

(endorsed 2011)

GUIDELINE

Based on human health concerns, methiocarb in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Methiocarb (CAS 2032-65-7) is in the carbamate class of chemicals. Other pesticides in this class include aldicarb, carbaryl, methomyl and pirimicarb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, methiocarb would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Methiocarb is an insecticide, acaricide and molluscicide used for the control of slugs and snails, mites, thrips, aphids, leaf-hoppers, fruit flies and soil insects.

There are registered products containing methiocarb in Australia. The products are for both professional and home garden use and include granular and soluble powder formulations for use in sprays. Use patterns include spreading pellets onto soil by hand or by sod-seeding machines in the home garden, and spraying wettable powder formulations onto soil by boom spray, airblast, or hand sprays in agriculture. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to methiocarb are home garden use and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of sources waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Data on levels of methiocarb in Australian drinking waters are not available. Given the environmental properties of methiocarb, which is highly water insoluble, it is likely that levels in drinking water would be very low and associated with particulate matter and sediments.

TREATMENT OF DRINKING WATER

Advanced treatment methods such as ozonation, ozone/biologically activated carbon and advanced oxidation are effective against this type of compound.

MEASUREMENT

Measurement at residue levels in water are by high performance liquid chromatography (HPLC) with post-column derivitisation and HPLC with tandem mass spectrometry.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for methiocarb is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day from a 2-year dietary study in dogs. The NOEL is based on reduced plasma cholinesterase activity. The ADI incorporates a safety factor of 100 and was established in 1986.

The ADI for methiocarb was first set in 1981 at 0.06 mg/kg bw/day, based on a NOEL of 6.25 mg/kg bw/day from a long-term dietary study in dogs, before being revised in 1983 to 0.001 based on a reassessment of data on decreased plasma acetylcholinesterase activity. In 1986, the ADI was revised to its current value on the basis that estimates of food consumption were replaced with actual data.

The acute reference dose (ARfD) of 0.03 mg/kg bw/day for methiocarb was established in 2001, based on NOELs of 3 mg/kg bw/day from developmental toxicity studies in rats and rabbits. The ARfD incorporates a safety factor of 100.

The previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Methiocarb is rapidly absorbed from the gastrointestinal tract, and distributed broadly. It is extensively metabolised and eliminated within 72 hours, mainly in the urine. Methiocarb has a low potential for bioaccumulation. The primary metabolites are methiocarb phenol, methiocarb sulfoxide phenol and methiocarb phenol sulfone.

Acute effects: Methiocarb has a high acute oral and low acute dermal toxicity. Symptoms of acute poisoning include salivation, lacrimation, vomiting, diarrhoea, muscular tremors, restlessness, convulsions, and paralysis. Methiocarb is not a skin sensitiser.

Short-term effects: In short-term dietary studies in rats, there are clinical symptoms indicative of central nervous system toxicity. Plasma, red blood cell and brain acetylcholinesterase activity was decreased at a dose of 10 mg/kg bw/day.

Long-term effects: Long-term dietary studies in rat, mouse and dog also showed effects on the central nervous system with decreased acetylcholinesterase activity in brain and other tissues, together with decreases in physical activity and grooming behaviours at dose levels above 0.2 mg/kg bw/day in dogs. This NOEL is the basis for the ADI.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for methiocarb.

Genotoxicity: Methiocarb is not considered to be genotoxic, based on short-term *in vitro* and *in vivo* studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits showed no evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Methiocarb is included in Schedule 5, 6 or 7 in the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for methiocarb was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a long-term (2-year) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Methomyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, methomyl in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Methomyl (CAS 16752-77-5) belongs to the carbamate class of insecticides. There are many other pesticides in this class, including carbaryl, methiocarb, and oxamyl (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, methomyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Methomyl is an insecticide for the control of fruit flies in agricultural settings, and domestic flies in home garden, public and industrial settings.

There are registered products that contain methomyl in Australia. The products are intended for professional and home garden use. They are applied by aerial and ground boom spray on agricultural crops and as baits in domestic and commercial buildings. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to methomyl are the use of home garden products and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of methomyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for methomyl in Australian waters could be found. In the USA, the maximum predicted concentrations for methomyl are 20 and 30 µg/L in groundwater and surface water, respectively (USEPA 1998).

TREATMENT OF DRINKING WATER

Oxidation has been reported to be an effective method of removing methomyl. Both ozone and chlorination (using chlorine gas) were successful treatment methods for methomyl removal; however, harmful by-products are formed during oxidation processes (Mason *et al.* 1990).

Activated carbon technologies are limited in their success in the removal of methomyl, and very large doses of powdered activated carbon are required to achieve any significant removal (Hu *et al.* 1998).

MEASUREMENT

The practical limit of quantification for methomyl in water is 1 µg/L by liquid chromatography with tandem mass spectrometry (Alder *et al.* 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for methomyl is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.25 mg/kg bw/day from a medium-term (3-month) dietary study in rats. The NOEL is based on decreased cholinesterase activity. The ADI incorporates a safety factor of 100, and was first established in 1991.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Methomyl is readily absorbed via the gastrointestinal tract in rats, and is extensively metabolised. The major metabolic pathway is via isomerisation to the E-isomer, then hydrolysis followed by rearrangement to form acetonitrile. The metabolites are eliminated in the urine almost completely within 24 hours as sulfate conjugates.

Acute effects: Methomyl has high acute oral toxicity and moderate acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 28-day dietary studies in mice and rats, there was decreased cholinesterase activity at 10 mg/kg bw/day and above. No other effects were observed. Medium-term (3-month) dietary studies reported decreased cholinesterase activity at 12 mg/kg bw/day in mice and decreased bodyweight gain, decreased kidney weight and adverse effects in the spleen in rats. A medium-term study in dogs was not considered acceptable for regulatory purposes. The lowest overall NOEL was 1.25 mg/kg bw/day in the medium-term study in rats. This NOEL is the basis for the current ADI.

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. In mice, decreased cholinesterase activity was reported at 13 mg/kg bw/day. In rats, decreased bodyweight gain and adverse effects on the spleen were reported at 10 mg/kg bw/day. In dogs, splenic haematopoiesis, and kidney swelling and pigmentation were reported at 10 mg/kg bw/day.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for methomyl.

Genotoxicity: Methomyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Reproduction studies in rodents reported decreased litter size and increased still births in first generation pups at the lowest dose, 3.75 mg/kg bw/day. Developmental studies in rodents reported increased embryo deaths at 1 mg/kg bw/day. The potential effects of methomyl on reproduction and development are the subject of a current review.

Poisons Schedule: Methomyl is included in Schedule 6 and 7 of the *Standard for the Uniform*

Scheduling of Medicines and Poisons No.1, 2010 (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for methomyl was determined as follows:

$$0.02 \text{ mg/L} = \frac{1.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 200}$$

where:

- 1.25 mg/kg bw/day is the NOEL based on a medium-term (3-month) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 200 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation., with an additional safety factor of 2 to account for uncertainty in the ADI (which may change as a result of the current review).

The World Health Organization has not established a health-based guideline value for methomyl and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Mason Y, Choshen E, Rav-Acha C (1990). Carbamate insecticides: Removal from water by chlorination and ozonation. *Water Research*, 24(1):11-21.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

USEPA (1998) *Reregistration Eligibility decision (RED) Methomyl* Prevention, Pescticides and Toxic Substances (7508C), United States Environment Protection Agency, EPA 738-R-98-021, December 1998

WHO (World Health Organization) (2004). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Methyl bromide

(endorsed 2011)

GUIDELINE

Based on human health concerns, methyl bromide in drinking water should not exceed 0.001 mg/L.

RELATED CHEMICALS

Methyl bromide (CAS 74-83-9) belongs to the fumigant class of chemicals. Other pesticides in this class include chloropicrin, dimethyl disulfide, ethylene dibromide and sulfuryl fluoride (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, methyl bromide would not be a health concern unless the concentration exceeded 0.001 mg/L. Excursions above this level would need to occur over a reasonably significant period to be a health concern, as the health-based guideline is based on medium-term effects.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Methyl bromide is a broad-spectrum fumigant effective against a variety of pests including insects, nematodes, rodents, bacteria, viruses, fungi, mites and weeds. It is used in grain silos, buildings, ships' holds and cargos, and in soil.

There are registered products that contain methyl bromide in Australia. The products are intended for professional use only, with restrictions on availability to authorised or licensed persons. Methyl bromide is available as liquefied gas (under pressure) to be applied either by hand equipment or machinery. Methyl bromide is currently in the phase-out stage due to environmental concerns, with very restricted uses allowed only under Critical Use Exemptions (CUEs) and for quarantine uses. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to methyl bromide is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Use of methyl bromide on soil may potentially lead to contamination of source waters through absorption into soil and subsequent entry into groundwater.

A major route of exposure to methyl-bromide is likely to be inhalation from gaseous sources such as leaking and venting from fumigation chambers, and gas escape from treated products.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of methyl bromide in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No reports of the treatment of methyl bromide in drinking water were found. Methyl bromide is a volatile halogenated methane and would be expected to respond to most treatment processes in a similar manner to other halogenated methanes such as dichloromethane and chloroform.

MEASUREMENT

Methyl bromide can be measured in drinking waters using the same techniques as those routinely applied to dihalomethanes and trihalomethanes. Most commonly these substances are analysed by liquid-liquid extraction followed by gas chromatography with electron caption detection. The typical limit of quantitation for this approach is less than 1 µg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for methyl bromide is 0.0004 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.4 mg/kg bw/day from a short-term (90-day) dietary rat study. The NOEL is based on injury to the forestomach. The ADI incorporates a safety factor of 1000 and was established in 2001.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Methyl bromide is readily and extensively absorbed from the gastrointestinal tract in rats. It is widely distributed to tissues, extensively metabolised to bromide, excreted in urine and bile, and exhaled as CO_2. Bromide accumulates in tissues in rats followed by slow elimination. The half-life of bromide has been reported to be 12 days in humans.

Acute effects: Methyl bromide has moderate acute oral toxicity and high dermal toxicity in rats. There are no quantitative data available on skin sensitisation. However, dermal exposure may result in redness, dermatitis, itching, swelling and blistering.

Short-term effects: Short-term dietary studies in rats reported focal hyperaemia and dose-related hyperplasia of the forestomach at doses of 2 mg/kg bw/day and above. The NOEL for these effects was 0.4 mg/kg bw/day and this is the basis for the current ADI. Inflammation, fibrosis and hyperkeratosis were reported at doses of 25 mg/kg bw/day and above. Methyl bromide is much more toxic via inhalation than via the oral route.

Long-term effects: A long-term dietary study in rats reported decreased bodyweight gain at a dose of 16.75 mg/kg bw/day. Relative brain and kidney weights were increased in males at higher doses.

Carcinogenicity: From oral administration studies in rats, there is some evidence of induction of forestomach squamous cell carcinoma. From inhalational studies in mice and rats, there is no evidence of carcinogenicity for methyl bromide.

Genotoxicity: Methyl bromide produced positive results in some *in vitro* assays in bacteria and cultured mammalian cells, as well as in mouse and rat bone marrow cells *in vivo* and in *Drosophila*. It was negative in the mouse dominant lethal assay. Overall, it has some genotoxic potential; however, there is no evidence that this leads to cancer formation.

Reproductive and developmental effects: Two-generation reproduction studies in rats and rabbits did not produce any evidence of reproductive effects. A developmental toxicity study in rabbits by inhalation exposure produced developmental effects at maternotoxic dose levels only. No oral exposure study was available.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Methyl bromide is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), with an Appendix J (Conditions for availability and use of Schedule 7 poisons) rider restricting its availability to authorised or licensed persons. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.001 mg/L for methyl bromide was determined as follows:

$$0.001 \text{ mg/L} = \frac{0.4 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 0.4 mg/kg bw/day is the NOEL based on a short-term (90-day) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation, and an additional 10 because the NOEL is based on a short-term study.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

Metiram

(endorsed 2011)

GUIDELINE

Metiram degrades in the environment to ethylene thiourea (ETU), hence the health-based guideline for metiram is based on the toxicity of ETU. Based on human health concerns, the environmental degradant of metiram, ETU, in drinking water should not exceed 0.009 mg/L.

RELATED CHEMICALS

Metiram (CAS 9006-42-2) belongs to the ethylenebis-dithiocarbamate class of chemicals. Other pesticides in this class include mancozeb and zineb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, the environmental degradant of metiram, ethylene thiourea (ETU), would not be a health concern unless the concentration exceeded 0.009 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Metiram is a fungicide for the control of early and late blight in potatoes, and fungal diseases in apples, pears, grapevines, stone fruit, turf and certain vegetable crops.

There are registered products that contain metiram in Australia. The products are intended for professional use and are available as concentrated solutions to be applied in diluted form using ground or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: Metiram hydrolyses rapidly in the environment to ETU and carbon disulfide (CS_2), both of which have higher toxicity than metiram. It is considered highly unlikely that residues of metiram or its degradants will be present in food. Metiram residues are grouped with other dithiocarbamates (mancozeb, metham, metiram, propineb, thiram, zineb and ziram) in the maximum residue limit definition.

Agricultural use of metiram may potentially lead to contamination of source waters by both metiram and ETU through adsorption into soil and subsequent entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Metiram and ETU have been monitored in some drinking water supplies in Australia, with values below the limit of quantitation (Barwon Water 2007). The highest measured value in a public drinking water well in the USA was reported to be 0.21 µg/L (USEPA 2005).

TREATMENT OF DRINKING WATER

Powdered activated carbon filtration, granulated activated carbon filtration, and reverse osmosis have been demonstrated to be highly effective processes at removing certain pesticides including dithiocarbamates (USEPA 2001). Dithiocarbamates are also degraded by hydrogen peroxide, ultraviolet irradiation and Fenton-type advanced oxidation processes (Ikehata and El-Din 2006).

ETU is degraded by ozone at 3 mg/L and chlorine dioxide at 20 mg/L, producing several degradation compounds (Hwang *et al*. 2003).

MEASUREMENT

The analytical methods for metiram rely on acid hydrolysis to release CS_2, which is then measured colorimetrically or by gas chromatography. Metiram degrades in the environment to ETU, hence the analytical methods reported are for the determination of ETU in water. United States Environmental Protection Agency (USEPA) Method 509 for the determination of ETU in water using gas chromatography with nitrogen-phosphorus detector can achieve a limit of quantitation (LOQ) of 2.7 µg/L (Munch and Graves 1992). After extraction with dichloromethane in the presence of thiourea and sodium L-ascorbate, ETU can be analysed by gas chromatography with alkali flame ionization detection and mass spectrometric confirmation. The LOQ is less than 0.1 µg/L in water (Van Der Poll *et al*. 1993). ETU in water can also be analysed by fluorimetric determination based on the inhibitory effect of ETU on the oxidation of thiamine to thiochrome by mercury(II) (Pérez-Ruiz *et al*. 1998). ETU has been determined in water by a cathodic stripping voltammetry method, with a LOQ of 1.4 µg/L (Carvalho *et al*. 2004).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for metiram is 0.02 mg per kg body weight (mg/kg bw), based on a lowest-observed-effect level (LOEL) at the lowest dose tested of 5 mg/kg bw/day 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, and was first established in 1988. There is currently no ADI for ETU.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Metiram is readily absorbed via the gastrointestinal tract and is widely distributed in tissues and blood. It is moderately metabolised to ETU, and hydrolysed to carbon disulfide (CS_2). It is slowly excreted as ETU in the urine and faeces, and as CS_2 in the breath within 7 days.

Acute effects: Metiram has low acute oral and dermal toxicity. It is a skin sensitiser in guinea pigs. ETU has low acute oral toxicity.

NOTE: Important general information is contained in PART II, Chapter 6

Short-term effects: In a 3-month dietary study with metiram in rats, atrophy of skeletal muscle fibres in females was seen at 15 mg/kg bw/day, and hind-limb paralysis in females was seen at the highest dose tested, 45 mg/kg bw/day. Reversible decreases in iodine uptake into the thyroid were seen at all doses tested, and reversible decreases in thyroxine levels were seen at 45 mg/kg bw/day.

In a 26-week oral gavage study with metiram in monkeys, levels of thyroxine and triiodothyronine in the thyroid gland were decreased at the lowest dose tested of 5 mg/kg bw/day and above. Decreases in serum thyroxine and partially reversible increases in thyroid weight and thyroid hyperplasia were seen at the next highest doses of 15 mg/kg bw/day and 75 mg/kg bw/day (highest dose tested). A NOEL was not obtained in this study. The LOEL of 5 mg/kg bw/day in this study, with 250-fold safety factor, is the basis for the current ADI for metiram.

In short-term studies with ETU, the thyroid was the target organ. In a dietary study in rats over 14 days, histological changes including thyroid hyperplasia, bone marrow depletion, and lymphatic lesions occurred from 25 mg/kg bw/day. When administered in the drinking water of rats over 28 days, decreased levels of thyroxine and triiodothyronine, increased levels of thyroid stimulating hormone in serum, and thyroid follicular necrosis were seen at doses from 10.6 mg/kg bw/day. Other effects seen at 17.6 mg/kg bw/day and above include proximal tubule kidney cell hypertrophy and vacuolisation.

In 3- and 4-month dietary studies in rats and mice with ETU, effects in rats included follicular cell hypertrophy and thyroid hyperplasia from 3 mg/kg bw/day and above. At higher doses there was also increased relative thyroid weight and decreased iodine uptake into the thyroid (8 mg/kg bw/day), decreased levels of thyroxine and increased levels of thyroid stimulating hormone in serum, and increased absolute thyroid weights (10 mg/kg bw/day), thyroid adenomas (12.5 mg/kg bw/day). In mice, thyroid adenomas and pituicyte vacuolisation occurred from 12.5 mg/kg bw/day, hepatocellular hypertrophy from 37.5 mg/kg bw/day, and thyroid hyperplasia from 75 mg/kg bw/day. The lowest overall NOEL was 2 mg/kg bw/day (rats) in these studies.

Long-term effects: In 96-week studies with metiram in mice and 2-year studies in rats by dietary administration, there was decreased food consumption and bodyweight gain at the highest dose tested, 150 mg/kg bw/day, in mice, and an increased incidence of skeletal muscle atrophy at the highest dose tested, 16 mg/kg bw/day, in rats. No other effects were seen in these studies.

In a 1-year rat study with ETU, there was increased thyroid vascularisation and thyroid acinar cell papillation at the lowest dose tested, 0.025 mg/kg bw/day. At 1.25 mg/kg bw/day, there was decreased bodyweight gain. Increased relative thyroid weight occurred at 7 mg/kg bw/day and thyroid tumours occurred at 15 mg/kg bw/day.

In a 2-year rat study with ETU, thyroid hyperplasia, elevated TSH and decreased triiodothyronine and thyroxine were seen at the lowest dose, 0.25 mg/kg bw/day. Thyroid carcinomas were observed at 8.7 mg/kg bw/day. In a 2-year mouse study with ETU, decreased bodyweight gain, increased thyroid stimulating hormone (TSH), thyroid cell hypertrophy and hyperplasia and thyroid adenomas and carcinomas were observed at the lowest dose tested, 16 mg/kg bw/day.

Carcinogenicity: Based on a 2-year study in mice and rats, there is no evidence of carcinogenicity for metiram. In mice, ETU produced thyroid follicular-cell tumours and tumours of the liver and anterior pituitary gland. However, due to its nongenotoxicity and disturbance of thyroid function, ETU would not be expected to produce thyroid cancer in humans exposed to concentrations that do not alter thyroid hormone homeostasis.

Genotoxicity: Metiram is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies. ETU was positive in some *in vitro* short-term assays, but overall, it is not considered to be genotoxic.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 3-generation reproduction study and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development. Developmental studies on rats and rabbits with ETU showed effects on development only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Metiram is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.009 mg/L for the degradant of metiram, ETU, was determined as follows:

$$0.009 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 1}{2 \text{ L/day} \times 1000}$$

where:

- 0.25 mg/kg bw/day is the LOEL based on a long-term (2-year) dietary study in rats on ETU.
- 70 kg is taken as the average weight of an adult.
- The proportionality factor is 1 since metiram has no residues in food and is degraded to ETU in the environment. It is assumed, therefore, that 100% of the ADI (nominal in this case) for ETU will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the LOEL for ETU derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation, and an additional factor of 10 because a LOEL was used to derive the guideline.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Metolachlor/s-Metolachlor

(endorsed 2011)

GUIDELINE

Based on human health concerns, metolachlor in drinking water should not exceed 0.3 mg/L.

RELATED CHEMICALS

Metolachlor (CAS 51218-45-2) belongs to the chloroacetamide class of chemicals. Other pesticides in this class include dimethenamid and propachlor. Metolachlor is a racemic mixture of the R- and S-isomers; S-metolachlor is the purified S-isomer (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, metolachlor would not be a health concern unless the concentration exceeded 0.3 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Metolachlor is a pre-emergent herbicide for the control of grasses and broad-leaf weeds in agricultural crops.

There are registered products that contain metolachlor or its isomer s-metolachlor in Australia. These products are intended for professional use and are available as concentrated solutions to be applied in diluted form using boom and hand-held ground sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to metolachlor and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of metolachlor may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of metolachlor in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Metolachlor can be a relatively difficult pesticide to treat in drinking water. Oxidation by chlorine or ozone are only partially effective at typical doses, and adsorption to activated carbon can be incomplete (Ormad *et al.* 2008). However, a combination of ozone, activated carbon and coagulation-flocculation can be effective (Ormad *et al.* 2008).

MEASUREMENT

Metolachlor can be measured in drinking waters by gas chromatography with nitrogen–phosphorus detection. The limit of detetion for this method is 0.75–0.01 µg/L (WHO 2004).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for metolachlor is 0.08 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 7.5 mg/kg bw/day from a medium-term (6-month) dietary study in dogs. The NOEL is based on decreased bodyweight gain. The ADI incorporates a safety factor of 100, and was established in 1987.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metolachlor and its isomer S-metolachlor demonstrate similar toxicological profiles. Therefore, the toxicological endpoints that occur at the lowest dose level for either chemical (both referred to as metolachlor) have been reported below.

Metabolism: Metolachlor is readily and extensively absorbed in the gastrointestinal tract of rats. It is extensively metabolised and excreted in urine and faeces. Metabolites have not been identified.

Acute effects: Metolachlor has low acute oral and dermal toxicity. It is a skin sensitiser in guinea-pigs.

Short-term effects: Medium-term dietary studies conducted in rats and dogs reported biochemical changes and changes in bodyweight and organ weight as the most sensitive toxicological effects. In a 13-week study in rats, there were effects indicative of mild liver toxicity, reduced bodyweight gain and increases in relative and absolute organ weights at 200 mg/kg bw/day. A 6-month study in dogs reported decreased bodyweight gain, food consumption and absolute liver weights at 25 mg/kg bw/day. The NOEL of 7.5 mg/kg bw/day from this study is the basis for the current ADI.

Long-term effects: Long-term dietary studies have been conducted in mice, rats and dogs. In a 2-year dietary study in mice there were changes in spleen weight at 150 mg/kg bw/day. In a 2-year rat study there was decreased bodyweight gain and food consumption, and an increase in pituitary carcinomas and liver neoplastic nodules at 150 mg/kg bw/day. In a 1-year dietary study in dogs, there was decreased bodyweight gain at 32 mg/kg bw/day.

Carcinogenicity: There was some evidence of carcinogenicity in rats at high dose levels, but the threshold noted for this effect is well in excess of the likely level of human exposure.

Genotoxicity: Metolachlor is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Metolachlor is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.3 mg/L for metolachlor was determined as follows:

$$0.3 \text{ mg/L} = \frac{7.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 7.5 mg/kg bw/day is the NOEL based on a medium-term (6-month) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a health-based guideline value of 0.01 mg/L for metolachlor (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Metribuzin

(endorsed 2011)

GUIDELINE

Based on human health concerns, metribuzin in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Metribuzin (CAS 21087-64-9) belongs to the triazinone class of chemicals. Other pesticides in this class include hexazinone, metamitron and toltrazuril (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, metribuzin would not be a health concern unless the concentration exceeded 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.

GENERAL DESCRIPTION

Uses: Metribuzin is a pre- and post-emergent herbicide for the control of broad-leaf weeds and grasses in agricultural crops.

There are registered products that contain metribuzin in Australia. The products are intended for professional use and are available as concentrated solutions, granular formulations or wettable powders to be applied in diluted form using ground boom and aerial sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to metribuzin and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of metribuzin may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of metribuzin in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of metribuzin in drinking water have been identified.

MEASUREMENT

Metribuzin may be measured in drinking waters by gas chromatography with mass spectrometry, with a limit of reporting of 0.1 µg/L (QFSS 2009).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for metribuzin is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2 mg/kg bw/day 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, and was established in 1982.

The acute reference dose (ARfD) of 0.25 mg/kg bw for metribuzin was established in 2007, based on a NOEL of 25 mg/kg bw/day from a developmental study in rats. The ARfD incorporates a safety factor of 100.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Metribuzin is rapidly absorbed via the gastrointestinal tract in rats. It is readily metabolised and rapidly excreted in the urine and faeces with little tissue retention after 96 hours. The major metabolite recovered from rats is N-acetylcysteine.

Acute effects: Metribuzin has low to moderate acute oral toxicity and low dermal toxicity. It is not a skin sensitiser.

Short-term effects: A short-term dermal study conducted in rabbits reported elevated serum levels of thyroid hormone (thyroxine) in female rabbits at doses of 200 mg/kg bw/day and above. Short-term dietary studies performed in rats reported increased absolute liver weights at the high dose of 4.5 mg/kg bw/day. Associated histopathological effects were not observed.

Long-term effects: Long-term dietary studies conducted in mice, rats and dogs showed the main effect to be changes in absolute and relative organ weights. In a 2-year study in mice, increased liver, spleen, and kidney weights and evidence of anaemia were observed at 500 mg/kg bw/day. In a 2-year study in rats, decreased relative and absolute heart weights were observed at 5.7 mg/kg bw/day, and effects on the thyroid hyperplasia and fluctuating levels of triiodothyronine and thyroxine at 13 mg/kg bw/day and above. In a 2-year study in dogs, anaemia, increased mortality, increased relative and absolute organ weights and lesions in heart, liver, kidney and adrenal glands were observed at 52.5 mg/kg bw/day. The overall NOEL was 2 mg/kg bw/day in rats, and this is the basis for the current ADI.

Carcinogenicity: Based on a 2-year study in rats, metribuzin is not considered to be carcinogenic.

Genotoxicity: Metribuzin is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and a developmental study in rats did not produce any evidence of effects on reproduction or foetal development. In the developmental study, effects on the dams included increased thyroid weights and fluctuations in thyroid hormones at doses of 75 mg/kg bw/day and above. The NOEL of 25 mg/kg bw/day from this study was used to set the ARfD.

Poisons Schedule: Metribuzin is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for metribuzin was determined as follows:

$$0.07 \text{ mg/L} = \frac{2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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Metsulfuron-methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, metsulfuron-methyl in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

Metsulfuron-methyl (CAS 74223-64-6) belongs to the sulfonylurea class of chemicals. There are many other pesticides in this class including azimsulfuron, chlorsulfuron, ethoxysulfuron, halosulfuron-methyl, iodosulfuron methyl-sodium salt, sulfometuron-methyl, sulfosulfuron, triasulfuron, tribenuron-methyl and trifloxysulfuron (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, metsulfuron-methyl would not be a health concern unless the concentration exceeded 0.04 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Metsulfuron-methyl is used as a post-emergent herbicide for the control of weeds in native pastures, rights of way, commercial and industrial areas, domestic and public service areas and agricultural crops.

There are registered products that contain metsulfuron-methyl in Australia. The products are intended for professional use and are available in wettable powder and granular formulations. Product labels indicate products are to be diluted and applied by boom, hand-held and aerial spray methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to metsulfuron-methyl and its metabolites are residues in food and contact with treated weeds. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of metsulfuron-methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on metsulfuron-methyl occurrence in Australian drinking water supplies were found.

TREATMENT OF DRINKING WATER

No specific data on the treatment of metsulfuron-methyl in drinking water have been identified.

MEASUREMENT

Metsulfuron-methyl can be measured in water after filtration by direct injection on a triple quadrapole liquid chromatography–mass spectrometry instrument in multiple reaction monitoring mode, with a limit of reporting of 10 µg/L. Metsulfuron can also be analysed by solid phase extraction (SPE) followed by high performance liquid chromatography with diode array detection, achieving a limit of detection of 10 µg/L (Ruberu *et al.* 2000). SPE followed by liquid chromatography with electrospray mass spectrometric detection can achieve method detection limits of 3 ng/L for drinking water samples (Corcia *et al.* 1999).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for metsulfuron is 0.01 mg per kg of bodyweight (0.01 mg/kg bw), based on a no-observed-effect level (NOEL) of 1 mg/kg bw/day from a long-term (2-year) dietary rat study. The NOEL is based on decreased bodyweight gain. The ADI incorporates a safety factor of 100 and was established in 1985.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Metsulfuron-methyl is readily absorbed via the gastrointestinal tract in rats. It is not extensively metabolised and is rapidly excreted mostly unchanged in the urine (90%) and faeces. Less than 2% was retained in the tissue in rats.

Acute effects: Metsulfuron-methyl has low acute oral and dermal toxicity. Metsulfuron-methyl is not a skin sensitiser in guinea pigs.

Short-term effects: Medium-term dietary studies in rats and dogs reported decreased bodyweight gain and clinical evidence of mild toxicity in both species at doses of 12 mg/kg bw/day and above. Medium-term studies in mice did not report any toxic effects at doses up to 750 mg/kg bw/day.

Long-term effects: Long-term dietary studies conducted in mice, rats and dogs reported decreased bodyweight gain and decreased food consumption in all species at doses of 12 mg/kg bw/day and above. The most sensitive NOEL was 0.93 mg/kg bw/day based on decreased bodyweight gain in a 2-year dietary study in rats. This NOEL was used to set the current ADI.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for metsulfuron-methyl.

Genotoxicity: Metsulfuron-methyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A two-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any effects on reproductive parameters or on foetal development.

Poisons Schedule: Metsulfuron-methyl is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

NOTE: Important general information is contained in PART II, Chapter 6

The health-based guideline of 0.04 mg/L for metsulfuron-methyl was determined as follows:

$$0.04 \text{ mg/L} = \frac{1 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Ruberu SR, WM Draper, Perera SK (2000). Multiresidue HPLC methods for phenyl urea herbicides in water. *Journal of Agricultural and Food Chemistry,* 48(9):4109-4115.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Mevinphos

(endorsed 2011)

GUIDELINE

Based on human health concerns, mevinphos in drinking water should not exceed 0.005 mg/L.

RELATED CHEMICALS

Mevinphos (CAS 7786-34-7) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes chlorfenvinphos, chlorpyrifos, dichlorvos and diazinon (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, mevinphos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Mevinphos is an anticholinesterase acaricide (miticide) and insecticide for the control of moths in *Brassica* crops (cabbages, cauliflowers, broccoli and brussel sprouts).

There is at least one registered product that contains mevinphos in Australia. Mevinphos products are intended for professional use and are available as concentrated solutions to be applied in diluted form, by boom spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to mevinphos and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of mevinphos may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on mevinphos occurrence in Australian drinking water supplies were found.

TREATMENT OF DRINKING WATER

A reverse osmosis (RO) membrane challenge test was conducted by injecting 1200 µg/L of mevinphos before treatment. RO removed 96% of the initial concentration of mevinphos (1200 µg/L), and the post-membrane carbon filter further removed 95% of the remaining mevinphos, from 40 µg/L to 2.1 µg/L (USEPA 2005). In another challenge test, the concentration of mevinphos remained the same after ultraviolet (UV) light and ozone treatment; however, the activated carbon filter located after the UV and ozone treatment removed 99% of the pesticide (USEPA 2007).

MEASUREMENT

Mevinphos is one of the organophosphorus pesticides analysed by the United States Environmental Protection Agency (USEPA) Method 622 (Pressley *et al.* 2002). The sample is solvent-extracted and the extract is dried with sodium sulfate concentrated and analyzed by gas chromatography using a flame photometric or phosphorus/nitrogen detector. The concentrated can also be analysed by gas chromatography–mass spectrometry in selected ion monitoring mode. The method can achieve a limit of quantitation (LOQ) of 0.05 mg/L. Hollow fiber liquid phase micro-extraction with gas chromatography by flame thermionic detection can achieve a LOQ of 40 ng/L in drinking water (Lambropoulou and Albanis 2005). A solid-phase microextraction method coupled with a flame photometric can achieved a LOQ for mevinphos of 420 µg/L (Su and Huang 1999).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for mevinphos is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.016 mg/kg bw/day (1 mg/person/day using a mean bodyweight of 62.5 kg) from a 30-day human volunteer study. The NOEL is based on inhibition of erythrocyte cholinesterase. The ADI incorporates a safety factor of 10 and was established in 1998.

The previous ADI established in 1996 was 0.0008 mg/kg bw based on a NOEL of 0.016 mg/kg bw/day (1 mg/person/day) in a human volunteer study and using a safety factor of 20. An additional factor of 2 was included because of the decrease in slow motor fibre nerve conduction velocity observed in a different human volunteer study at 0.025 mg/kg bw/day.

The acute reference dose (ARfD) of 0.003 mg/kg bw for mevinphos was based on a LOEL of 0.025 mg/kg bw/day from a 28-day human volunteer study. The ARfD incorporates a safety factor of 10 and was established in 2000.

The previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Mevinphos is rapidly and extensively absorbed via the gastrointestinal tract and rapidly metabolised and excreted, predominantly as carbon dioxide in expired air (78%), with only 14% in the urine over 24 hours. There were four major metabolites in the urine.

Acute effects: Mevinphos has high acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 3-, 12- and 13-week dietary studies in rats at dose levels up to 20 mg/kg bw/day, the principal sign of toxicity at the higher dose levels was death. Four dogs also died in a dietary study at a dose of 15 mg/kg bw/day. In a 30-day five-person human volunteer study, erythrocyte cholinesterase activity was decreased at 1.5 mg/person/day. The NOEL was 0.015 mg/kg bw/day (1 mg/person/day) and this NOEL is the basis for the ADI. In a 28-day eight person volunteer study, plasma and erythrocyte cholinesterase activity was decreased at 0.025 mg/kg bw/day. There was also a decrease in slow fibre motor conduction at this dose level. This LOEL, the only dose tested, is the basis for the ARfD.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: In a 2-year dietary study in rats at dose levels up to 0.6 mg/kg bw/day, there were no treatment-related effects on general health or bodyweight gain. No histopathological changes were observed. In a 2-year dietary study in dogs at doses up to 0.75 mg/kg bw/day, plasma and erythrocyte cholinesterase activity were decreased at 0.075 mg/kg bw/day and above and increased with time. At the two-year period, brain cholinesterase activity was significantly decreased at 0.25 mg/kg/day in females and at 0.75 mg/kg in males and females. All but two high dose male animals survived in good health.

Carcinogenicity: Based on a 2-year study in rats and dogs, there is no evidence of carcinogenicity for mevinphos.

Genotoxicity: Mevinphos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Mevinphos is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.005 mg/L for mevinphos was determined as follows:

$$0.005 \text{ mg/L} = \frac{0.015 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.015 mg/kg bw/day is the NOEL established in a short-term (30-day) study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from the human study to allow for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Molinate

(endorsed 2011)

GUIDELINE

Based on human health concerns, molinate in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Molinate (CAS 2212-67-1) belongs to the thiocarbamate class of pesticides. Other herbicides in this class include EPTC, methiobencarb, pebulate, thiobencarb and vernolate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, molinate would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Molinate is a post-emergence herbicide for the control of grass weeds in rice only.

There are registered products that contain molinate in Australia. The products are intended for professional use. The chemical is available as concentrated solutions to be applied in diluted or undiluted form to rice crops soon after sowing. It may be applied by aerial application, or directly to flooded rice bays by drip applicators mounted on a tractor or a four-wheel drive spray bike. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The possible sources of public exposure to molinate and its metabolites are residues in rice and drinking water. Residue levels in rice produced according to good agricultural practice are generally low and maximum residue limits (MRLs) are at the level of detection.

The agricultural use of molinate involves direct application into water bays of rice crops, which may then enter source waters for drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Molinate was the most commonly applied herbicide to rice crops in southern New South Wales in 1994-1995. It was detected in irrigation drains after application to rice fields at levels up to 0.7 mg/L (Bowmer *et al.* 1998). Molinate was detected on two occasions in the Mulwala supply offtake on the Murray river, at 0.0072 and 0.0005 mg/L (7.2 and 0.5 µg/L). Over a 55-day period of monitoring supply water in the irrigated areas, molinate was found in 90% of the analysed samples, with a maximum concentration of 0.0036 mg/L (3.6 µg/L) (Bowmer *et al.* 1998). The high frequency of molinate detection was due to samples being taken in early summer, when the herbicide is used in rice crops.

Rice-growing areas are within the Murray Darling Basin on the Murrumbidgee and Murray rivers in south-western New South Wales and Victoria. Molinate has been detected in the Coleambally irrigation area, Murrumbidgee region, New South Wales and Murray irrigation area (Ball 2001).

TREATMENT OF DRINKING WATER

Ozonation, granular activated carbon, preoxidation by chlorine and preoxidation by chlorine combined with activated carbon adsorption removes 100% of molinate during drinking water treatment (Ormad *et al*. 2008).

MEASUREMENT

Capillary gas chromatography with a selective nitrogen–phosphorus detector for the determination of molinate can achieve a limit of quantitation (LOQ) of 0.03 µg/L (Worthing and Hance 1991). United States Environmental Protection Agency (USEPA) method 525.2 for the determination of organic compounds in drinking water by liquid-solid extraction and capillary column gas chromatography–mass spectrometry (GC/MS) can achieve a LOQ of 0.05 µg/L to 0.087 µg/L for molinate (Munch 1995a). USEPA method 507 can achieve a LOQ of 0.15 µg/L (Munch 1995b). Molinate can be extracted from water by liquid/liquid extraction with dichloromethane and analysed by gas chromatograpy–mass spectometry in selected ion monitoring mode, with a LOQ of 0.5 µg/L. Liquid chromatography–mass spectrometry with direct injection can achieve a LOQ of 2.2 µg/L (Yu *et al*. 2003). Solid phase extraction and high performance liquid chromatography with ultraviolet detection can achieve a LOQ of 0.1 µg/L. Solid phase micro extraction followed by gas liquid chromatography employing either a nitrogen-phosphorus detector or mass spectrometry can achieve LOQ of 0.11 µg/L and 0.02 µg/L respectively (Choudhury *et al*. 1996).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for molinate is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day from a 3-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, and was established in 1986.

The previous ADI of 0.0001 mg/kg bw established in 1984 was based on the same NOEL of 0.2 mg/kg bw/day from the 3-generation rat reproduction study, but included a safety factor of 2000 due to the absence of long-term studies. Following the review of long-term studies in 1986, the NOEL of 0.2 mg. kg bw/day remained the lowest available, but the safety factor was reduced to 100 and the current ADI was established.

The previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Molinate is readily and extensively absorbed via the gastrointestinal tract in rats. It is metabolised to more polar products such as molinate sulfoxide (35%) and hydroxymolinate (26%). The majority of an administered dose is excreted within 48 hours, with 82% in urine, 11% in faeces and less than 1% expired as carbon dioxide.

Acute effects: Molinate is of moderate acute oral toxicity and low dermal toxicity. It is not a skin sensitiser.

NOTE: Important general information is contained in PART II, Chapter 6

Short-term effects: A 3-week dietary study in rats reported weakness in the hind limbs, and depressed bodyweight and food consumption at 80 mg/kg bw/day. Interference in blood clotting occurred at higher dose levels. Three-month dietary studies in rats reported pathological changes in the liver, kidney, testis, ovary and adrenal glands at 70 mg/kg bw/day. In 3-month dietary study in dogs, there were increases in thyroid gland weight at 60 mg/kg bw/day.

Long-term effects: Long-term dietary studies in rats reported increased testes weight at 2 mg/kg bw/day and above, and decreased bodyweight gain and increased kidney weight at 6 mg/kg bw/day.

Carcinogenicity: Based on a 2-year study in rats, there is no evidence of carcinogenicity for molinate.

Genotoxicity: Molinate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats noted a reduction in the number of litters, with an associated reduction in litter size and pup survival, in all generations at the highest dose, 0.63 mg/kg bw/day. No effects were noted at the next lowest dose, 0.2 mg/kg bw/day. This NOEL is the basis for the ADI. Further detailed studies have shown that molinate causes infertility in rats through its effects on sperm membranes, interfering with sperm maturation and causing some degeneration of seminiferous tubules.

In a developmental toxicity study in mice, there were no effects on foetal development. In rabbits, there were maternotoxic and foetotoxic effects at dose levels well in excess of the likely level of human exposure. There were no teratogenic effects in the rabbit. Developmental and reproduction studies in rats evaluated by the USEPA (not evaluated in Australia) have reported effects on brain weight at 0.4 mg/kg bw/day and on reproductive parameters at 0.2 mg/kg bw/day (USEPA 2002).

Neurotoxicity: Degeneration and demyelination of the sciatic nerve (combined with muscle atrophy) in a long-term study in rats have been reported at the lowest dose of 0.3 mg/kg bw/day by the USEPA (not yet evaluated in Australia).

Poisons Schedule: Molinate is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), with an Appendix J rider limiting availability to authorised or licensed persons. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.004 mg/L for molinate was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 200}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a 3-generation reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 200 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation, with an additional factor of 2 to take into account the uncertainty resulting from the new data on neurotoxicity and developmental effects, which have yet to be evaluated in Australia.

The World Health Organization has a health-based guideline value of 0.006 mg/L for molinate (WHO 2004).

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Molybdenum

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of molybdenum in drinking water should not exceed 0.05 mg/L.

GENERAL DESCRIPTION

Molybdenum is present in ground and surface waters at very low concentrations, generally below 0.01 mg/L. Higher concentrations have been reported in the vicinity of molybdenum mining operations. Fly ash deposited onto soils from coal-fired power stations can be a significant source of molybdenum. Application of fertilisers may also increase the concentration of molybdenum in ground and surface water.

Molybdenum is used in the production of steel, electrical components such as spark plugs, and nonferrous metal alloys. Molybdenum compounds are used as lubricants in oils and greases, and in fertilisers to overcome molybdenum deficiency in soils.

Many foods contain significant amounts of molybdenum. Legumes, grains and liver have the highest concentrations and food is a significant source of intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for molybdenum.

TREATMENT OF DRINKING WATER

There are no published methods for the removal molybdenum from drinking water.

MEASUREMENT

The concentration of molybdenum in drinking water can be determined by inductively coupled plasma emission spectroscopy or graphite furnace atomic absorption spectroscopy (APHA Method 3500-Mo Parts B or C 1992). Limits of determination are 0.04 mg/L and 0.005 mg/L respectively.

HEALTH CONSIDERATIONS

Molybdenum is an essential trace element for humans and other animals. The estimated requirement is between 0.15 mg/day and 0.5 mg/day for adults.

Approximately 30–70% of dietary molybdenum is absorbed in the gastrointestinal tract. Highest concentrations of molybdenum are found in the liver, kidney and bones. There does not appear to be any significant bioaccumulation of molybdenum in the body. Approximately 90% of ingested molybdenum is excreted in the urine.

Data are scarce on the long- and short-term toxicity of molybdenum in humans. One study of people consuming up to 0.2 mg/L of molybdenum in drinking water for 2 years reported no adverse effects. Another study has linked high intake of molybdenum in food with gout-like symptoms, joint pains of the legs and hands, and enlargement of the liver.

A number of long- and short-term animal studies have been undertaken, with considerable variability in the results depending on the chemical nature of the compound and the animal species. Effects included changes in skin and fur pigment, enlargement of joints, weight loss, diarrhoea and emaciation. Not all these effects were observed in each study and effects usually occurred only at high doses.

No relevant data are available on the carcinogenicity of molybdenum. Tests for mutagenicity with bacteria have been inconclusive.

DERIVATION OF GUIDELINE

The guideline value for molybdenum in drinking water was determined as follows:

$$0.05 \text{ mg/L} = \frac{0.5 \text{ mg/day} \times 0.2}{2 \text{ L/day}}$$

where:

- 0.5 mg/day is the upper range of the estimated adult requirement for molybdenum.
- 0.2 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.

Studies with animals and humans, while unable to establish a no-effect level, reported no adverse effects due to molybdenum in drinking water at concentrations of 0.05 mg/L (Chappell *et al*. 1979).

Adverse human health effects have been reported with molybdenum intakes of 10 mg/day (Chappell *et al* 1979). This is a hundred times higher than the guideline value, assuming that water consumption is 2 litres per day.

The World Health Organization guideline value of 0.07 mg/L was determined using a different approach which, upon review, was considered to be questionable. The difference between the two values is not significant.

REFERENCES

APHA Method 3500-Mo Part B (1992). Molybdenum: Atomic Absorption Spectrometric method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

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NOTE: Important general information is contained in PART II, Chapter 6

Monochloramine

CAS NO 10599-90-3

(endorsed 2014)

GUIDELINE

Based on health considerations, the concentration of monochloramine in drinking water should not exceed 3 mg/L (equivalent to 5 mg Cl as Cl_2/L in chloraminated systems).

GENERAL DESCRIPTION

Monochloramine is used as a disinfectant for drinking water supplies. It is increasingly being used in conjunction with chlorine, or in its own right, to provide primary disinfection of drinking water entering the distribution system and/or maintain a disinfectant residual through the distribution network. Although it is not as strong an oxidant as chlorine, monochloramine can be quite useful and effective in distribution systems with long water ages as it persists for longer. Where monochloramine is used overseas, concentrations typically range from 1.5 to 2.5 mg/L (as Cl_2).

Use of monochloramine for primary disinfection at the treatment facility needs to be considered carefully in terms of the range of C.*t* (disinfectant concentration × contact time) values achievable prior to the first customer.

Use of monochloramine can significantly reduce the level of disinfection by-products compared to that produced by similar levels of chlorine. If not managed proactively, however, use of chloramine can lead to nitrification in the distribution system resulting in a reduction of its effectiveness.

Monochloramine is formed by the addition of ammonia and chlorine in drinking water. This reaction can also result in the formation of dichloramine and trichloramine, both of which have lower taste and odour thresholds than monochloramine, and which should be minimised. The preferential formation of monochloramine is affected by the pH and the physical arrangements of adding the two chemicals.

Monochloramine has an odour threshold of 0.5 mg/L.

For additional information refer to the Disinfection Information Sheet for Chloramines.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Monochloramine is used as a disinfectant in some Australian reticulated supplies, and concentrations up to 4-5 mg/L (as total chlorine) have been applied at the start of long distribution systems to achieve concentrations ranging from 0.5-1.5 mg/L at the ends of distribution systems.

TREATMENT OF DRINKING WATER

Monochloramine can be removed from drinking water by the use of granular activated carbon, or by reducing agents such as sodium sulphite or sodium bisulphite.

MEASUREMENT

The concentration of monochloramine in drinking water can be determined by the DPD ferrous titrimetric method (APHA Method 4500-Cl Part F 2012) or by amperometric titration (APHA Method 4500-Cl Part D 2012). The limit of determination is typically 0.1 mg/L for the DPD method and can be lower for amperometric titration. Water utilities should refer to Standard Methods when selecting a method (APHA 2012).

HEALTH CONSIDERATIONS

In studies with rats it has been shown that monochloramine is readily absorbed and does not accumulate in tissues. It is metabolised rapidly to the chloride ion and excreted in urine in mammals. No specific toxic effects have been reported for monochloramine from either short-term or long-term studies. However, monochloramine is toxic to fish.

In humans, short-term exposure to concentrations of up to 24 mg/L of monochloramine in drinking water did not produce adverse effects. Similarly, volunteers given water containing up to 5 mg/L of monochloramine for 12 weeks did not exhibit adverse effects.

Acute haemolytic anaemia has been reported in haemodialysis patients when tap water containing chloramines was used for dialysis (Eaton *et al*. 1973; Kjellstrand *et al*. 1974; Tipple *et al*. 1988). Chloramines present in water are harmful to people on kidney dialysis and to animal species in aquaria; therefore, it is important for water utilities using chloramination to inform consumers at risk. Water suppliers that disinfect with chloramines need to contact coordinators of home dialysis and renal dialysis clinics to advise on the presence and concentrations of chloramines in drinking water.

Carcinogenicity studies have reported a slight increase in the incidence of mononuclear cell leukaemia in female rats exposed to monochloramine for 2 years, at doses of approximately 10 mg/kg bodyweight per day. There was no evidence of carcinogenic activity in male rats, or male and female mice.

Monochloramine exhibited weak mutagenic activity in one test using bacteria but was negative in another test (Shih and Lederberg 1976; Thomas *et al*. 1987). It did not induce chromosome aberrations in mammalian cells.

Based on inadequate evidence in humans and experimental animals, the International Agency for Research on Cancer concluded that chloramines are not classifiable as to their carcinogenicity to humans (Group 3) (IARC 2004).

No data are available on the health effects of dichloramine or trichloramine in drinking water.

DERIVATION OF GUIDELINE

The guideline value for monochloramine in drinking water was derived as follows:

$$3\ \text{mg/L} = \frac{9.4\ \text{mg/kg bodyweight per day} \times 70\ \text{kg}}{2\ \text{L/day} \times 100}$$

where:

- 9.4 mg/kg bodyweight per day is the no-observed-adverse-effect level (NOAEL) based on 2-year drinking water study using rats (NTP 1992). A similar value was obtained from a human study but this was of a limited duration.
- 70 kg is taken as the average weight of an adult.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOAEL derived from an animal study (10 for interspecies variations, and 10 for intraspecies variations).

Where monochloramine is measured by determining mg Cl as Cl_2 by standard DPD ferrous titrimetric methods the equivalent guideline value is:

$$5\ \text{mg/L} = \frac{9.4\ \text{mg/kg bodyweight per day} \times 70\ \text{kg} \times 71\ (\text{molecular weight } Cl_2)}{2\ \text{L/day} \times 100 \times 51.5\ (\text{molecular weight } NH_2Cl)}$$

It is assumed that all monochloramine intake is from drinking-water.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Naphthalophos

(endorsed 2011)

GUIDELINE

The health concerns associated with naphthalophos have not been fully evaluated and therefore a health-based guideline value for naphthalophos in drinking water cannot be set.

RELATED CHEMICALS

Naphthalophos (CAS 1491-41-4) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes acephate, chlorfenvinphos, diazinon and profenofos (Tomlin 2006).

HUMAN RISK STATEMENT

There are currently insufficient data on which to base a human risk statement.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Naphthalophos is a parasiticide for the control of organophosphate-susceptible gastrointestinal roundworms in sheep and lambs.

There are registered products that contain naphthalophos in Australia. Products containing naphthalophos are intended for professional use and are administered orally to sheep and lambs using drench guns. Products are typically diluted in water in original packaging before being transferred into the backpack reservoir of a drenching gun. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to naphthalophos and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The veterinary use of naphthalophos provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on occurrence of naphthalophos in water could be found.

TREATMENT OF DRINKING WATER

No information on efficiency of drinking water treatment to remove naphthalophos could be found.

MEASUREMENT

No method to measure naphthalophos in water could be found.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for naphthalophos is 0.0001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.25 mg/kg bw/day. The ADI incorporates a safety factor of 2500 and was established in 1971. The toxicological endpoint used to establish this ADI is unknown. The reason for such a large safety factor is also unknown, although it is likely to be due to the limited toxicological database for naphthalophos.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: There are no metabolic or kinetic studies available for naphthalophos.

Acute effects: Naphthalophos has moderate acute oral toxicity in rats and mice and moderate dermal toxicity in rats. No other acute toxicity data are available for naphthalophos.

A quantitative evaluation of the dermal absorption of naphthalophos is not available. However the moderate acute dermal toxicity in rats suggests that it is well absorbed dermally.

Short-term and long-term effects, carcinogenicity, genotoxicity, reproductive and developmental effects: No repeat-dose studies, or developmental or reproductive studies have been evaluated in Australia. Therefore the potential toxicity from exposure to naphthalophos cannot be adequately determined. There are no short-term studies available for naphthalophos. However, as an organophosphate compound, there is potential for cumulative anti-cholinesterase toxicity through repeated minor exposure.

Poisons Schedule: Naphthalophos is included in Schedule 6 or 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

Due to its current status as a chemical under review in Australia, a health-based guideline value for naphthalophos in drinking water is not recommended at this stage.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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NOTE: Important general information is contained in PART II, Chapter 6

Napropamide

(endorsed 2011)

GUIDELINE

Based on human health concerns, napropamide in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Napropamide (CAS 15299-99-7) belongs to the alkanamide class of chemicals. Another pesticide in this class is diphenamid (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, napropamide would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Napropamide is a pre-emergent herbicide for the control of grass weeds in tomato, almond, grape, and stone fruit crops and commercial farms.

There is at least one registered product that contains napropamide in Australia. Napropamide products are intended for agricultural use and are available as a concentrated water-soluble granule formulation to be diluted and sprayed onto soil and then incorporated mechanically or by irrigation. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to napropamide and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of napropamide may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on the occurrence of napropamide in Australian waters. Napropamide is broken down very quickly in water, with a half-life as rapid as seven minutes (EXTOXNET 1993). In water, the breakdown is predominantly mediated by the action of sunlight (photolysis). Napropamide was not detected in groundwater in the USA in a national survey in 1988 (Williams *et al*. 1988).

TREATMENT OF DRINKING WATER

No specific data on the treatment of napropamide in drinking water have been identified.

MEASUREMENT

Napropamide can be analysed by high-performance liquid chromatography with ultraviolet detection, with a limit of quantitation of 0.3 µg/L (USEPA Method 632.1).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for napropamide is 0.1 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 11 mg/kg bw/day from a long-term (2-year) dietary study in rats. The NOEL is based on liver spongiosis and decreased bodyweight gains. The ADI incorporates a safety factor of 100 and was established in 1994.

The previous ADI was 0.4 mg/kg bw based on a NOEL of 40 mg/kg bw/day in a long-term dietary study in rats and a medium-term dietary study in dogs. It was set in 1987.

The previous health value was 1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Napropamide is readily absorbed from the gastrointestinal tract in rats. Over 80% of the dose is excreted in urine and faeces within 48 hours, and excretion is complete by 96 hours. There is no evidence of accumulation in blood or tissues.

Acute effects: Napropamide has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea-pigs.

Short-term effects: Short-term (13-week) dietary studies were conducted in rats and dogs. In dogs, effects included increased absolute liver weights, and increased levels of glutamic transaminase and alkaline phosphatase enzymes in serum at 100 mg/kg bw/day. In rats, no toxic effects were seen up to the highest dose tested, 50 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice and rats and long-term dietary studies in dogs. The study in rats reported hepatic spongiosis and increased absolute liver and kidney weights at doses of 45 mg/kg bw/day and above. Effects in both mice and dogs were confined to decreased bodyweight gains at the highest doses tested (427 mg/kg bw/day for mice, 500 mg/kg bw/day for dogs). The lowest overall NOEL was 11 mg/kg bw/day (rat), based on liver spongiosis and decreased bodyweight gain.

Carcinogenicity Based on a 2-year dietary study in rats and an 18-month dietary study in mice, there is no evidence of carcinogenicity for napropamide.

Genotoxicity: Napropamide is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of reproductive effects, delayed development or teratogenicity.

Poisons Schedule: Napropamide is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for napropamide was determined as follows:

$$0.4 \text{ mg/L} = \frac{11 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 11 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES.

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Nicarbazin

(endorsed 2011)

GUIDELINE

Based on human health concerns, nicarbazin in drinking water should not exceed 1 mg/L.

RELATED CHEMICALS

Nicarbazin (CAS 330-95-0) does not belong to a recognised chemical class. It is a synthetic complex composed of an equimolar amount of 4,4'-dinitrocarbanilide (DNC) and 2-hydroxy-4,6-dimethylpyrimidine (HDP). There are no related pesticides (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, nicarbazin would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Users: 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.

There are registered products containing nicarbazin in Australia. The products are intended for professional use and are available as concentrated granular and powder formulations for addition to feed. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to nicarbazin and its metabolites is residues in food. Residue levels in chicken products produced according to good veterinary practice are generally low.

The veterinary use of nicarbazin provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of nicarbazin in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of nicarbazin in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

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.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for nicarbazin is 0.4 mg per kg of bodyweight (mg/kg bw) based a no-observed-effect level (NOEL) of 200 mg/kg bw/day in a rat developmental study, with a safety factor of 500.

The previous ADI of 2 mg/kg bw established in 1982 was based on a NOEL of 200 mg/kg bw/day from a 2-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.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Nicarbazin consists of equimolar amounts of 4,4'-dinitrocarbanilide (DNC) and 2-hydroxy-4,6-dimethylpyrimidine (HDP). HDP is readily absorbed via the gastrointestinal tract while DNC is not. There is no evidence of bioaccumulation. Elimination is mainly via the urine for HDP and via the faeces for DNC.

Acute effects: Nicarbazin has a low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: Information on short-term effects is very limited. The available data indicate that in rats there are effects on the kidney at 500 mg/kg bw/day, while in dogs there is bile duct proliferation at 1600 mg/kg bw/day.

Long-term effects: A 2-year dietary study in rats reported no treatment-related effects up to 300 mg/kg bw/day of DNC plus 100 mg/kg bw/day of HDP. A 2-year dietary study in dogs reported transitory liver enzyme changes and slight effects on bile duct at highest dose only, namely, 600 mg/kg bw/day of DNC plus 200 mg/kg bw/day of HDP. The NOEL was 180 mg/kg bw/day DNC plus 60 mg/kg bw/day HDP.

Carcinogenicity: Based on long-term studies in rats, there is no evidence of carcinogenicity for nicarbazin.

Genotoxicity: Nicarbazin was weakly positive in *in vitro* bacterial studies, but *in vivo* studies were negative. There is insufficient information to determine its genotoxic potential.

Reproductive and developmental effects: There are no studies available to examine the potential effects of nicarbazin on reproductive parameters. A developmental study in rats reported effects on the dams and foetuses at 600 mg/kg bw/day, but the study was of poor quality. The NOEL was 200 mg/kg bw/day and is the basis of the current ADI.

Poisons Schedule: Nicarbazin is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 1 mg/L for nicarbazin was determined as follows:

$$1 \text{ mg/L} = \frac{200 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 500}$$

where:

- 200 mg/kg bw/day is the NOEL based on a developmental study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 500 is a safety factor applied to the NOEL from a developmental study conducted in rats. The safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variations, and an additional safety factor of 5 for limitations in the current database.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Nickel

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of nickel in drinking water should not exceed 0.02 mg/L.

GENERAL DESCRIPTION

Drinking water generally contains very low concentrations of nickel. Concentrations reported overseas are usually less than 0.01 mg/L. Higher concentrations, up to 0.5 mg/L, have been reported where water has been in prolonged contact with nickel-plated tap and plumbing fittings; however, these higher concentrations are unusual.

Nickel is used in the electroplating industry and in alloys used in the chemical, marine, nuclear and aerospace industries. It is used as a catalyst in industrial processes, and in oil refining. Main releases to the environment are from the burning of fossil fuels and in waste discharges from electroplating industries.

Nickel is present in many foods. Highest concentrations occur in cocoa, soy beans and some cereals. It has been estimated that the average daily dietary intake is between 0.1 mg/day and 0.3 mg/day.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, concentrations of nickel range up to 0.03 mg/L, with typical concentrations less than 0.01 mg/L.

TREATMENT OF DRINKING WATER

Nickel can be co-precipitated with iron and manganese oxides.

MEASUREMENT

The nickel concentration in drinking water can be determined using inductively coupled plasma emission spectroscopy or graphite furnace atomic absorption spectroscopy (APHA Method 3500-Ni Parts B and C 1992). The limits of determination are approximately 0.02 mg/L and 0.005 mg/L respectively. Lower concentrations can be determined with pre-concentration using chelation or solvent extraction techniques.

HEALTH CONSIDERATIONS

Intestinal absorption of soluble nickel in drinking water can be as high as 27%, compared with only 0.7% from food. After absorption, nickel appears to be distributed to most organs, with higher amounts in the kidneys, lung and liver. It can cross the human placenta.

An extensive review and summary of the human and animal toxicity data for nickel is available (IPCS 1991).

In humans, long-term exposure may result in toxic effects to the kidney. Increased beta-microglobulin concentrations were reported among electroplating workers exposed to high amounts of nickel.

Nickel is known to be a common skin allergen and can cause dermatitis, particularly in younger women. While skin is sensitised, oral intake of low doses (0.0083 mg/kg body weight per day) may provoke contact dermatitis in sensitised individuals.

Several epidemiological studies have demonstrated that inhalation of nickel can cause lung, sinus and nasal cancer. There is no evidence that other organs are affected, or that nickel is carcinogenic when ingested.

Animal studies have reported altered body weights, some evidence of liver toxicity and mild kidney toxicity with high nickel doses (over 100 mg/kg body weight per day). Nickel has also affected the immune system in laboratory mice.

Some nickel compounds are carcinogenic when injected into laboratory animals but not when administered orally. Tests for mutagenicity with strains of bacteria have mostly been negative but gene mutations and chromosome aberrations have been reported in mammalian cells.

The International Agency for Research on Cancer has concluded that nickel compounds are carcinogenic to humans (Group 1, sufficient evidence of carcinogenicity in humans) (IARC 1990).

DERIVATION OF GUIDELINE

The guideline value for nickel in drinking water was derived as follows:

$$0.02 \text{ mg/L} = \frac{5 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 5 mg per kg body weight per day is the no-effect level for altered organ-to-body-weight ratios in a 2-year study with rats (Ambrose 1976).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in applying the results of animal studies to humans (10 for interspecies variations, 10 for intraspecies variations and 10 to compensate for the lack of adequate studies on chronic effects and for increased intestinal absorption when taken on an empty stomach). An additional factor for carcinogenicity was not included as effects only occurred on inhalation (no effects were observed on ingestion) and were localised to the lung and nasal passages.

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IPCS (International Programme on Chemical Safety) (1991). Nickel. Environmental Health Criteria, 108. World Health Organization, IPCS.

NOTE: Important general information is contained in PART II, Chapter 6

Nitrate and nitrite

(endorsed 2011)

GUIDELINE

Nitrate: Based on health considerations, the guideline value of 50 mg-NO_3/L (as nitrate) has been set to protect bottle-fed infants under 3 months of age. Up to 100 mg-NO_3/L can be safely consumed by adults and children over 3 months of age.

Where a water supply has between 50 and 100 mg-NO_3/L nitrate, active measures are required to ensure that those caring for infants are aware of the need to use alternative water sources in making up bottle feeds for babies under 3 months of age. Water may be used for bottle-fed infants if the nitrate concentration is between 50 and 100 mg/L, but medical authorities need to be increasingly vigilant and the water must also be known to be microbiologically safe.

Nitrite: Based on health considerations, the concentration of nitrite in drinking water should not exceed 3 mg-NO_2/L (as nitrite).

GENERAL DESCRIPTION

Nitrate and nitrite ions are naturally occurring oxides of nitrogen that make up part of the nitrogen cycle.

Nitrate is formed from the oxidation of organic wastes such as manure, by the action of nitrogen-fixing bacteria in soils, or from lightning strikes through air. Nitrates are also manufactured for use in explosives and inorganic fertilisers.

Intensification of farming practices and sewage effluent disposal to streams have led to increasing amounts of nitrate in some waters, particularly groundwater.

The nitrite ion is relatively unstable and can be formed by the reduction of nitrate in poorly oxygenated waters. It is rapidly oxidised to nitrate and is seldom present in well oxygenated or chlorinated supplies. Chemical and biological processes can result in further reduction to various compounds, including ammonia, or oxidation back to nitrate.

Food, particularly vegetables and cured meat, is the major source of nitrate intake for humans.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, nitrate concentrations range up to 51 mg NO_3/L, with typical concentrations usually less than 0.15 mg NO_3/L. Nitrite is generally not present in significant concentrations, although operational difficulties in chloramination can lead to nitrite formation due to the action of nitrifying bacteria.

Very high nitrate concentrations (up to 1300 mg NO_3/L) have been recorded in some groundwater supplies in rural areas.

TREATMENT OF DRINKING WATER

Conventional water treatment is not effective for nitrate removal. Nitrate reduction facilities are expensive to operate and involve the use of anion exchange resins.

MEASUREMENT

The nitrate concentration in drinking water can be determined by a colorimetric procedure following reduction of nitrate to nitrite using a cadmium column (APHA Method 4500-NO_3 Part E 1992). The limit of determination is 0.01 mg/L. Nitrite can be determined separately using the same procedure but without the reduction column (APHA Method 4500-NO_2 Part B 1992). Alternatively, nitrate and nitrite can be determined using ion chromatography (APHA Method 4110 Part B 1992).

HEALTH CONSIDERATIONS

The toxicity of nitrate to humans is thought to be solely due to its reduction to nitrite. The major biological effect of nitrite in humans is its involvement in the oxidation of normal haemoglobin to methaemoglobin, which is unable to transport oxygen to the tissues. This condition is called methaemoglobinaemia. Young infants are more susceptible to methaemoglobin formation than older children and adults. Other susceptible groups include pregnant women and people with a deficiency of glucose-6-phosphate dehydrogenase or methaemoglobin reductase.

Recently the World Health Organization (WHO 2007) reviewed the toxicity and health information for nitrate and nitrite and retained the drinking water guideline of 50 mg-NO_3/L based on epidemiological evidence for methaemoglobinaemia in infants because it is protective for bottle-fed infants and consequently for other parts of the population. The WHO recommended that water should not be used for bottle-fed infants when nitrate levels are above 100 mg/L, but that it may be used if medical authorities are increasingly vigilant when the nitrate concentration is between 50 and 100 mg/L. However, *the water must also be known to be microbiologically safe*. This caveat was included because the dose response data for methaemoglobin formation is complicated by the more-often-than-not concomitant presence of bacterial contamination and the fact that nitrite formation from nitrate in infants is markedly enhanced by gastrointestinal infections. Indeed some cases of infant methaemoglobinaemia have been described in which increased endogenous nitrite synthesis as a result of gastrointestinal infection appeared to be the only causative factor (FAO/WHO 1996, WHO 2007).

The central role that gastrointestinal infection plays in the aetiology of the disease has lead to an opinion that exogenous nitrate in drinking water is not a significant contributor to the prevalence of methaemoglobinaemia, and that current limits of nitrate in drinking water based solely on the health threat of infantile methaemoglobinaemia may be unnecessarily strict (Avery 1999). Indeed, a recent exposure assessment based on drinking water nitrate levels greater than 50 mg NO_3/L could not identify an exposure-response relationship that related drinking water nitrate level to methaemoglobinaemia (Fewtrell 2004). Nevertheless the collective data indicate that concentrations less than the current 50 mg NO_3/L are not commonly associated with methaemoglobinaemia (Fan and Steinberg 1996, FAO/WHO 1996, WHO 2007).

In animals, laboratory experiments suggest that neither nitrite nor nitrate acts directly as a carcinogen. There is concern that nitrite may react with foods rich with secondary amines to form N-nitroso compounds in the stomach: many of these compounds are known to be carcinogenic in animals. Some epidemiological evidence suggests a relationship between nitrate and gastric cancer in humans, but this has not been confirmed in more definitive analytical studies.

Nitrate is not mutagenic in tests with bacteria and mammalian cells *in vitro*. Chromosome aberrations have been observed in the bone marrow of rats but may be due to the formation of N-nitroso compounds. Nitrite is mutagenic in both *in vivo* and *in vitro* experiments using mammalian cells.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF GUIDELINE

The guideline value of 50 mg NO_3/L for nitrate is set to protect young infants, the most sensitive group (USEPA 1990, WHO 2007). Up to 100 mg NO_3/L can be used by adults and children over 3 months of age without significant health effects.

If the value of 50 mg NO_3/L is exceeded, the local health authority should be informed so that parents can be advised to use rainwater or bottled water in making up feeds for babies under 3 months of age. Water with concentrations up to 100 mg NO_3/L may be used if medical authorities are vigilant and the water is free of microbial contamination (WHO 2007).

The guideline level for nitrite of 3 mg NO_2/L is based on a relative potency for nitrite and nitrate with respect to methaemoglobin formation. WHO (2007) developed the same value for nitrite based on human data that show methaemoglobinaemia caused in infants by doses of nitrite ranging from 0.4 to more than 200 mg/kg of bodyweight. The guideline (rounded value) was derived by using the lowest level of the range (0.4 mg/kg of bodyweight), a bodyweight of 5 kg for an infant and a drinking-water consumption of 0.75 litre.

Because it is possible that nitrate and nitrite may occur simultaneously in drinking-water, and the two have a common toxic effect (methaemoglobinaemia), these compounds should be considered together when judging compliance with the Guidelines. The sum of the ratios of the concentration (C) of each to its guideline value (GV) should not exceed unity (WHO 2007). This is a standard screening risk assessment approach based on the assumption of dose additivity. Thus for infants:

$$(C_{Nitrate}/GV_{Nitrate}) + (C_{Nitrite}/GV_{Nitrite}) \leq 1 = (C_{Nitrate}/50\ mg/L) + (C_{Nitrite}/3\ mg/L) \leq 1$$

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Nitrilotriacetic acid (NTA)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of nitrilotriacetic acid in drinking water should not exceed 0.2 mg/L.

GENERAL DESCRIPTION

NTA may be present in drinking water that has been contaminated with sewage, for example by sewage discharge into a river or stream that is then used for drinking water. It is likely to be present in the form of metal complexes rather than the free acid. NTA has been detected in water supplies of municipalities in Canada and the United States at a mean concentration of less than 0.004 mg/L, with a small number of supplies exceeding 0.01 mg/L.

NTA is a chelating agent and forms soluble metal complexes with a number of metal ions including calcium and magnesium. It is used in laundry detergents as a replacement for phosphate, particularly in countries where legislation restricts the use of phosphate-based detergents. It is also used in the treatment of boiler water to prevent scale formation, and in the photographic, metal plating, textile manufacturing, and paper and cellulose industries. It is not widely used in Australia.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

NTA has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

No published reports are available on water treatment procedures to remove NTA from drinking water.

MEASUREMENT

Analysis can be undertaken using gas chromatography with a nitrogen-specific detector after converting NTA to the tri-n-butyl ester (Aue *et al.* 1972, Malaiyandi *et al.* 1979). The limit of determination is 0.0002 mg/L.

HEALTH CONSIDERATIONS

NTA is poorly absorbed by humans compared to experimental animals. It is rapidly excreted unchanged, but may be briefly retained in bone, probably due to the formation of complexes with calcium ions.

Data on the health effects in humans are scarce.

A number of long-term toxicity studies with animals have all shown similar results. No adverse effects are observed with low doses, but higher doses (30 mg/kg body weight per day) can cause some adverse effects to the kidney and urinary tract. The formation of kidney, urinary tract and bladder tumours has been reported in rats after prolonged exposure to high doses, but the tumours are believed to be the result of chelation of metal ions in the urinary tract.

Tests for mutagenic activity using bacteria have been negative; however, the NTA–iron complex is mutagenic in mammalian cells *in vitro*.

The International Agency for Research on Cancer has concluded that NTA is possibly carcinogenic to humans (Group 2B, no data in humans but sufficient evidence in animals) (IARC 1990).

DERIVATION OF GUIDELINE

The assessment of the toxicological data for NTA by the World Health Organization (WHO) has been used without review. The guideline value was determined as follows:

$$0.2 \text{ mg/L} = \frac{10 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.5}{2 \text{ L/day} \times 1000}$$

where:

- 10 mg/kg body weight per day is the no-effect level from a 2-year feeding study using rats (Nixon *et al*. 1972).
- 70 kg is the average weight of an adult.
- 0.5 is the proportion of total daily intake attributable to the consumption of water, based on a WHO assessment of distribution.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for potential carcinogenic effects).

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NOTE: Important general information is contained in PART II, Chapter 6

N-Nitrosodimethylamine (NDMA)

(endorsed 2011)

GUIDELINE

Based on health considerations, the concentration of NDMA in drinking water should not exceed 0.0001 mg/L (100 ng/L).

Action to reduce NDMA is encouraged, but must not compromise disinfection, as non-disinfected water poses significantly greater risk than NDMA.

GENERAL DESCRIPTION

N-Nitrosodimethylamine ($C_2N_6N_2O$)(CAS No. 62-75-9) is a member of the dialkylnitrosamine family. Other names for the compound include *N*-methyl-*N*-nitrosomethanamine, dimethylnitrosamine, and nitrous dimethylamine. The compound is also referred to by the acronyms NDMA, DMN and DMNA. The most recognisable acronym in the context of water treatment and water recycling is NDMA.

NDMA is a polar compound with a molecular weight of 74.08 g/mol, a water solubility of >10 g/100 ml (at 19ºC) and a Log Octanol/Water partition coefficient of –0.57. Pure NDMA exists as yellow liquid with a density of 1.006 g/cm^3, a boiling point of 151-154ºC and a vapour pressure of 1080 Pa at 25ºC.

NDMA is used as an industrial solvent, an anti-oxidant, a rubber accelerator, and in the preparation of polymers, where it may be used as an initiator or a plasticiser. The compound has been used in the production of rocket fuel, as a biocide for nematodes, and an intermediate for 1,1-dimethylhydrazine to inhibit nitrification of soils.

NDMA is formed under mildly acidic conditions by the reaction of natural and synthetic secondary, tertiary or quaternary amines with nitrate and nitrite. Precursor amines include alkylamines, dimethylamine (DMA), tetramethylthiuram disulfide (thiram) and polyelectrolytes used in water and wastewater treatment. NDMA is also produced as a by-product of chloramination of drinking water (due to the presence of dimethylamine in source waters subject to wastewater discharges or the oxidation of natural organic matter by chlorine in the presence of ammonia) and to a lesser extent by chlorination. NDMA formation can be facilitated in soils by biochemical pathways in micro-organisms, and this compound is resistant to microbial degradation under both aerobic and anaerobic conditions. Ozonation of drinking water contaminated with the fungicide tolyfluamide can also lead to the formation of NDMA.

NDMA can exist in the liquid and vapour phase and may be associated with airborne particulates. The compound has been detected in indoor air contaminated with tobacco smoke at concentrations of up to 240 ng/m^3. Detectable levels in outdoor air have been reported in the immediate vicinity of point sources (e.g. chemical production facilities). NDMA has been detected in preserved foods, such as smoked and salted fish and meat and sausages cured by nitrates. Studies conducted in the 1970s and 1980s found NDMA in foodstuffs at levels up to 17,200 ng/kg for cured meat products such as bacon, 68,000 ng/kg for smoked cheese and 9,200 ng/L for beer; although these levels should be viewed with caution as the concentrations were determined using analytical methods available at the time. Moreover, since that time, efforts have been made to reduce the amount of NDMA in foods by limiting the amount of allowable nitrate in preservation, prohibiting the use of nitrate for certain food groups, and the inclusion of nitrosation inhibitors.

In addition to pre-formed NDMA occurring in some foods, NDMA is generated in the stomach through nitrosation of secondary amines in ingested food, especially fish and meat. This process also involves reaction with nitrate and nitrite from foodstuffs and nitrate formed in the stomach, and is influenced by other food components that may enhance or inhibit nitrosation reactions. For these reasons, it is difficult to estimate the amount of NDMA formed endogenously in the human body.

NDMA is absorbed via the gastrointestinal and respiratory tracts, and may also be absorbed through the skin, but at much lower rates. Distribution in the body is uniform and rapid, and it is metabolised rapidly, with an estimated half life of 4 hours, based on observations in rodents. Excretion is primarily via carbon dioxide in expired air, with only a small percentage persisting as NDMA in the urine.

A worst case estimate for NDMA exposure from contaminated outdoor air and consumption of food and water indicated 5.0-16.0 ng/kg of body weight per day for a 29-50 year old adult (WHO 2006). Drinking water was estimated to account for 0.3-1.0 ng/kg of body weight per day based on a mean NDMA concentration of 12 ng/L and a maximum concentration of 40 ng/L in water. Food was estimated to account for 4.3-11 ng/kg of body weight per day. Cigarette smoking was a more significant source of NDMA exposure, with smokers estimated to have an intake of 1.0-80 ng/kg of bodyweight per day from mainstream smoke, and people with heavy exposure to smoke-contaminated indoor air, an intake of 40-130 ng/kg bodyweight per day from smoke. These estimates did not take into account the endogenous formation of NDMA in the digestive tract, and they indicate that drinking water forms only a minor component of exposure to exogenous NDMA (less than 10%).

Another assessment, incorporating estimates of the possible range of endogenous NDMA formation using data from *in vivo* and *in vitro* studies, indicated that drinking water contributed around 2.7% of daily NDMA intake when only exogenous sources were assessed, but only about 0.02% when endogenous NDMA formation was also taken into account (Fristachi and Rice 2007).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

There are no data in the public domain or peer reviewed literature on NDMA in Australian drinking water distribution systems and water treatment plants. Anecdotal evidence suggests a bi-modal distribution, with several water authorities indicating that NDMA is present at levels at or near the limit of determination of 1 to 2 ng/L, whereas preliminary sampling and analysis by other authorities indicates levels in the range of 60-90 ng/L. A recent report from South Australia has indicated that NDMA may originate from rubber components of newly commissioned drinking water pipelines, regardless of the disinfectant used. This may account at least partly for the divergent results reported by different water suppliers.

MEASUREMENT

Analytical methods for NDMA detection have been developed with a sensitivity at the nanogram per litre (ng/L) level. The methods developed by the United States Environmental Protection Agency (USEPA 2004) and the Ontario Ministry of the Environment (OME 2004) include a concentration and separation step prior to quantification by gas chromatography and mass spectrometry. Internal standards for each method are based on the use of the deuterated analogue of NDMA, NDMA-d6, as the surrogate. The OME method was developed specifically for use in drinking water. In this method, NDMA is extracted onto Ambersorb 572 and eluted using dichloromethane. NDMA is separated from the solvent using capillary column gas chromatography, and quantified by high resolution mass spectrometry at a detection level of 0.4 ng/L, with a reporting detection level of 1.0 ng/L. The USEPA method was developed for large scale surveys and can be used to detect NDMA and seven other nitrosamines. Following solid phase extraction and elution, the nitrosamines may be separated by gas chromatography and quantified via chemical ionisation tandem mass spectrometry, with a detection level of 0.28 ng/L and a limit of determination of 1.6 ng/L.

NOTE: Important general information is contained in PART II, Chapter 6

HEALTH CONSIDERATIONS

NDMA is absorbed through the gastrointestinal tract and subsequently distributes uniformly and rapidly. It can cross the placenta and may be present in breast milk. The metabolic half life in rodents is around 4 hours. It is excreted largely via exhaled carbon dioxide, with limited amounts excreted unchanged in urine.

NDMA is carcinogenic in experimental animals through several exposure routes, including ingestion in drinking water. In 1987 the International Agency for Research on Cancer (IARC) classified NDMA as a Group 2A chemical, probably carcinogenic to humans. The mechanism by which NDMA causes cancer is believed to involve biotransformation in the liver by microsomal enzymes, generating the methyldiazonium ion which subsequently forms DNA adducts.

A number of epidemiological studies have shown an association between NDMA intake from food and increased risks of gastric or colorectal cancer, although the data are not sufficient to derive a quantitative dose-response relationship for cancer risk in humans. These studies did not consider exposure to NDMA from drinking water, or endogenous generation of NDMA in the body.

Various other N-nitrosamine compounds with structures related to NDMA are known to occur in water supplies. The toxicological properties of these compounds have not been well characterised, however it is believed likely that some are also carcinogenic.

DERIVATION OF GUIDELINE VALUE

The World Health Organization has derived a guideline value for NDMA in drinking water based on a study of hepatic biliary cystadenomas in rats that used a wide range of NDMA exposure doses (from 0.033 mg/L to 16.896 mg/L). This dataset was used to derive a tumorigenic dose (TD_{05}) for NDMA corresponding to a dose level that causes a 5% increase in tumour incidence over the background level. The TD_{05} values were used to calculate a unit risk, which represents the increase in risk per unit increase in dose. Using the most sensitive endpoint observed in the animal study and conservative assumptions, a guideline value of 100 ng/L was derived, corresponding to an excess lifetime cancer risk of 1 in 100,000. This methodology treats the risk from exposure to NDMA in drinking water in isolation from other sources of NDMA exposure.

While adopting the same numerical value, a different approach has been taken to derive the guideline value for NDMA in Australian drinking water supplies. In assessing the potential public health benefits associated with regulation of this compound, the following factors were considered:

- NDMA has been demonstrated to be carcinogenic in animals, and is probably carcinogenic in humans.
- NDMA levels in drinking water may be an indicator of the presence of structurally related compounds, some of which may also have carcinogenic properties.
- The current level of exposure to NDMA from food is uncertain, due to lack of recent analytical data; however, even with changes in food preservation techniques since the 1970s, it is probable that exposure through food is at least 5 to 10 times greater than exposure from drinking water.
- There is evidence that exposure from endogenous formation of NDMA in the stomach may greatly exceed dietary exposures from both food and water.

In these circumstances, the adoption of a guideline value corresponding to a 1 in 1,000,000 lifetime cancer risk (the usual target level for health risks from carcinogens in these Guidelines) was deemed inappropriate, as this would impose a disproportionate regulatory burden on water suppliers while having little impact on total population exposures. Nevertheless, it was judged to be prudent to limit levels of NDMA in drinking water, given that this will probably reduce exposure to a range of related but as yet largely uncharacterised *N*-nitrosamine compounds that may pose potential health risks. For these reasons, a guideline value of 100 ng/L has been adopted.

NOTE: Important general information is contained in PART II, Chapter 6

LIMITING FORMATION IN DRINKING WATER

Reducing the occurrence of NDMA in drinking water systems may conflict with the goals of maintaining a persistent chlorine residual in distributions and controlling levels of other disinfection by-products such as trihalomethanes and haloacetic acids. The potential for NDMA formation may be reduced by avoiding chloramination through the removal of ammonia prior to disinfection, or by operating the system for breakpoint chlorination. If NDMA is a problem, treatment using UV irradiation in the prescence of hydrogen peroxide is an option to reduce NDMA levels while maintaining a chloramine residual. NDMA cannot be removed by air stripping or adsorption, due to its vapour pressure, solubility in water and limited partitioning at interfaces. It is only partially removed (<50%) by liquid phase pressure-driven separation processes such as reverse osmosis.

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NOTE: Important general information is contained in PART II, Chapter 6

Norflurazon

(endorsed 2011)

GUIDELINE

Based on human health concerns, norflurazon in drinking water should not exceed 0.05 mg/L.

RELATED CHEMICALS

Norflurazon (CAS 27314-13-2) belongs to the pyridazinone class of chemicals. Another pesticide in this class is maleic hydrazide (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, norflurazon would not be a health concern unless the concentration exceeded 0.05 mg/L. 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 3-month study.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Norflurazon is a pre-emergent herbicide for the control of annual grasses, broad-leaf and perennial weeds in agricultural crops.

There is at least one registered product containing norflurazon in Australia. Norflurazon products are intended for professional use and are available as a concentrated solution that is diluted and applied by aerial and ground spray to soil. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to norflurazon and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of norflurazon may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data were found on the occurrence of norflurazon in Australian waters. Norflurazon has been detected in several wells in Florida, USA, at levels approaching or in some cases exceeding 0.03 mg/L (the US Health Advisory Level) (USEPA 1996).

TREATMENT OF DRINKING WATER

No specific data on the treatment of norflurazon in drinking water have been identified.

MEASUREMENT

Norflurazon can be analysed by gas chromatography with a nitrogen–phosphorous specific detector (USEPA Method 645).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for norflurazon is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.5 mg/kg bw/day from a medium-term dietary study in dogs. The NOEL is based on increased liver weights. The ADI incorporates a safety factor of 100 and was first established in 1984.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Norflurazon is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, and is rapidly excreted in urine and faeces, with excretion being complete by 4 days.

Acute effects: Norflurazon has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea pigs.

Short-term effects: In short-term (21-day) dietary studies in rats, there was increased testis and kidney weight without accompanying histopathological changes at 100 mg/kg bw/day and above.

In medium-term dietary studies in rats, increased kidney weight without accompanying changes in histopathology was reported at a dose level of 127 mg/kg bw/day. In medium-term dietary studies in dogs, increased liver weight was reported at 10 mg/kg bw/day, with a NOEL of 1.5 mg/kg bw/day. This NOEL is the basis for the current ADI.

Long-term effects: Long-term dietary studies in mice and rats reported decreased bodyweight and food consumption and significant changes in relative organ weights. The overall NOEL was 18 mg/kg bw/day in rats.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for norflurazon.

Genotoxicity: Norflurazon is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and a developmental toxicity study in rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Norflurazon is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.05 mg/L for chemical was determined as follows:

$$0.05 \text{ mg/L} = \frac{1.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.5 mg/kg bw/day is the NOEL based on a medium-term (3-month) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Omethoate

(endorsed 2011)

GUIDELINE

Based on human health concerns, omethoate in drinking water should not exceed 0.001 mg/L.

RELATED CHEMICALS

Omethoate (CAS 1113-02-6) belongs to the organophosphate class of chemicals. There are many other pesticides in this class including dimethoate, fenthion, parathion, profenofos and ethoprophos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, omethoate would not be a health concern unless the concentration exceeded 0.001 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Omethoate is an insecticide and acaricide (miticide) for the control of aphids, flies, caterpillars, bugs, moths, mites and fleas. Omethoate is a metabolite of dimethoate.

There are registered products containing omethoate in Australia. The products are intended for both professional and home garden use. Omethoate is formulated as a liquid concentrate, to be diluted and sprayed onto plants and bare earth. It can be applied to a variety of crops including pastures, legumes, oilseeds, faba bean, poppies, ornamentals, citrus, apples, cotton, lupins, onions, pears and potatoes. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to omethoate are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice and potential dietary exposure are generally low.

Agricultural use of omethoate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of omethoate in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of omethoate in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Omethoate can be determined in water by hydrophilic interaction liquid chromatography with tandem mass spectrometry, with a limit of quantitation of 0.05 µg/L (Hayama *et al*. 2008). A capillary electrophoresis method has also been developed for the analysis of omethoate with a method detection limit of 50 µg/L (Tao *et al*. 2008). A variety of solid phase extraction materials may be used for the effective extraction of omethoate from water (Geiss and Gebert 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for omethoate is 0.0004 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.04 mg/kg bw/day from 2-year dietary study in rats. The NOEL was based on inhibition of acetylcholinesterase. The ADI incorporates a safety factor of 100 and was established in 2005.

The acute reference dose (ARfD) of 0.003 mg/kg bw/day for omethoate was established in 2005, 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.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Omethoate is absorbed rapidly and extensively from the gastrointestinal tract in rats and is rapidly eliminated in the urine, mainly as unchanged omethoate (88% eliminated after 8 hours). It is widely distributed throughout the body with the highest levels found in the thyroid. Identified metabolites include N-methyl-methyl-sulfinyl-acetamide, O-desmethylated omethoate, O,O dimethyl phosphoric acid and O,O-dimethyl phosphorothioic acid.

Acute effects: Omethoate has high acute oral toxicity and moderate acute dermal toxicity. It can cause skin sensitisation in guinea pigs.

Short-term and long-term effects: Short-term dermal exposure studies and long-term dietary exposure studies in rats reported symptoms indicative of nervous system toxicity. A 2-year dietary study in rats reported inhibition of red blood cell and brain cholinesterase activity at dose levels equivalent to 0.12 mg/kg bw/day and above. The NOEL of 0.04 mg/kg bw/day from this study is the basis of the ADI.

Carcinogenicity: There was evidence of benign thyroid tumours at high dose levels in rats. These levels were well in excess of the expected levels of human exposure.

Genotoxicity: Omethoate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A multigeneration reproduction study in rats reported no evidence of effects on reproductive parameters. Developmental studies in rats and rabbits reported maternal and foetal toxicity as a result of cholinesterase inhibition at 1 mg/kg bw/day in rats and 0.2 mg/kg bw/day in rabbits. There was no evidence of teratogenicity.

Neurotoxicity: Omethoate did not cause delayed neurotoxicity in tests conducted on hens.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Omethoate is in Schedules 5, 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.001 mg/L for omethoate was determined as follows:

$$0.001 \text{ mg/L} = \frac{0.04 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.04 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated amount (maximum) of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Organotins
dialkyltins
tributyltin oxide

(endorsed 1996)

GUIDELINE

Dialkyltins: Data are inadequate to set a guideline value for drinking water.

Tributyltin oxide: Based on health considerations, the concentration in drinking water should not exceed 0.001 mg/L.

GENERAL DESCRIPTION

The group of compounds known as the organotins comprises a large number of compounds with different properties and applications. Of these the dialkyl and tributyltin compounds have some application in the water industry and are the ones most likely to be found in drinking water supplies.

The dialkyltins are widely used as stabilisers in plastic, and may leach out of PVC water pipes for a short time after installation. In one study, dibutyltin sulfide was detected at a concentration of 0.01 mg/L in water that was in static contact with PVC pipes.

Tributyltins are used as biocides and have occasionally been detected in raw water in Canada, the United States, the United Kingdom and Switzerland, probably because of their use as antifouling agents on boats. The use of tributyl-organotin compounds, particularly tributyltin oxide, in antifouling paints has now been banned in a number of countries because it is extremely toxic to aquatic life. Tributyltin is also used as a biocide in boiler waters. Other organotins are unlikely to be found in water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Organotins have not been found in Australian drinking waters. They are included here to provide guidance in the unlikely event of contamination, and because they have been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

No published reports are available on water treatment procedures that can be used to remove organotins from drinking water.

MEASUREMENT

The organotins can be analysed using a solvent extraction procedure (Greaves and Unger 1988). They are extracted using a hexane–tropolone mixture and derivatised to form hexylbutyltins. Analysis is by gas chromatography with flame photometric detection. Limits of determination are less than 0.000002 mg/L (2 ng/L).

HEALTH CONSIDERATIONS

Few data are available on the absorption and distribution of organotins in the body, but animal studies have reported that some of the compounds are poorly absorbed, and distributed primarily to the liver and kidney.

An extensive review and summary of the human and animal toxicity data for tributyltin compounds is

available (IPCS 1990).

The dialkyltins have low general toxicity. A study using rats fed dialkyltin for 3 months reported depressed growth and mild anaemia only at the highest dose used (4mg/kg body weight per day). No toxic effects were observed at lower doses. Other studies with rats and dogs reported similar results. Carcinogenicity bioassays with animals have been inconclusive.

No data are available on the ingestion of tributyltin oxide in humans, although occupational information and dermal exposure are known to cause irritation. A number of long-term animal studies have been undertaken using tributyltin oxide. A 2-year chronic toxicity study using rats concluded that doses of 50 mg/kg body weight per day can induce toxicity to some organs including the thyroid and pituitary glands. A no-effect level of 0.5 mg/kg body weight per day was established from this study (Wester *et al.* 1990). An immunotoxicity study on the suppression of resistance to nematodes in rats identified a no-effect level of 0.025 mg/kg body weight per day (Vos *et al.* 1990). The latter immunotoxicity study is considered more sensitive but the significance to humans is questionable. The no-effect levels agree to about an order of magnitude.

Tributyltin oxide was not mutagenic with bacteria and yeast but caused a significant increase in the number of benign tumours of the pituitary gland when fed to rats for 2 years.

DERIVATION OF GUIDELINE

The guideline value of 0.001 mg/L for tributyltin oxide in drinking water was determined as follows:

$$0.001 \text{ mg/L} = \frac{0.025 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.025 mg/kg body weight per day is the no-effect level from a 18-month immunotoxicity study using rats (Vos *et al.* 1990).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 100 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations and 10 for intraspecies variations).

The World Health Organization guideline value of 0.002 mg/L was based on 20% of total daily intake coming from drinking water. The proportion contributed by drinking water to the total Australian intake is probably less.

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NOTE: Important general information is contained in PART II, Chapter 6

Oryzalin

(endorsed 2011)

GUIDELINE

Based on human health concerns, oryzalin in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Oryzalin (CAS 19044-88-3) belongs to the dinitroaniline class of chemicals. Other pesticides in this class include butralin and pendimethalin (Tomlin 2006).

HUMAN RISK STATEMENT

There are currently insufficient data on which to base a human health risk statement.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Oryzalin is a herbicide used for the pre-emergent control of certain annual grasses and broad-leaf weeds in non-bearing and bearing fruit and nut orchards, vineyards, nursery stock, ornamentals and amenity plantings. In addition, it is used for the pre-emergent control of annual ryegrass, phalaris, wireweed (hogweed) and deadnettle in wheat, barley and canola.

There are registered products containing oryzalin in Australia. The products are intended for professional use and are available as a granular formulation, suspension concentrates or emulsifiable concentrates. The concentrates are diluted and applied by ground boom, hand spray or overhead irrigation, and the granules spread by hand or mechanical spreader. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to oryzalin is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of oryzalin may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for oryzalin in Australian waters could be found. In the USA, the highest predicted concentration of oryzalin in surface and groundwater was 90 and 0.9 µg/L, respectively (USEPA 2004). The highest measured concentration in surface and groundwater was 1.9 and 0.018 µg/L, respectively, while concentrations of oryzalin in US drinking water samples ranged from 0.01 to 0.07 µg/L (USEPA 2004).

TREATMENT OF DRINKING WATER

No data on drinking water treatment removal efficiency were found for oryzalin.

MEASUREMENT

Oryzalin in water can be measured by high performance liquid chromatography, with a method detection limit of 0.14 µg/L (USGS 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for oryzalin is 0.1 mg per kg body weight (mg/kg bw), based on a no-observed-effect level (NOEL) of 12 mg/kg bw/day 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 previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

No evaluation report on the toxicity of oryzalin is currently available from the Office of Chemical Safety and Environmental Health (OCSEH).

Metabolism: No studies have been evaluated in Australia.

Short-term/long-term effects: No studies have been evaluated in Australia.

Carcinogenicity: No studies have been evaluated in Australia. Oryzalin has not been evaluated by International Agency for Research in Cancer.

Genotoxicity: No studies have been evaluated in Australia.

Reproductive and developmental effects: No studies have been evaluated in Australia.

Poisons Schedule: Oryzalin is not scheduled in the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for oryzalin was determined as follows:

$$0.4 \text{ mg/L} = \frac{12 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 12 mg/kg bw/day is the NOEL on which the existing ADI was based; however further details are unknown.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is assumed to be the safety factor applied to the ADI, which is a safety factor typically applied to a NOEL derived from animal studies. The safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation. This is consistent with US reports.

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

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USGS (United States Geological Survey) (2006). Pesticides in the Nation's Streams and Ground Water, 1992–2001. National Water Quality Assessment Program, USGS.

NOTE: Important general information is contained in PART II, Chapter 6

Oxamyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, oxamyl in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Oxamyl (CAS 23135-22-0) belongs to the carbamate class of chemicals. There are many pesticides in this class including aldicarb, methomyl, carbaryl and methiocarb (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, oxamyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Oxamyl is an insecticide for the control of weevil borers and nematodes in agricultural crops.

There is at least one registered product containing oxamyl in Australia. Oxamyl products are intended for professional use and are available as a liquid concentrate formulation applied by stem injection and hand spray to banana crops, and by irrigation to tomato and capsicum crops. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to oxamyl and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of oxamyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data on occurrence of oxamyl in Australian waters could be found. The United States Environmental Protection Agency estimates environmental concentration of 0.001 mg/L in surface waters and 0.004 mg/L in groundwater in the USA (USEPA 2007).

TREATMENT OF DRINKING WATER

No specific data on the treatment of oxamyl in drinking water have been identified.

MEASUREMENT

Oxamyl can be measured by routine high-performance liquid chromatography–mass spectrometry analysis, with a limit of reporting of 0.001 mg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for oxamyl is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day from a developmental study in rats. The NOEL is based on reduced foetal weights. The ADI incorporates a safety factor of 100 and was established in 1993.

The previous ADI for oxamyl was 0.03 mg/kg bw/day, based on NOELs of 2.5 mg/kg bw/day from long-term dietary studies in rats and dogs. The ADI was amended in 1993 following consideration of the developmental study in rats that demonstrated a lower overall NOEL.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Oxamyl is readily and extensively absorbed in rats. It is not extensively metabolised, and is excreted in the urine almost completely within 168 hours.

Acute effects: Oxamyl has high acute oral toxicity and low dermal toxicity. It is not a skin sensitiser in guinea pigs.

Short-term effects: Short-term (21-day) dermal studies in rabbits and short-term (29-day) dietary studies in rats reported decreases in cholinesterase in plasma, brain, and red blood cells, but no clinical signs of nervous system toxicity at 10 mg/kg bw/day.

Three-month dietary studies in rats and dogs reported decreased bodyweight gain at 15 mg/kg bw/day (rats), and increased serum alkaline phosphatase without associated organ histopathology (dogs), at doses of 15 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies in mice, rats and dogs reported decreased bodyweight gains (all species), hyperactivity and decreased plasma cholinesterase (rats and dogs), and tremors, decreased red blood cell counts, increased absolute brain weights, and inhibition of brain cholinesterase activity (dogs) at 1.3 mg/kg bw/day and above. The lowest overall NOEL was 0.9 mg/kg bw/day (dogs). No other effects were seen in rats and mice.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for oxamyl.

Genotoxicity: Oxamyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In reproduction studies in rats, there was no evidence of effects on reproductive parameters. Developmental studies in rats reported reduced foetal bodyweight at 0.5 mg/kg bw/day and above, and maternotoxicity at 0.8 mg/kg bw/day. The NOEL was 0.2 mg/kg bw/day and is the basis for the current ADI.

Poisons Schedule: Oxamyl is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for oxamyl was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.2 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a developmental study in rats using gavage administration.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for oxamyl and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2006).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Queensland Health (2007). Organochlorine, organophosphorous and synthetic pyrethroid pesticide, urea and triazine herbicides and PCBs in water. QHFSS SOP 16315.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

USEPA (United States Environmental Protection Agency) (2007). Interim Reregistration Eligibility Decision. Oxamyl – List A, case 0253. USEPA.

WHO (World Health Organization) (2006). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

Paraquat

(endorsed 2011)

GUIDELINE

Based on human health concerns, paraquat in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Paraquat (CAS 4685-14-7 (paraquat); CAS 1910-42-5 (paraquat dichloride)) belongs to the bipyridinium class of compounds, which also includes the herbicide diquat (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, paraquat would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Paraquat is a non-selective herbicide for the control of grasses and broad-leaf weeds in agricultural and horticultural crops.

There are registered products that contain paraquat (mainly as the dichloride) in Australia. These products are intended for professional use and are available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to paraquat is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of paraquat may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data for paraquat in Australian water could be found. Paraquat dichloride binds so strongly to soil clay particles that it is extremely unlikely to be found in groundwater supplied as a drinking water source (Health Canada 1986, USEPA 1997).

TREATMENT OF DRINKING WATER

Techniques effective in removing paraquat from water include adsorption by charcoal, ion exchange (66% and 70%) and modified peat (95% to 99%). Chlorine dioxide has been found to oxidize paraquat concentrations of 15 and 30 mg/L within minutes above pH 8.7. The use of bentonite, a clay adsorbent, for 10 minutes, followed by a 15-minute coagulation period, resulted in 90% removal of paraquat present at 1 mg/L (Health Canada, 1986).

MEASUREMENT

Paraquat can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 1 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for paraquat is 0.004 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.45 mg/kg bw/day 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 and was established in 1992.

The acute reference dose (ARfD) of 0.004 mg/kg bw/day for paraquat is based on the same NOEL as the ADI (0.45 mg/kg bw/day from a one-year dietary study in the dog). The NOEL is based on lung lesions at the next highest dose, 0.93 to 1.0 mg/kg bw/day. These lung lesions were evident also for shorter exposures. The ARfD incorporates a safety factor of 100, and was established in 2003.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Paraquat is poorly absorbed via the gastrointestinal tract, and is not extensively metabolised. Within 72 hours after administration, up to 80% appears unchanged in the faeces, up to 20% in urine, and less than 1% remains in the body. The small amount of urinary metabolites has not been identified. At 72 hours, there is no evidence of accumulation in most tissues, although paraquat may persist and accumulate in mouse brain.

Acute effects: Paraquat has moderate acute oral toxicity and low acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 3-6 week dietary studies in mice, rats, rabbits and dogs, pathological changes in the lung, gastrointestinal tract and kidneys at dose levels above 2-4 mg/kg bw/day were reported. Significantly decreased food consumption and decreased bodyweight gain, and a dose-dependent increase in the mortality rate were also common observations. In a 13-week dietary study in dogs, there were macroscopic lung lesions and histopathological signs of alveolitis from 1.5 mg/kg bw/day. Alveolitis was detected in all dogs at 3 mg/kg bw/day.

In a one-year dietary study in dogs, there was an increased incidence of pulmonary lesions associated with chronic pneumonitis from 0.9 mg/kg bw/day. The NOEL was 0.45 mg/kg bw/day and this is the basis for the ADI and ARfD.

Long-term effects: A 2-year dietary study in mice reported clinical signs of toxicity at 1.9 mg/kg bw/day and an increased incidence of pulmonary adenomas at 15 mg/kg bw/day. A 2-year dietary study in rats reported cataracts and lenticular abnormalities of the eye from 2.5 mg/kg bw/day. At higher dose levels, lesions in the lungs included focal subpleural abnormalities, chronic pneumonitis, and proliferative lesions in the alveolar epithelium. Other effects included hydrocephalus, degeneration of the nerve fibres of the sciatic nerve and an increase in the numbers of cysts or cystic spaces in the spinal cord.

NOTE: Important general information is contained in PART II, Chapter 6

Carcinogenicity: There was evidence of proliferative lesions in the alveolar epithelium in a 2-year rat study, but only at dose levels well in excess of the likely level of human exposure. Long-term studies in mice showed no evidence of carcinogenicity.

Genotoxicity: Paraquat was clastogenic (causes chromosome breaks) in some *in vitro* short-term assays, but there was no evidence of genotoxicity in *in vivo* studies.

Reproductive and developmental effects: Two and three-generation dietary reproduction studies in rats and developmental toxicity studies in mice, rats and rabbits showed no evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: In studies in mice and rats, paraquat produced evidence of neurodegeneration and induced changes in the brain similar to Parkinson's disease. There is equivocal epidemiological evidence in some countries linking pesticide usage and the incidence of Parkinson's disease.

Poisons Schedule: Paraquat is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). The Standard also indicates that aqueous solutions of paraquat must be coloured blue or green, and must contain a stenching agent. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for paraquat was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.45 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.45 mg/kg bw/day is the NOEL based on a long-term (1-year) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

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USEPA (United States Environmental Protection Agency) (1997). Reregistration eligibility decision (RED) – Paraquat dichloride. EPA 738-F-96-018. USEPA.

NOTE: Important general information is contained in PART II, Chapter 6

Parathion

(endorsed 2011)

GUIDELINE

Based on human health concerns, parathion in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Parathion (ethyl parathion)(CAS 298-00-0) belongs to the organophosphate class of chemicals. Other pesticides in this class include methyl parathion, disulfoton, ethion, and chlorpyrifos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, parathion would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Parathion is an insecticide and acaricide (miticide) for the control of aphids, mites and caterpillars in commercial vegetable, fruit, tobacco and cotton crops.

There are currently no registered products containing parathion in Australia, but de-registered compounds could still be detected in water. Previously registered products were intended for professional use; these products were soluble concentrates intended to be diluted and applied by aerial and ground spray.

Exposure sources: If used in the future, the main source of public exposure to parathion and its metabolites, based on the previous use pattern, would be through residues in food. Residue levels in food produced according to good agricultural practice are generally low.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Parathion is typically not detected in Australian drinking waters and is not reported in drinking waters internationally under conditions of good agricultural practice. Its presence in drinking waters has not been reported by the World Health Organization (WHO 2004a).

TREATMENT OF DRINKING WATER

No specific data on the treatment of parathion in drinking water have been identified.

MEASUREMENT

Parathion is effectively extracted from water using liquid-liquid extraction with dichloromethane followed by gas chromatographic analysis employing nitrogen-phosphorus detection. The typical limit of detection using this procedure is 10 ng/L (Culea and Gocan 2000).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for parathion is 0.005 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.05 mg/kg bw/day for a reduction in erythrocyte cholinesterase activity in a 3-week oral toxicity study in humans. The ADI incorporates a safety factor of 10. It was first set in 1967 and reaffirmed in 1997.

The acute reference dose (ARfD) of 0.01 mg/kg bw for parathion was established in 2000, 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.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Parathion is readily and extensively absorbed via the gastrointestinal tract. It is extensively metabolised, and is rapidly excreted in the urine and faeces, almost completely within 48 hours. The main metabolite is paraoxon-ethyl, which is of similar acute toxicity to the parent compound.

Acute effects: Parathion has high acute oral and dermal toxicity in animals and humans. The potential for skin sensitisation is unknown, due to its high dermal toxicity. Clinical symptoms of toxicity were typical of cholinesterase inhibition and included tremors, prostration, coma, piloerection, ataxia, and salivation.

Short-term effects: An dietary study in humans for up to 21 days reported reduced erythrocyte cholinesterase activity at the highest dose tested, 0.1 mg/kg bw/day. The NOEL was 0.05 mg/kg bw/day and this NOEL is the basis for the current ADI.

Long-term effects: Long-term dietary studies in rats and dogs reported reduced plasma and erythrocyte cholinesterase activity at doses of 0.03 mg/kg/day and above. In rats, reduced brain cholinesterase activity, retinal atrophy, and myelin degeneration in optical nerves were seen at the highest dose tested, 1.9 mg/kg bw/day.

Carcinogenicity: The evidence from several long-term rodent studies is inadequate to assess carcinogenicity for parathion.

Genotoxicity: Parathion is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Two-generation reproduction studies in rats up to 2.8 mg/kg bw/day and developmental studies in rats and rabbits up to 1.5 mg/kg bw/day found no evidence for effects on reproduction or foetal development.

Neurotoxicity: In a 10-day study in hens, there was no evidence of delayed neurotoxicity due to parathion.

Poisons Schedule: Parathion is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for parathion was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.05 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.05 mg/kg bw/day is the NOEL based on a short-term (3-week) dietary study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from human studies. This safety factor covers intraspecies variation.

The World Health Organization has not established a health-based guideline value for parathion and it is excluded from the list of agricultural chemicals guideline value derivation because it "occurs in drinking-water at concentrations well below those at which toxic effects may occur" (WHO 2004b).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

Culea M, Gocan S (2000). Organophosphates. In: Nollet LM, Dekker M (eds). *Handbook of Water Analysis*, New York, pp571-608.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

WHO (World Health Organization) (2004a). Parathion in Drinking-water; Background Document for Development of WHO Guidelines for Drinking Water.

WHO (World Health Organization) (2004b). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Parathion-methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, parathion-methyl in drinking water should not exceed 0.0007 mg/L.

RELATED CHEMICALS

Parathion-methyl (CAS 298-00-0) belongs to the organophosphate class of pesticides, and is structurally related to parathion. This is one of the largest classes of pesticides, and other members include acephate, chlorpyrifos, ethion, phorate, and terbufos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, parathion-methyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Parathion-methyl is an insecticide for the control of pests in agricultural crops.

There are registered products that contain parathion-methyl in Australia. The products are intended for professional use on vegetables, citrus, pome and stone fruit, grapevines, and cotton crops. Products are capsule suspensions or liquid concentrates that are applied in diluted form to crops by ground boom or aerial sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to parathion-methyl and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of parathion-methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of parathion-methyl in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Parathion methyl is completely removed from water by chlorination when the chlorine dose is adjusted to match chlorine demand (Ormad *et al*. 2008).

Ozonation and activated carbon adsorption for parathion-methyl removal has also been reported with moderate success (Ormad *et al*. 2008). Conventional coagulation/flocculation provides a relatively low removal rate (30%). Jar testing is recommended to optimise dose rates if parathion-methyl is detected.

MEASUREMENT

Parathion-methyl can be measured in drinking water by gas chromatography–mass spectrometry. The typical limit of detection is 0.1 µg/L (QFSS 2009).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for parathion-methyl is 0.0002 mg per kg of bodyweight (mg/kg bw), based on a NOEL of 0.02 mg/kg bw/day from long-term (1-year and 2-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, and was established in 1997.

The previous ADI was 0.03 mg/kg bw/day. It was established in 1990 based on a NOEL of 0.3 mg/kg bw/day for erythrocyte cholinesterase inhibition in a 30-day dietary study in humans. The ADI was amended in 1997 to its current level after submission of long-term studies in rats showing effects at levels below this NOEL.

The ARfD of 0.03 mg/kg bw for parathion-methyl was established in 2000, 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 previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Parathion-methyl is readily and extensively absorbed from the gastrointestinal tract. Metabolism was extensive and proceeded by sulfonation, conjugation, and oxidation. The metabolites are of similar or lower toxicity to parathion-methyl. Excretion of parent compound and metabolites is rapid, proceeding through urine and being almost complete by 24 hours.

Acute effects: Parathion-methyl has high acute oral and dermal toxicity in rats. Parathion-methyl is not a skin sensitiser in guinea pigs. Clinical symptoms of toxicity were typical of cholinesterase inhibition and included tremors, prostration, coma, piloerection, ataxia, and salivation.

Short-term effects: A five-day dermal study in rats reported brain cholinesterase inhibition at 1 mg/kg bw/day and above. Clinical symptoms were observed at higher dose levels. A 28-day dermal study in rats reported brain and erythrocyte cholinesterase inhibition at 0.3 mg/kg bw/day and above. A 13-week dietary study in rats reported erythrocyte cholinesterase inhibition at 0.23 mg/kg bw/day and brain cholinesterase inhibition at higher doses. There were no associated histopathological changes. The NOEL in this study was 0.02 mg/kg bw/day.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: Long-term dietary studies were undertaken in rats, dogs, and mice. Effects were typical of organophosphates and in rats included neuronal degeneration and lethargy at doses of 0.1 mg/kg bw/day and above. In mice and rats, effects included behavioural changes and brain and erythrocyte cholinesterase inhibition at doses of 0.5 mg/kg bw/day. Brain demyelination also was seen in rats by 6 months at doses of 2 mg/kg bw/day. In dogs, erythrocyte cholinesterase was inhibited at the lowest dose tested, 0.03 mg/kg bw/day.

The lowest overall NOEL was 0.02 mg/kg bw/day based on neuronal degeneration and decreased physical activity in the rat. This NOEL is the basis for the current ADI.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for parathion-methyl.

Genotoxicity: Parathion-methyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats reported reduced pup survival during weaning at 1 mg/kg bw/day, without evidence of adverse effects in dams. Developmental studies in rats and rabbits did not identify any effects on foetal development.

Neurotoxicity: Short-term dietary studies in rats, mice and dogs reported symptoms indicative of nervous system toxicity but only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Parathion-methyl is included in Schedule 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.0007 mg/L for parathion-methyl was determined as follows:

$$0.0007 \text{ mg/L} = \frac{0.02 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.02 mg/kg bw/day is the NOEL based on long-term (1-year and 2-year) dietary studies in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for parathion-methyl based on the shown evidence that the chemical "occurs in drinking-water at concentrations well below those at which toxic effects may occur" (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Pebulate

(endorsed 2011)

GUIDELINE

Based on human health concerns, pebulate in drinking water should not exceed 0.03 mg/L.

RELATED CHEMICALS

Pebulate (CAS 1114-71-2) belongs to the thiocarbamate class of chemicals. Other pesticides in this class include molinate, butylate, and EPTC (ethyl dipropylthiocarbamate) (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pebulate would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pebulate is a selective herbicide for the control of grassy weeds in tobacco and tomato crops.

There is at least one registered product containing pebulate in Australia. Pebulate products are intended for professional use and are available as a concentrated solution to be applied in diluted form by roller application to foliage, and by boomspray to soil. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to pebulate and its metabolites are residues in food and in tobacco used for cigarettes and cigars. Residue levels in food and tobacco produced according to good agricultural practice are generally low.

Agricultural use of pebulate may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on pebulate occurrence in Australian drinking water supplies were found.

TREATMENT OF DRINKING WATER

No specific data on the treatment of pebulate in drinking water have been identified.

MEASUREMENT

United States Environmental Protection Agency method 525.2 (USEPA 1995) for the determination of organic compounds in drinking water by liquid-solid extraction and capillary column gas chromatography–mass spectrometry (GC-MS) can achieve a limit of quantitation (LOQ) of 0.08 µg/L to 0.11 µg/L for pebulate. Pebulate can be extracted from water by liquid/liquid extraction with dichloromethane and analysed by GC-MS in selected ion monitoring mode, with a LOQ of 0.5 µg/L. USEPA method 634 for the determination of thiocarbamate pesticides in industrial and municipal wastewaters by gas chromatography is also approved for the analysis of pebulate in water (USEPA 1993). USEPA method 507 for the determination of nitrogen and phosphorus containing pesticides in water by gas chromatograpy (GC) with a nitrogen-phosphorus detector can achieve a LOQ of 0.05 µg/L (Munch 1995). Solid-phase microextraction (SPME) followed by gas–liquid chromatography employing a nitrogen-phosphorus detector can achieve a LOQ of 0.04 µg/L, and SPME-GC employing mass spectrometry can achieve a LOQ of 0.01 µg/L (Choudhury *et al*. 1996).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pebulate is 0.007 mg per kg of bodyweight (mg/kg bw), based on no-observed-effect levels (NOELs) of 0.7 and 0.75 mg/kg bw/day from a long-term dietary study and a reproduction study in rats, respectively. The NOELs are based on decreased bodyweight and slight lens disjunction in eyes at 7 mg/kg bw/day in the long-term study, and decreased bodyweight in parents and offspring at 7.5 mg/kg bw/day in the reproduction study. The ADI incorporates a safety factor of 100, and was established in 1990.

The previous ADI of 0.01 mg/kg bw was set in 1982.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Pebulate was rapidly absorbed and extensively metabolised in oral dosing studies in rats. Excretion was mainly through expired air and to a lesser extent by urine and faeces, and was complete by 24 hours. The major metabolites were mercapturic acids.

Acute effects: Pebulate has low acute oral and dermal toxicity. Pebulate is not a skin sensitiser.

Short-term effects: In medium-term dietary studies in rats and dogs, there was reduced cholinesterase activity in brain and red blood cells, as well as reduced red blood cell count, at doses of 16 mg/kg bw/day.

Long-term effects: Long-term studies were conducted in rats (2-years) and dogs (1-year). In rats, there was decreased bodyweight and slight lens disjunction in the eyes at doses of 7 mg/kg bw/day. In dogs, minor decreases in bodyweight and increases in serum platelet count were seen at doses of 50 mg/kg bw/day. The overall NOEL was 0.7 mg/kg bw/day in the rat study, which is partly the basis for the ADI.

Carcinogenicity: Based on a 2-year study in mice and rats, there is no evidence of carcinogenicity for pebulate.

Genotoxicity: Only short-term *in vitro* studies are available; these report no evidence that pebulate is genotoxic.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A two-generation study in rats found no effects on reproductive parameters. Decreased bodyweights in parents and offspring were seen at doses of 7.5 mg/kg bw/day. The NOEL was 0.75 mg/kg bw/day, which is partly the basis for the ADI. Development studies in rats and rabbits found no effects on foetal development.

Poisons Schedule: Pebulate is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.03 mg/L for pebulate was determined as follows:

$$0.03 \text{ mg/L} = \frac{0.7 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.7 mg/kg bw/day is the NOEL based on a 2-generation studies and long-term (2-year) dietary studies in rats. The effects at higher levels were decreased bodyweights and lens disjunction.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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Pendimethalin

(endorsed 2011)

GUIDELINE

Based on human health concerns, pendimethalin in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Pendimethalin (CAS 40487-42-1) belongs to the dinitroaniline class of chemicals. Other pesticides in this class include trifluralin and oryzalin (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pendimethalin would not be a health concern unless the concentration exceeded 0.4 mg/L. While the health-based guideline is based on long-term effects, there is evidence for maternotoxicity after short-term exposure at levels near the no-observed-effect level (NOEL) used to derive the health-based guideline. Therefore, excursions above the health-based guideline even for a short period are of concern.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pendimethalin is a selective herbicide for the control of broad-leaf weeds and annual grasses in soybean, cotton, wheat, barley, vegetable and turf crops.

There are registered products that contain pendimethalin in Australia. Pendimethalin products are intended for professional use. They are in emulsifiable concentrate or granular formulations, and are applied by aerial spray or ground spray to crops or soil, or mixed with irrigation water for use on fields. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to pendimethalin and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of pendimethalin may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of pendimethalin in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of pendimethalin in drinking water have been identified.

MEASUREMENT

Pendimethalin can be determined in drinking waters by gas chromatography-mass spectrometry. The typical limit of detection is 0.01 µg/L (WHO 2004).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pendimethalin is 0.1 mg per kg of bodyweight (mg/kg bw), based on a NOEL of 12.5 mg/kg bw/day from a long-term (2-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, and was first established in 1987.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Pendimethalin is poorly absorbed in the gastrointestinal tract, with most excreted unchanged in the faeces and the remainder being extensively metabolised and rapidly excreted in urine. Excretion is complete by 96 hours.

Acute effects: Pendimethalin has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea pigs.

Short-term effects: In 30-day dietary studies in rats and dogs, decreased bodyweight gain, and increased absolute liver weights and blood glucose levels were seen in rats at doses of 320 mg/kg bw/day and above. Toxic effects were not seen in dogs even up to high exposure levels of 1000 mg/kg bw/day.

In a 3-month dietary study with pendimethalin in dogs, the only effect was a small decrease in bodyweight gain at the highest dose tested, 1000 mg/kg bw/day.

Long-term effects: In long-term dietary studies in mice, rats and dogs, decreased bodyweight gain and mild liver effects (increased serum alkaline phosphatase, mild inflammation, biliary hyperplasia, hepatic haemosiderosis) were seen in all three species at various doses. The lowest overall NOEL was 12.5 mg/kg/day from a 2-year dietary study in dogs. This NOEL is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for pendimethalin.

Genotoxicity: Pendimethalin is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In 2- and 3-generation studies in rats, and in developmental studies in rats and rabbits, there was no evidence of effects on reproductive parameters or on foetal development. However, maternotoxicity in these studies at 30 mg/kg bw/day is close to the NOEL used as a basis for the ADI.

Poisons Schedule: Pendimethalin is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for pendimethalin was determined as follows:

$$0.4 \text{ mg/L} = \frac{12.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 12.5 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a health-based guideline value of 0.02 mg/L for pendimethalin (WHO 2004). This was based on an ADI of 5 mg/kg bw and an uncertainty factor of 1000 (100 for inter- and intra-species variation and 10 for a combination of the use of a lowest-observed-adverse-effect level instead of a no-observed-adverse-effect level and limitations of the database).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

WHO (World Health Organization) (2004). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Pentachlorophenol

(endorsed 2011)

GUIDELINE

Based on human health concerns, pentachlorophenol in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Pentachlorophenol (CAS 87-86-5) belongs to the chlorinated hydrocarbon class of chemicals. Other pesticides in this class include endosulfan (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pentachlorophenol would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pentachlorophenol is an insecticide and fungicide used formerly as a wood preservative. It has also been used formerly as a pre-harvest defoliant, pre-emergence herbicide and an aquatic biocide.

There are no registered products containing pentachlorophenol in Australia, but de-registered compounds may still be detected in water. When used previously, products containing pentachlorophenol or its salt variant were intended for professional use only.

Exposure sources: If used in the future, the main source of public exposure to pentachlorophenol and its metabolites would be through residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of pentachlorophenol, in the future, may potentially lead to contamination of source waters through processes such as leaching from treated wood, run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data in Australian water could be found. Although pentachlorophenol has been banned in most countries, it can still often be found in surface and groundwater at low µg/L concentrations and in drinking water usually in the range 0.01-0.1 µg/L (Health Canada 1987, WHO 2003).

TREATMENT OF DRINKING WATER

Available data indicate that concentrations of chlorophenols are not reduced significantly during conventional drinking water treatment processes. Although few relevant data are available, it is likely that concentrations below 1 µg/L can commonly be achieved by packed tower aeration and granular activated carbon adsorption (Health Canada 1987).

MEASUREMENT

Pentachlorophenol can be measured by routine gas chromatography mass spectrometry analysis, with a limit of reporting of 0.25 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

No acceptable daily intake (ADI) or acute reference dose (ARfD) values have been established for pentachlorphenol in Australia.

An ADI for pentachlorophenol was set at 0.003 mg per kg of bodyweight (mg/kg bw) by the United States National Academy of Sciences. This ADI was based on a no-observed-effect level (NOEL) of 3 mg/kg bw/day from a long-term (2-year) dietary study in rats. The NOEL is based on decreased bodyweight, liver effects and liver tumours. The ADI incorporates a safety factor of 1000 and was established in 1977.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Pentachlorophenol is readily absorbed via the gastrointestinal tract and through the skin in animals and humans. After exposure, the highest tissue levels were found in the liver and kidneys. Pentachlorophenol is excreted rapidly, either unchanged or as the metabolites, tetrachlorhydroquinone and glucuronides. The half-life for elimination in humans is 17 days.

Acute effects: Pentachlorophenol has moderate to high acute oral toxicity and moderate dermal toxicity. The skin sensitisation potential of pentachlorophenol is unknown.

Short-term effects: In short-term dietary studies in mice, rats and pigs, the main effects observed were on the liver in the form of increased relative liver weight and increased enzyme activity (particularly aryl hydrocarbon hydroxylase), together with histopathological changes. In mice, these effects, as well as increased mortality, were observed from 30 mg/kg bw/day. In pigs, liver weight changes were observed at 10 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice and rats. The liver was the main organ affected, with changes in enzyme levels and liver weight commonly noted at the lower doses, and histopathological changes and in some cases tumour formation at higher dose levels. In mice, decreased bodyweight, liver lesions, hepatocellular adenomas and carcinomas and benign adrenal medulla pheochromocytomas were observed at the lowest dose, 15 mg/kg bw/day. Female mice also showed haemangiosarcomas of the spleen and liver at 30-45 mg/kg bw/day. In rats, reduced bodyweight gain and pigment accumulation in the liver were observed from 10 mg/kg bw/day.

Carcinogenicity: Studies in mice showed an increased incidence of tumours in the spleen, liver and adrenal gland from 15 mg/kg bw/day. This dose level is well in excess of the likely level of pentachlorophenol in drinking water.

Genotoxicity: Pentachlorophenol is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies, despite some weak evidence for chromosomal effects.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: In a one-generation reproduction study in rats, there was evidence of foetotoxicity at high dose levels (25 mg/kg bw/day) only.

In a developmental toxicity study in rats, delayed foetal development was observed at 4 mg/kg bw/day, and embryonic death and maternotoxicity were seen at doses of 43 mg/kg bw/day.

Poisons Schedule: Pentachlorophenol is included in Schedule 6 and 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for pentachlorophenol was determined as follows:

$$0.01 \text{ mg/L} = \frac{3 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 3 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation, with an additional safety factor of 10 due to the limitation of the toxicological data available at the time the ADI was set.

The World Health Organization has a health-based guideline value of 0.009 mg/L for pentachlorophenol (WHO 2004). This guideline value is considered provisional because of the variations in metabolism between experimental animals and humans.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

PER-FLUOROALKYL AND POLY-FLUOROALKYL SUBSTANCES (PFAS)

CAS NUMBERS 1763-23-1 (PFOS), 335-67-1 (PFOA), 355-46-4 (PFHxS)

GUIDELINE

Based on human health considerations, the sum of the concentrations of perfluorooctane sulfonate (PFOS) and perfluorohexane sulfonate (PFHxS) in drinking water should not exceed 70 nanograms per litre (ng/L), which is equivalent to 0.07 micrograms per litre (µg/L).

Based on human health considerations, the concentration of perfluorooctanoic acid (PFOA) in drinking water should not exceed 560 ng/L, which is equivalent to 0.56 µg/L.

GENERAL DESCRIPTION

Per- and poly-fluoroalkyl substances (PFAS) are manufactured chemicals that do not occur naturally in the environment. PFAS chemicals include perfluorooctane sulfonate (PFOS), perfluorooctanoic acid (PFOA) and perfluorohexane sulfonate (PFHxS) amongst a large group of other compounds. PFAS are persistent in the environment, show the potential for bioaccumulation and biomagnification, and are toxic in animal studies (potential developmental, reproductive and systemic toxicity).

Due to PFAS water and heat resistance, they have been used in a wide range of consumer products including surface treatments such as non-stick cookware, and notably in aqueous film forming foam used to extinguish fires. While the import of some PFAS in Australia has been reduced since 2002 (Environmental Health Standing Committee, 2017), historical use in firefighting foams has resulted in detections of PFAS at a number of sites including airports, firefighting training facilities and federal government sites. PFAS has also been found in groundwater, surface water, sewage treatment plant effluents and landfill leachates in international studies (Ahrens *et al.*, 2016; Banzhaf *et al.*, 2017).

Humans can be exposed to PFAS present in food, consumer products, dust and drinking water (Health Canada, 2016a; Health Canada, 2016b). The major sources of PFAS are expected to be food and consumer products, including solution-treated carpeting and treated apparel (Tittlemier et al., 2007); however, the proportion of exposure from drinking water can increase in individuals living in areas with drinking water containing PFAS (Health Canada, 2016a; Health Canada, 2016b). Exposure to PFOS and PFOA from both inhalation and dermal routes during showering and bathing is considered negligible (Health Canada, 2016a; Health Canada, 2016b).

LEVEL DETECTED IN AUSTRALIAN WATER

While some water that is in proximity to contaminated sites has been monitored for PFAS, this has not been done routinely for Australian drinking water supplies.

Low concentrations of PFAS have been reported in water supplies not impacted by contaminated sites; however, these are unlikely to be of human health concern. A study of drinking water collected from 34 sampling locations around Australia found that levels of PFOS and PFOA were not quantifiable in approximately half the samples (limit of quantification (LOQ) of 0.66 ng/L and 0.5 ng/L, respectively), and PFHxS was not quantifiable in more than 70% of samples (LOQ 0.92 ng/L). Concentrations ranged from <0.66 to 16 ng/L for PFOS, <0.92 to 14 ng/L for PFHxS and <0.5 to 9.7 ng/L for PFOA (Thompson et al., 2011a).

TREATMENT OF DRINKING WATER

Standard water treatment technologies including coagulation followed by physical separation, aeration, chemical oxidation, UV irradiation, and disinfection have little or no effect on PFOS or PFOA concentrations (Dickenson and Higgins, 2016; Health Canada, 2016).

Granular activated carbon (GAC) and anion exchange (AIX) can remove many PFAS but are less effective at removing shorter chain PFAS, and may only be effective for a limited time. Reverse osmosis is likely to remove shorter chain PFAS (Thompson *et al*., 2011b). Disposal or treatment of the membrane concentrate stream needs to be considered (WRF, 2016; Dickenson and Higgins, 2016). Researchers are still investigating the most effective and efficient approach to treating PFAS in drinking water and therefore available resources should be taken into consideration during water treatment.

MEASUREMENT

PFAS can be measured by solid phase extraction followed by a liquid chromatograph coupled to electrospray ionization tandem mass spectrometry (MS/MS) operated in negative ion mode (National Measurement Institute (NMI), 2017; Health Canada, 2016). In drinking water the limit of reporting for this analysis is below the guideline values for these chemicals (NMI, 2017). Other methods may be available (for example, time-of-flight mass spectrometry and ion trap mass analysers). Complementary techniques such as oxidative conversion may be used to determine the presence of precursor compounds, which are capable of biotransforming in the environment to form stable chemicals (e.g. PFOS and PFOA) (Houtz and Sedlak, 2012). As with all analytical chemistry, it is essential to ensure a method limit of detection sensitive enough for the level at which the guideline value is set.

Appropriate sampling, storage and transportation are critical for analysis. The potential for sample contamination during both sample collection and analysis is very high due to PFAS being used in other products, including waterproof sample labels, and therefore should be carried out by trained personnel.

A laboratory measurement uncertainty of +/- 20-30% was shown in water samples tested for PFOS and PFOA in the NMI's Proficiency Test Report AQA 16-06 PFOS/PFOA in Fish, Soil and Water (2016). Robust averages were calculated using the procedure set out in ISO13528:2015(E). Reported or estimated uncertainties should be considered carefully when comparing results (NMI, 2016).

HEALTH CONSIDERATIONS

Food Standards Australia New Zealand (FSANZ) conducted a review of the available literature for the purposes of determining Australian Tolerable Daily Intakes (TDIs) for PFOS, PFOA and PFHxS (2017b). FSANZ concluded that available human epidemiology data are not suitable to support the derivation of TDI for PFOS or PFOA, which is consistent with the findings of other regulatory agencies. Therefore, FSANZ has recommended TDIs based on extensive toxicological databases in laboratory animals (FSANZ, 2017).

The following summarises FSANZ findings:

- It is not possible to identify any causal associations between PFOS, PFOA and PFHxS and human health effects from epidemiological studies due to limitations in study design and inconsistency in study results (FSANZ, 2017).
- While there is evidence of associations with increased serum cholesterol and decreased body weights at birth, it is not possible to determine whether PFOS or PFOA cause the changes, or whether other factors are involved. As these are observational studies, FSANZ considers that the meaning and clinical significance of the associations for PFOS and PFOA for decreased birth weight and increased cholesterol in humans are uncertain and should be interpreted with caution (FSANZ, 2017).

NOTE: Important general information is contained in PART II, Chapter 6

- There are studies showing both negative and positive associations between increasing PFOS and PFOA concentrations and compromised antibody production in humans. However, to date there is no convincing evidence for increased incidence of infective disease associated with PFOS or PFOA effects on human immune function (FSANZ, 2017).
- Epidemiological studies have not provided convincing evidence of a correlation between PFOS and PFHxS and any cancer type in human beings. Although associations between PFOA and some human cancers have been suggested from some epidemiological studies, results have often been contradictory, and a causal relationship cannot be established with reasonable confidence (FSANZ, 2017). The International Agency for Research on Cancer (IARC) Monograph found that there is limited evidence of carcinogenicity in humans for PFOA and classified it as possibly carcinogenic to humans (Group 2B) (IARC, 2017).

DERIVATION OF GUIDELINE

PFOS

The health-based guideline value of 70 ng/L for PFOS was determined as follows:

$$\text{70 ng/L equivalent to 0.07 µg/L} = \frac{\text{20 ng/kg body weight/day x 70 kg x 0.1}}{\text{2 L/day}}$$

where:

- A Tolerable Daily Intake (TDI) of 20 ng/kg bodyweight per day has been established by FSANZ on the basis of decreased parental and offspring body weight gains in a multigenerational reproductive toxicity study in rats.
- Because of the large differences observed in the half-lives of PFOS in humans compared to animals, pharmacokinetic modelling was applied to the serum PFOS concentrations measured in experimental animals at the no-observed-adverse-effect level (NOAEL) to calculate the human equivalent dose. The FSANZ TDI incorporates an uncertainty factor of 30, applied to the human equivalent dose (HED: A dose in humans anticipated to provide the same degree of effect as that observed in animals at a given dose), which includes a default factor of 3 to account for interspecies differences in toxicodynamics and a default factor of 10 for intraspecies differences in the human population.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that drinking water accounts for 10% of the TDI.
- 2 L/day is the reference value of water consumed by an adult.
- The rounding conventions described in Chapter 6 have not been applied in the derivation of the health based guideline value for PFOS in order to align with guidance published by the Department of Health.

PFHxS

FSANZ found that there was insufficient toxicological and epidemiological evidence to justify establishing a TDI for PFHxS. In the absence of a TDI, FSANZ concluded that it is reasonable to consider that the TDI for PFOS is likely to be conservative and protective of human health as an interim measure. Effectively this means that the guideline value for PFOS should apply to the sum of PFOS and PFHxS.

NOTE: Important general information is contained in PART II, Chapter 6

PFOA

The health-based guideline value of 560 ng/L for PFOA was determined as follows:

$$560 \text{ ng/L which is equivalent to } 0.56 \text{ µg/L} = \frac{160 \text{ ng/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day}}$$

where:

- A Tolerable Daily Intake of 160 ng/kg bodyweight/day has been established by FSANZ on the basis of a NOAEL for foetal toxicity in a developmental and reproductive study in mice.
- Because of the large differences observed in the half-lives of PFOA in humans compared to animals, pharmacokinetic modelling was applied to the serum PFOA concentrations measured in experimental animals at the NOAEL and above to calculate the human equivalent dose. The FSANZ TDI incorporates an uncertainty factor of 30, applied to the HED, which includes a default factor of 3 to account for interspecies differences in toxicodynamics and a default factor of 10 for intraspecies differences in the human population.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that drinking water accounts for 10% of the TDI.
- 2 L/day is the reference value of water consumed by an adult.
- The rounding conventions described in Chapter 6 have not been applied in the derivation of the health based guideline value for PFOA in order to align with guidance published by the Department of Health.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Permethrin

(endorsed 2011)

GUIDELINE

Based on human health concerns, permethrin in drinking water should not exceed 0.2 mg/L.

RELATED CHEMICALS

Permethrin (CAS 52645-53-1) is in the pyrethroid class of chemicals. Other pesticides in this class include cyfluthrin, cypermethrin, alpha-cypermethrin and deltamethrin (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, permethrin would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Permethrin is an insecticide used for the control of mosquitoes and flies in domestic and agricultural settings, seed infestation in food industry settings, and fleas on dogs.

There are many registered products containing permethrin in Australia. The products are intended for both professional and home garden use. Use patterns include sprays and drenches for livestock in agricultural settings, paint formulations on timber as a preservative in industrial settings, shampoos for dogs, sprays for insects in domestic settings, and sprays for application directly to clothing. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to permethrin are home garden use as an insecticide, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on the concentrations of permethrin in Australian drinking waters or in drinking water overseas.

TREATMENT OF DRINKING WATER

There are no identified reports of the treatment of permethrin in drinking water.

MEASUREMENT

Several methods have been reported for the analysis of permethrin in water, including gas chromatography with micro-electron capture detection (limit of detection [LOD] 2.18 ng/L, Casas *et al*. 2006; LOD 3 ng/L, Mekebri *et al*. 2008), liquid chromatography with electrospray ionisation mass spectrometry (LOD 0.4 ng/L in groundwater and 0.7 ng/L in sea water) (Gil-Garcia *et al*, 2006), and gas chromatography–high resolution mass spectrometry (LOD 0.15ng/L) (Woudneh and Oras 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for permethrin is 0.05 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day from a 2-year dietary study in rats and a 1-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 and was established in 1986.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Permethrin is rapidly absorbed from the gastrointestinal tract and widely distributed in the body. It is rapidly eliminated, mainly in the urine and faeces as polar metabolites in the form of glucuronide conjugates, benzyl alcohols, and weak acids. Permethrin has a low potential for bioaccumulation. The primary metabolites are *m*-phenoxybenzyl alcohol and *m*-phenyxybenzoic acids.

Acute effects: Permethrin has low acute oral and dermal toxicity. Symptoms of acute poisoning were indicative of nervous system poisoning and included tremors, hyperexcitability, salivation and paralysis. It is not a skin sensitiser.

Short-term effects: A 10-day dietary study in rats produced clinical symptoms indicative of an effect on the nervous system (impaired muscle relaxation) at 30 mg/kg bw/day. Recovery from these effects was observed one week after dosing. Medium-term studies were conducted in rats and dogs. Rats were most sensitive to permethrin, with liver centrilobular hypertrophy observed in males at 7.5 mg/kg bw/day. Dogs reported increased liver weight from 50 mg/kg bw/day and decreased bodyweight at 500 mg/kg bw/day.

Long-term effects: A long-term (2-year) dietary study with permethrin in rats, and a 1-year oral dosing study in dogs showed the main effects to be on the liver, and central and peripheral nervous systems. Symptoms included increased serum glucose levels and absolute liver weight at the highest dose tested of 25 mg/kg bw/day (rats), and tremors, incoordination and convulsions at doses of 100 mg/kg bw/day and above (dogs). The NOEL in both studies was the next lowest dose levels tested, 5 mg/kg bw/day, and this is the basis for the current ADI.

Carcinogenicity: Based on long-term studies in rats, there is no evidence of carcinogenicity for permethrin.

Genotoxicity: Permethrin is not considered to be genotoxic, based on *in vitro* or *in vivo* short-term studies.

Reproductive and developmental effects: In a 3-generation reproduction study in rats and developmental toxicity studies in rats and rabbits, there was no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Permethrin is either exempt from scheduling or in Schedule 4, 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on the concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.2 mg/L for permethrin was determined as follows:

$$0.2 \text{ mg/L} = \frac{5.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 5.0 mg/kg bw/day is the NOEL based on a long-term (1-year) oral dosing study in dogs and a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has established a guideline value of 0.3 mg/L for permethrin (WHO 2006).

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

pH

(endorsed 1996)

GUIDELINE

Based on the need to reduce corrosion and encrustation in pipes and fittings, the pH of drinking water should be between 6.5 and 8.5.

New concrete tanks and cement-mortar lined pipes can significantly increase pH and a value up to 9.2 may be tolerated, provided monitoring indicates no deterioration in microbiological quality.

GENERAL DESCRIPTION

pH is a measure of the hydrogen ion concentration of water. It is measured on a logarithmic scale from 0 to 14. A pH of 7 is neutral, greater than 7 is alkaline, and less than 7 is acidic.

One of the major objectives in controlling pH is to minimise corrosion and encrustation in pipes and fittings. Corrosion can be reduced by the formation of a protective layer of calcium carbonate on the inside of the pipe or fitting, and the formation of this layer is affected by pH, temperature, the availability of calcium (hardness) and carbon dioxide. If the water is too alkaline (above pH 8.5), the rapid deposition and build-up of calcium carbonate that can result may eventually block the pipe.

When pH is below 6.5 or above 11, the water may corrode plumbing fittings and pipes. This, however, will depend on other factors such as the material used, the concentration and type of ions in solution, the availability of oxygen, and the water temperature. Under some conditions, particularly in the presence of strong oxidising agents such as chlorine, water with a pH between 6.5 and 7 can be quite corrosive.

Chlorine disinfection efficiency is impaired above pH 8.0, although the optimum pH for monochloramine disinfectant formation is between 8.0 and 8.4. In chloraminated supplies chlorine can react with ammonia to form odorous nitrogen trichloride below pH 7.

Chlorination of water supplies can decrease the pH, while it can be significantly raised by lime leached from new concrete tanks or from pipes lined with asbestos cement or cement mortar. Values of pH above 9.5 can cause a bitter taste in drinking water, and can irritate skin if the water is used for ablutions.

MEASUREMENT

pH can be determined potentiometrically using a standard glass electrode and reference (APHA Method 4500-H^+ 1992).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies pH ranges between 6 and 10.8.

CONTROL IN DRINKING WATER SUPPLIES

The pH of water can be adjusted by the addition of acid or alkali. Usually lime, soda ash, sodium hydroxide, or a combination of lime and carbon dioxide are used (AWWA 1990).

HEALTH CONSIDERATIONS

A direct relationship between pH and human health is difficult to determine, as pH is closely associated with other aspects of water quality. Consumption of food and beverages with quite low or high pH is common and does not result in adverse health effects. Some carbonated soft drinks, for instance, have a

pH of 2.5, orange fruit juice has a pH of about 3.8, and the pH of milk is 6.7.

In humans, extreme values of pH result in irritation of the eyes, skin and mucous membranes. Eye irritation and exacerbation of skin disorders have been associated with pH values above 11. Gastrointestinal irritation may occur in sensitive individuals at pH values above 10. Below pH 4, redness and irritation of the eyes have been reported, with the severity increasing with decreasing pH. Below pH 2.5, damage to the epithelium is irreversible and extensive.

pH may have an indirect effect on bacteriological quality through its effects on disinfection processes. It can affect the solubility of heavy metals, particularly lead and copper from pipes, and the formation of trihalomethanes (see Section 6.3.2 in Chapter 6 on disinfection by-products) (USEPA 1989).

In studies using animals, solutions of differing pH have been injected into the abdominal skin of mice, resulting in irritation at pH 10 after 6 hours. In rabbits, eye irritation was reported at pH 10 but not at pH 4.5.

Chromosome aberrations and gene mutations have been reported in cultured mammalian and invertebrate cells using different acids between pH 4 and 6.5.

The effect of pH on health will depend on the buffering capacity of the water used. This is related to the nature and amount of dissolved inorganic and organic material. Water with a low buffering capacity can change pH rapidly, but water with a high buffering capacity is resistant to pH change. Extreme values of pH in association with highly buffered water are of greater concern than when the water has a low buffering capacity.

DERIVATION OF GUIDELINE

The guideline value is based on minimising corrosion and encrustation of plumbing fittings and pipes. Water with a pH between 6.5 and 8.5 should deposit a protective coating of calcium carbonate and prevent corrosion. High pH can cause scaling and encrustation problems, while lower pH can result in corrosion.

New concrete tanks and cement–mortar lined pipes can significantly increase pH and a value up to 9.2 may be tolerated, provided microbiological monitoring indicates no deterioration in bacteriological quality.

Insufficient data are available to set a health-based guideline value for pH.

GUIDELINES IN OTHER COUNTRIES

The Canadian Guidelines, United States Regulations, European Economic Community Standards, and 1984 World Health Organization (WHO) Guidelines all recommend a pH range of 6.5 to 8.5. The 2006 WHO Guidelines do not provide a specific range of pH values.

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NOTE: Important general information is contained in PART II, Chapter 6

Picloram

(endorsed 2011)

GUIDELINE

Based on human health concerns, picloram in drinking water should not exceed 0.3 mg/L.

RELATED CHEMICALS

Picloram (CAS 2545-60-0) belongs to the pyridinecarboxylic acid class of chemicals. Other pesticides in this class include clopyralid, fluroxypyr and triclopyr (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, picloram would not be a health concern unless the concentration exceeded 0.3 mg/L. Excursions above this level over a short to medium period are of concern, as the health-based guideline is based on effects observed in a 3-month study.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Picloram is a post-emergent herbicide for the control of woody and herbaceous weeds and rhizomatous plants in cereal crops, conservation areas, reserves and parks, and in home gardens.

There are registered products that contain picloram as an ester or a salt in Australia. The products are intended for professional and home garden use. They are generally available as emulsifiable concentrates that are applied by aerial and ground spray, or by direct brushing onto foliage or pouring into the trunks of herbaceous and woody weeds. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to picloram and its metabolites are the use of home garden products, contact with treated weeds in parklands, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The use of picloram in parkland areas and agriculture may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of picloram in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Picloram is completely removed when water undergoes advanced oxidation with iron catalysed ultraviolet irradiation and peroxide (Fenton reaction) (Huston and Pignatello 1999). More research into the removal of picloram is recommended.

MEASUREMENT

Picloram may be measured in drinking waters by liquid chromatography–mass spectrometry, with a typical detection limit of 0.01 µg/L (QFSS 2009 pers comm).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for picloram is 0.07 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 7 mg/kg bw/day from a short-term (3-month) dietary study in dogs. The NOEL is based on increased liver weight. The ADI incorporates a safety factor of 100 and was first established in 1987.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Picloram is readily absorbed in the gastrointestinal tract. It is not extensively metabolised, and is rapidly excreted in the urine, almost completely within 48 hours.

Acute effects: Picloram and its esters and salts have low acute oral dermal toxicity. There is some evidence that picloram is a skin sensitiser in humans. Picloram esters and salts are skin sensitisers in guinea pigs.

Short-term effects: A 3-month oral toxicity study conducted in rats reported no adverse effects up to maximal levels of exposure relevant to humans. A 6-month dietary study in dogs reported increased liver weight at 35 mg/kg bw/day. The lowest overall NOEL was 7 mg/kg bw/day in dogs. This NOEL is the basis for the current ADI.

Long-term effects: Long-term dietary studies were conducted in rats and dogs. In both rats and dogs, the studies reported increases in liver weight, hepatocellular enlargement, and liver discolouration at doses of 60 mg/kg bw/day and above. The lowest overall NOEL was 20 mg/kg bw/day in the rat.

Carcinogenicity: There is limited evidence of picloram (technical grade) carcinogenicity in rats.

Genotoxicity: Picloram is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Two- and 3-generation reproduction studies in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Picloram is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.3 mg/L for picloram was determined as follows:

$$0.3 \text{ mg/L} = \frac{7 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 7 mg/kg bw/day is the NOEL based on a medium-term (3-month) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Piperonyl butoxide

(endorsed 2011)

GUIDELINE

Based on human health concerns, piperonyl butoxide in drinking water should not exceed 0.6 mg/L.

RELATED CHEMICALS

Piperonyl butoxide (CAS 51-03-6) is a derivative of safrole and does not belong to a recognised chemical class. There are no chemically-related pesticides (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, piperonyl butoxide would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Piperonyl butoxide is a synergist for pyrethrin and pyrethroid insecticides and parasiticides for the control of parasites and insects.

There are many registered products that contain piperonyl butoxide in Australia. It is only ever used in combination with insecticides and parasiticides to increase their efficacy. The products are intended for professional and domestic use. Products containing piperonyl butoxide are available as skin ointments, throat/ear drops, aerosol sprays, powders, shampoos and soluble concentrates. Products are applied topically when used as a parasiticide on pets or livestock, and are sprayed as aerosols or diluted solutions when used as an insecticide on fruit, cereal, and vegetable crops. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to piperonyl butoxide and its metabolites are dermal and inhalation exposure from the use of domestic insecticide products, and residues in foods. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of piperonyl butoxide may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater. The veterinary use of piperonyl butoxide provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of piperonyl butoxide in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of piperonyl butoxide in drinking water have been identified.

MEASUREMENT

Piperonyl butoxide may be measured in drinking water by gas chromatography–mass spectrometry. The limit of reporting for this method is typically 0.1 µg/L (QFSS 2009 pers comm).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for piperonyl butoxide is 0.1 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 16 mg/kg bw/day from a long-term study (1-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, and was established in 1997.

The previous ADI for piperonyl butoxide was 0.03 mg/kg bw, based on a NOEL of 3 mg/kg bw/day from the same long-term study in dogs. The ADI was amended in 1997 after a re-evaluation of this study.

The previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Piperonyl butoxide is poorly but rapidly absorbed from the gastrointestinal tract. The absorbed fraction is mostly distributed to the liver and fat, and undergoes extensive metabolism. Excretion occurs relatively rapidly, through the urine (30%) and faeces and is essentially complete within 7 days.

The metabolites of piperonyl butoxide inhibit detoxification enzymes in the liver and are responsible for the synergising effects.

Acute effects: Piperonyl butoxide has low acute oral and dermal toxicity, and is not a skin sensitiser. In humans, no adverse effects were seen after a single oral dose of 0.7 mg/kg bw

Short-term effects: A 4-week dietary study in rats reported histopathological changes in the liver at the lowest dose, 62.5 mg/kg bw/day. An 8-week dietary study in dogs reported decreased bodyweight, increased liver weight and hypertrophy, and decreased testis weights at 62 mg/kg bw/day. Medium-term studies mice reported decreased bodyweight gain, increased liver weight and hypertrophy, and clinical chemistry changes 100 mg/kg bw/day.

Long-term effects: In long-term dietary studies in dogs (1 year), mice (18 months), and rats (up to 22 months), changes included decreased bodyweight gain, increased liver and thyroid weight, and changes indicative of mild liver toxicity at doses of 62 mg/kg bw/day and above. Liver hyperplasia and increased kidney weight were also observed in rats and mice at higher doses. The lowest overall NOEL was 16 mg/kg bw/day in the 1-year study in dogs, and this is the basis for the ADI.

Carcinogenicity: Based on 18- to 22-month studies in mice and rats, there is no evidence of carcinogenicity for piperonyl butoxide.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: Piperonyl butoxide is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Piperonyl butoxide is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.6 mg/L for piperonyl butoxide was determined as follows:

$$0.6 \text{ mg/L} = \frac{16 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 16 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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QFSS (Queensland Forensic and Scientific Services) (2009). QFSS, Personal communication.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th edition, British Crop Production Council, UK.

Pirimicarb

(endorsed 2011)

GUIDELINE

Based on human health concerns, pirimicarb in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Pirimicarb 9 CAS 23103-98-2) belongs to the carbamate class of chemicals. There are many pesticides in this class, including aldicarb, bendiocarb, carbaryl, carbofuran, methiocarb, methomyl and oxamyl (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pirimicarb would not be a health concern unless the concentration exceeded 0.007 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pirimicarb is a post-emergent insecticide for the control of aphids in pastures and a variety of agricultural crops and ornamentals.

There are registered products that contain pirimicarb in Australia. The products are intended for professional use and are available as concentrated solutions, powders and granular formulations. Products are intended for application as a concentrated or dilute spray using high volume application spray equipment such as aircraft or ground boom. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to pirimicarb and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of pirimicarb may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Pirimicarb has been routinely monitored by water utilities in Australia. No detections above analytical limits of detection have been reported in the reviewed reports.

TREATMENT OF DRINKING WATER

Pirimicarb undergoes photochemical and metabolic degradation. Greater than 99.5% removal of pesticides has been reported with the ozonation, biological activated carbon filtration and reverse osmosis treatment (Bonne *et al.* 2000). Reverse osmosis alone was able to remove 99% of the influent concentration of pirimicarb in a challenger test conducted using two different type of membranes (Bonne *et al.* 2000).

MEASUREMENT

Pirimicarb can be analysed by on-line solid phase extraction followed by high-performance liquid chromatography-tandem mass spectrometry. The method can achieve a limit of quantitation (LOQ) of 0.4 µg/L. Solid-phase microextraction followed by gas chromatography–mass spectrometry can achieve a LOQ of 0.1 µg/L (Carabias-Martinez *et al.* 2005). Solid-phase extraction followed by high-performance liquid chromatography coupled to atmospheric pressure electrospray ionisation mass spectrometry can also achieve a LOQ of 0.1 µg/L (Nogueira *et al.* 2003). Solid-phase extraction followed by liquid chromatography with diode array detection can achieve a LOQ of 0.02 µg/L (Van Hoof *et al.* 2002). Single-drop microextraction followed by gas chromatography–mass spectrometry can achieve a LOQ of 50 ng/L (Saraji and Esteki 2008). Dispersive liquid–liquid microextraction coupled with high-performance liquid chromatography–diode array detection can achieve a LOQ of 0.6 ng/mL

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pirimicarb is 0.002 mg per kg of bodyweight (mg/kg bw), based on a lowest-observed-effect level (LOEL) of 0.4 mg/kg bw/day from a short-term (90-day dietary) study in dogs. The LOEL is based on haemotoxicity. The ADI incorporates a safety factor of 200, and was established in 1987.

The previous health value was 0.005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Pirimicarb is readily absorbed via the gastrointestinal tract of mammals. It is readily metabolised and rapidly excreted, mostly in expired air, with the remainder excreted in urine and faeces. It has a low potential for bioaccumulation.

Acute effects: Pirimicarb has moderate acute oral toxicity and moderate acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: Short-term dietary studies conducted in mice, rats, dogs and monkeys reported haematological effects in dogs as the most sensitive toxicological endpoint. A study in rats reported decreased bodyweight gain and food consumption at the highest dose of 75 mg/kg bw/day. A study in dogs reported increased incidence of megaloblasts in bone marrow at 0.4 mg/kg bw/day. This LOEL is the basis for the current ADI. Effects in dogs at higher doses included plasma cholinesterase inhibition, decreased bodyweight gain and effects indicative of bone marrow dysfunction. A study in monkeys reported plasma cholinesterase inhibition at doses of 7 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies have been conducted in mice, rats and dogs. In mice, no effects were reported up to doses of 60 mg/kg bw/day. A two-year study in rats reported decreased bodyweight gain at 25 mg/kg bw/day and above. Plasma cholinesterase was inhibited at the highest dose of 75 mg/kg bw/day. A study in dogs reported increased erythroid/myeloid ratio in females at the highest dose tested of 4 mg/kg bw/day.

Carcinogenicity: There was some evidence of an increased incidence of lung tumours in mice but only at very high dose levels, well in excess of the likely level of human exposure.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: Pirimicarb is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: One and three-generation reproductive studies in rats did not produce any evidence of reproductive effects. Developmental studies in mice, rats and rabbits reported foetotoxicity and maternotoxicity at high dose levels that are well in excess of the likely level of human exposure.

Neurotoxicity: Special neurotoxicity studies in rats by short-term oral administration found no evidence of delayed neurotoxicity at doses up to 25 mg/kg bw/day.

Poisons Schedule: Pirimicarb is included in Schedule 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for pirimicarb was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.4 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 200}$$

where:

- 0.4 mg/kg bw/day is the LOEL based on a short-term (90-day) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 200 is the safety factor applied to the LOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation, with an additional safety factor of 2 for the use of a LOEL instead of a no-observed-effect level.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Pirimiphos methyl

(endorsed 2011)

GUIDELINE

Based on human health concerns, pirimiphos methyl in drinking water should not exceed 0.09 mg/L.

RELATED CHEMICALS

Pirimiphos methyl (CAS 29232-93-7) belongs to the organophosphate class of chemicals. There are many other pesticides in this class including acephate, dichlorvos, fenthion, malathion, omethoate and trichlorfon (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pirimiphos methyl would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pirimiphos methyl is an insecticide for the control of pests such as cockroaches, fleas, ants, mosquitoes and flies in domestic, public, commercial and industrial areas, and agricultural buildings. It is also used as a fumigant to treat stored grain and peanuts.

There are registered products that contain pirimiphos methyl in Australia. The products are intended for professional and domestic use and are available as concentrated solutions to be applied in diluted form using pressurised hand-held spray equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The possible sources of public exposure to pirimiphos methyl and its metabolites are the use of domestic products, residues found in publicly accessible areas, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The use pattern of pirimiphos methyl for treatment of mosquito larvae involves direct application to water that may harbour larvae, and which may then enter source waters for drinking water. Other insecticidal uses of pirimiphos methyl may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on pirimiphos methyl occurrence in Australian drinking water supplies were found. Pirimiphos-methyl was considered by the World Health Organization (WHO) for addition to drinking water in containers as a mosquito larvicide treatment, particularly to control dengue fever. However, the

WHO does not recommended their use for direct application to drinking water unless no other effective and safe treatment is available (WHO 2008).

TREATMENT OF DRINKING WATER

Pirimiphos methyl can be completely mineralised by hydroxyl radicals (HO) generated by Electro-Fenton process (Guivarch *et al.* 2003) and it can be readily degraded in water by ozone-forming polar phenol derivatives (Chiron *et al.* 1998). Powdered activated carbon filtration and reverse osmosis have been demonstrated to be highly effective for the removal of organic chemicals including pesticides in water (Heijman and Hopman 1999).

MEASUREMENT

Pirimiphos methyl can be extracted from water by liquid/liquid extraction with dichloromethane. The extract is dried with sodium sulfate, concentrated, and analysed by gas chromatography–mass spectrometry in selected ion monitoring mode. The method can achieve a limit of quantitation (LOQ) of 0.06 µg/L. Solid-phase microextraction using ceramic/carbon materials followed by gas chromatography with a flame thermionic detector can achieve a LOQ of 15.6 ng/L (Zeng *et al.* 2008). Enzyme-linked immunosorbent assay can achieve pirimiphos detection limits of 0.01 µg/mL (Tang *et al.* 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pirimiphos methyl is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.25 mg/kg bw/day 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, and was established in 1991.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Pirimiphos methyl is readily absorbed via the gastrointestinal tract of rats and dogs, and is extensively metabolised to non-phosphorylated derivatives. In rats, pirimiphos methyl was excreted rapidly in both urine (85%) and faeces (15%), with 12 metabolites detected in urine but not identified.

Acute effects: Pirimiphos methyl has low acute oral and dermal toxicity. It methyl is not a skin sensitiser.

Short-term effects: Short-term dietary studies in rats reported decreased bodyweight gain and food consumption, and inhibition of brain and plasma cholinesterase, at doses of 4 mg/kg bw/day and above. Clinical signs of cholinesterase inhibition and haematological effects were reported at 200 mg/kg bw/day. A 13-week dietary study in dogs reported inhibition of erythrocyte cholinesterase at doses of 2 mg/kg bw/day. At doses of 10 mg/kg bw/day and above, clinical signs consistent with cholinesterase inhibition were observed, as well as decreased bodyweight gain and evidence of mild liver toxicity.

In two human volunteer studies (0.25 mg/kg bw/day for 28 or 56 days), there was no significant change in plasma and erythrocyte cholinesterase activity or liver function parameters. The NOEL from these studies was 0.25 mg/kg bw/day and is the basis of the current ADI.

NOTE: Important general information is contained in PART II, Chapter 6

Long-term effects: Long-term dietary studies in mice, rats and dogs reported cholinesterase inhibition to be the most sensitive toxicological effect. In mice, plasma and erythrocyte cholinesterase were inhibited at 25 mg/kg bw/day, with no associated clinical signs. In rats, plasma and brain cholinesterase were inhibited at 2.5 mg/kg bw/day, with slight anaemia at higher doses. In dogs, inhibition of plasma cholinesterase with associated clinical signs was reported at 2 mg/kg bw/day.

Carcinogenicity: Based on 2-year studies in dogs, mice and rats, there is no evidence of carcinogenicity for pirimiphos methyl.

Genotoxicity: Pirimiphos methyl is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation study in rats and developmental studies in rats and rabbits did not indicate any adverse effects on reproductive parameters or foetal development.

Neurotoxicity: Special neurotoxicity studies in rats by dietary administration found no evidence of delayed neurotoxicity.

Poisons Schedule: Pirimiphos methyl is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.09 mg/L for pirimiphos methyl was determined as follows:

$$0.09 \text{ mg/L} = \frac{0.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.25 mg/kg bw/day is the NOEL based on two short-term (28- and 56-day) studies involving human volunteers.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from human studies, to allow for intraspecies variation.

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Plasticisers
Di(2-ethylhexyl) phthalate (DEHP)
Di(2-ethylhexyl) adipate (DEHA)

(endorsed 1996)

GUIDELINE

Di(2-ethylhexyl) phthalate: Based on health considerations, concentrations in drinking water should not exceed 0.01 mg/L.

Di(2-ethylhexyl) adipate: The data are inadequate to determine a guideline value.

GENERAL DESCRIPTION

DEHP and DEHA are commonly used plasticisers in flexible polyvinyl chloride products. They may be present in drinking water that has been in contact with these products for long periods of time, or as the result of industrial spills. Overseas studies have detected DEHP in drinking water on a few occasions at concentrations from 0.00005 mg/L (50 ng/L) to 0.01 mg/L. DEHA has been detected at concentrations between 0.000001 mg/L (1 ng/L) to 0.0001 mg/L (100 ng/L) in treated drinking water.

DEHP is the most widely used plasticiser. It is also used as a replacement for polychlorinated biphenyls (PCBs) in electrical capacitors. DEHA is used as a lubricant and in hydraulic fluids. Exposure to DEHP and DEHA is widespread because of the broad range of products using these plasticisers. Food is the major source of exposure, and it has been estimated that adult daily intake of DEHP and DEHA, as a result of consumption of food in contact with plastic products, is 0.2 mg to 16 mg.

People receiving kidney dialysis treatment may be exposed to much higher amounts of these plasticisers. In the United States it has been estimated that each dialysis patient could be receiving up to 90 mg of DEHP per treatment.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data are available on DEHP or DEHA concentrations in Australian drinking waters. It is unlikely that concentrations would exceed those reported overseas.

TREATMENT OF DRINKING WATER

There are no published reports on methods for the removal of DEHP or DEHA from drinking water.

MEASUREMENT

Measurement can be undertaken using a liquid extraction procedure (USEPA Draft Method 506 1990). The water sample is extracted with a ternary solvent consisting of methylene chloride, hexane and ethyl acetate. The extract is concentrated and analysed by gas chromatography with photoionization detection. The limit of determination is lower than 0.01 mg/L.

HEALTH CONSIDERATIONS

In animals, DEHP and DEHA are efficiently absorbed from the gastrointestinal tract, although marked differences in absorption are seen between species. Metabolism also differs markedly between species. Highest concentrations of metabolites are seen in the liver and adipose tissue.

An extensive review and summary of the human and animal toxicity data for DEHP is available

(IPCS 1992).

Human volunteers fed up to 10 g of DEHP have experienced mild gastric disturbances, which occurred only at the highest dose. Dialysis patients receiving 150 mg per week intravenously showed no liver changes after one month, but had higher peroxisome numbers after a year. No data exist on the effects of ingested DEHA in humans.

Exposure to DEHP and DEHA can result in a significant increase in peroxisome proliferation in the liver cells of rats. An increase in peroxisome proliferation has been linked to the development of liver tumours in rodents. Humans are regarded as being less sensitive to chemically induced peroxisomal proliferation than rodents.

Long-term gavage (measured force-feeding) studies in rats using DEHP have reported that doses of 100 mg/kg body weight increased the activity of peroxisomal-associated enzymes, with higher doses resulting in depression of growth and enlargement of the liver and kidneys. Very high doses resulted in increased incidence of liver tumours. Short-term studies have reported increases in liver peroxisomal activity at lower doses (from 25 mg/kg body weight per day).

DEHP adversely affects reproduction in mice at 140 mg/kg body weight per day, and it is teratogenic and fetotoxic in mice with a no-effect level of 35 mg/kg body weight per day.

A short-term study using DEHA in rats and mice reported peroxisomal proliferation with a no-effect level of 100 mg/kg body weight per day. Longer-term studies are available, but have used much higher doses. DEHA adversely affects reproduction in rats at doses from 128 mg/kg body weight per day.

Neither DEHP nor DEHA exhibited mutagenic activity when applied to bacteria or to mammalian cells.

The International Agency for Research on Cancer has concluded that DEHA is not classifiable as to its carcinogenicity to humans (Group 3, no adequate evidence in humans and limited evidence in animals) and that DEHP is possibly carcinogenic to humans (Group 2B, no adequate evidence in humans but sufficient evidence in animals) (IARC 1982).

Derivation of guidelThe guideline values were determined as follows:

i) DEHP

$$0.01 \text{ mg/L} = \frac{25 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.01}{2 \text{ L/day} \times 1000}$$

where:

- 25 mg/kg body weight per day is the lowest effect level based on a 14-day study using rats and hamsters (IPCS 1992). Although longer-term studies are available, they report no-effect levels at higher doses.
- 70 kg is the average weight of an adult.
- 0.01 is the proportion of total daily intake attributable to the consumption of water. Sufficient data are available to indicate that food is by far the major source of exposure, and that drinking water contributes approximately 1% of total daily intake.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 because effects were observed at the lowest dose).

An additional safety factor for carcinogenic effects was not applied, as rats are by far the most sensitive species with respect to the sensitive end-point of peroxisomal proliferation.

NOTE: Important general information is contained in PART II, Chapter 6

The World Health Organization (WHO) guideline value of 0.008 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

ii) DEHA

The WHO has calculated a guideline value of 0.08 mg/L for DEHA based on a short-term developmental toxicity study (ICI 1988). The data are not considered to be adequate to determine an Australian guideline value.

REFERENCES

IARC (International Agency for Research on Cancer) (1982). IARC Monographs on the Evaluation of Carcinogenic Risk of Chemicals to Humans: Some industrial chemicals and dyestuffs. World Health Organization, IARC, 29.

ICI (1988). Di(2-ethylhexyl)adipate: teratogenicity study in the rat. ICI Report No. CTL/P/2119.

IPCS (International Programme on Chemical Safety) (1992). Diethylhexyl phthalate. Environmental Health Criteria, 131. World Health Organization, IPCS.

USEPA Draft Method 506 (1990). Determination of phthalate and adipate esters in drinking water by liquid–liquid extraction or liquid–solid extraction and gas chromatography with photoionization detection. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

Polihexanide

(endorsed 2011)

GUIDELINE

Based on human health concerns, polihexanide in drinking water should not exceed 0.7 mg/L.

RELATED CHEMICALS

Polihexanide (CAS 50641-36-6) is a polymer of chlorhexidine. There are no related pesticides (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, polihexanide would not be a health concern unless the concentration exceeded 0.7 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Polihexanide is a disinfectant used to control microorganisms in veterinary hospitals and animal accommodations, and as a sanitiser for milk-handling equipment.

There is at least one registered product containing polihexanide in Australia. Polihexanide products are intended for professional use and are available as a concentrate. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to polihexanide are residues in food (dairy products), and exposure to treated surfaces.

Use of polihexanide as a disinfectant may potentially lead to contamination of source waters through processes such as run-off or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of polihexanide in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of polihexanide in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

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.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) and acute reference dose (ARfD) for polihexanide is 0.2 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 20 mg/kg bw/day from a rabbit developmental study. The NOEL was based on maternotoxicity in pregnant rabbits. The ADI and ARfD incorporate a safety factor of 100, and were established in 2007.

A health value has not been previously established by NHMRC for polihexanide.

HEALTH CONSIDERATIONS

Metabolism: Polihexanide is poorly absorbed via the gastrointestinal tract and is rapidly excreted mainly in the faeces (94%), with the absorbed portion excreted in urine. The metabolic fate of polihexanide is unknown.

Acute effects: Polihexanide has a low acute oral and dermal toxicity. It is a skin sensitiser in guinea pigs.

Short-term effects: Repeat-dose dermal exposure in rats caused reddening and inflammation of the skin at 200 mg/kg bw/day. Ninety-day dietary studies were conducted in rats and dogs. In rats, there was reduced bodyweight gain and haemosiderin deposits in the liver at 68 mg/kg bw/day. In dogs, there were haemosiderin deposits in the spleen at 68 mg/kg bw/day.

Long-term effects: Long-term studies were conducted in mice (2-years), rats (2-years) and dogs (1-year). In mice, there were treatment-related effects in the liver (increase in haemangiosarcomas) and recto-anal junction (inflammation, hyperplasia and squamous cell carcinomas) at 180 mg/kg bw/day. In rats, there was some evidence of an increase in haemangioma/haemangiosarcomas in the liver at 100 mg/kg bw/day. In dogs, there was evidence of systemic toxicity at 45 mg/kg bw/day.

Carcinogenicity: Polihexanide induced an increased incidence in haemangiomas/haemangiosarcomas in the liver of mice at a high dose level that is well in excess of the normal level of human exposure. The increased incidence of squamous cell carcinomas in the recto-anal junction was considered to be a consequence of irritation/inflammation at the high dose level and not relevant to human exposure.

Genotoxicity: Polihexanide is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproduction and developmental effects*:* A reproduction study in rats and developmental studies in rats and rabbits did not show any evidence of effects on reproductive parameters or on foetal development. The NOEL for maternal toxicity in rabbits was 20 mg/kg bw/day, and this was the basis for the ADI.

Poisons Schedule: Polihexanide is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.7 mg/L for polihexanide was determined as follows:

$$0.7 \text{ mg/L} = \frac{20 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 20 mg/kg bw/day is the NOEL based on a developmental study in rabbits.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor applied to the NOEL from a developmental study conducted in rabbits. The safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variations.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Polycyclic aromatic hydrocarbons (PAHs)

(endorsed 2011)

GUIDELINE

Based on health considerations, the concentration of benzo[a]pyrene in drinking water should not exceed 0.00001 mg/L (10 ng/L). Data are inadequate to set guidelines for other PAHs, however comparative carcinogenic potency can be used to determine an approximate risk when complex mixtures of PAHs are present in drinking water.

GENERAL DESCRIPTION

The polycyclic aromatic hydrocarbons are a large group of organic compounds with two or more fused aromatic rings. Several hundred have been identified in air, emitted from various combustion and pyrolysis sources. The principal PAHs include phenanthrene, fluoranthene, pyrene, anthracene, benzo(a) pyrene, benzofluoranthene, chrysene, anthanthrene and naphthalene.

PAHs are widespread throughout the environment. They are formed in forest fires and in the combustion of fossil fuels, and are present in emissions from coke ovens, aluminium smelters and motor vehicles. Contamination of drinking water can occur by direct atmospheric deposition and by leaching from bituminous liners in water distribution systems.

There are very few data on concentrations of PAHs in drinking water supplies. The few data that exist are mainly for benzo(a)pyrene (BaP). The typical concentration of BaP in drinking water in the United States is estimated to be 0.00000055 mg/L (0.55 ng/L).

Background levels of PAHs in drinking water range from 4 to 24 ng/L (0.0004 to 0.0024 µg/L) (ATSDR 2008). The typical level of BaP in drinking water in the United States is estimated to be 0.55 ng/L (0.00055 µg/L) (WHO 1996, WHO 1998). The median value for daily intake for PAHs from exposure via drinking water has been estimated to be 0.006 µg/day (Menzie *et al.* 1992). Daily intake of total PAHs has also been estimated to be 0.027 µg (Santodonato *et al.* 1981), while the daily intake of BaP in drinking water is estimated to range from 0.1 to 1 ng (Santodonato *et al.* 1981, WHO 1996). In general it is suggested that PAHs in drinking water only contribute no more than 1% of total PAH intake (WHO 1996).

Food is the major source of intake of PAHs. Highest concentrations occur in smoked foods, leafy vegetables and the burnt fat of meats. Intake from foods is extremely variable but significantly higher (by at least an order of magnitude) than from drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

PAHs have not been found in Australian drinking waters. They are included here to provide guidance in the unlikely event of contamination, and because they have been detected occasionally in drinking water supplies overseas. One potential contributor to PAHs in drinking water in Australia would be periodic intense and extensive bush fires in water storage catchments.

TREATMENT OF DRINKING WATER

The conventional water treatment processes of coagulation, settling and filtration are capable of reducing the BaP concentration of raw waters to less than 0.000001 mg/L (1 ng/L), even if the influent concentration is high. It is likely that other PAHs would be similarly reduced. Granular activated carbon would also be effective in the removal of these compounds.

MEASUREMENT

Concentrations of a wide range of PAHs in water can be determined by the use of gas chromatography–mass spectrometry (GC-MS) combined with suitable extraction and pre-concentration procedures. Alternatively, the use of fluorescence detection combined with high performance liquid chromatography (HPLC) provides a sensitive method for PAHs in water (USEPA Draft Method 550, 1990). Typically, solvent extraction employing dichloromethane or solid phase extraction using resins or commercially available adsorption cartridges or discs are used for extraction and concentration, prior to final determination by GC-MS or HPLC.

HEALTH CONSIDERATIONS

Most of the toxicological literature deals specifically with BaP. Few studies are available for the other PAHs. Some PAH compounds have been found to be carcinogenic by non-oral routes, but others are known to have low potential for carcinogenicity.

BaP is absorbed principally through the gastrointestinal tract and the lungs. The rate of absorption increases with increased intake of polyunsaturated fatty acids. BaP is rapidly distributed to the organs and may be stored in mammary and adipose tissue. Metabolism occurs mainly in the liver.

The International Agency for Research on Cancer (IARC) has upgraded BaP from group 2B to group 1 (carcinogenic to humans), based on mechanistic considerations and other relevant data. This evaluation is presented in full in IARC monograph 92. In addition, dibenz[a,h]anthracene and dibenzo[a,l]pyrene have been upgraded to group 2A (probably carcinogenic to humans), with supporting evidence from other relevant data. Certain substances containing complex mixtures of PAHs are classified as known human carcinogens (Group 1) by IARC. These include: coal tar pitches, coal tars and cigarette smoke condensate.

In experiments with animals, many PAH mixtures have been associated with an increased incidence of cancer. BaP is one of the most potent carcinogenic compounds, with primary tumours having been reported in a variety of studies, using different administration techniques, in mice, rats, hamsters, guinea pigs, rabbits, ducks and monkeys. Tumours have mostly appeared only at the site of administration.

BaP is metabolically activated to a series of dihydrodiol expoxides by the mixed function oxidases, particularly cytochrome P450 1A1, in combination with epoxide hydrolase. One particular dihydrodiol epoxide (+ anti isomer) is highly mutagenic and in its ultimate carcinogenic form (a carbonium ion), will bind to nucleophilic sites on DNA to product covalent DNA adducts. If these adducts are misrepaired, they may produce mutations in tumour suppression genes and cancer-causing oncogenes, which can lead to cancer. Other carcinogenic PAHs operate in a similar manner through metabolic activation and DNA adduct formation. The sensitive determination of DNA adducts can be useful in determination of human exposure to carcinogenic

DERIVATION OF GUIDELINE

Data are insufficient to set guideline values for PAHs except for BaP. The use of relative potencies of other PAHs can, however, give guidance to their relative contribution to risk caused by their presence in drinking water. Relative potencies of the most commonly found PAHs are given in Table 1.

NOTE: Important general information is contained in PART II, Chapter 6

The relative carcinogenic potencies of a number PAHs have been determined and are reported in the literature. Table 1 presents those data with summarised relative potencies sourced from the World Health Organization (WHO 1998) and additional data as referenced.

Table 1: *Relative carcinogenic potency of selected PAHs*

PAH	Relative potency with BaP as unity
Benz[a]anthracene	0.1*
Benzo[a]pyrene	1*
Benzo[b]fluoranthene	0.1*
Benzo[j]flouranthene	0.1*
Benzo[k]flouranthene	0.1*
Dibenz[a,h]anthracene	1*
Indeno[1,2,3,c,d]pyrene	0.1*
Benzo[g,h,i]perylene	0.01**
Benz[a]anthracene	0.1** and ***
Chrysene	0.01** and ***
Dibenz[a,h]anthracene	5**
Dibenz[a,e]pyrene	1***
Dibenz[a,h]pyrene	10***
Dibenz[a,i]pyrene	10***
Dibenz[a,l]pyrene	10***

* Sourced from WHO (1998)

** Sourced from Nisbet and LaGoy (1992)

*** Sourced from CA EPA (2002)

A number of points in relation to Table 1 are worth noting. PAHs with relative carcinogenic potencies of less than 0.01 (100 times less carcinogenic than BaP) are not reported due to the lower level of risk they pose in water. There are three PAHs listed in Table 1 with relative carcinogenic potencies ten times that of BaP, and these PAHs should be given attention when risk assessments of PAHs in drinking water are undertaken. Slope factors for carcinogenic risk assessment of PAHs are provided by the California Environmental Protection Agency (CA EPA 2002). Additional data on slope factors and drinking water unit risk for BaP are given in the IRIS database (USEPA 2008).

While it is recognised that a guideline is available only for BaP, this can be used in conjunction with relative potencies given in Table 1 to gain an estimate of acceptable levels when complex mixtures of PAHs are present.

On the basis of a feeding study using mice (Neal and Rigdon 1967), the excess risk of lifetime consumption of water with a BaP concentration of 0.00007 mg/L (70 ng/L) was conservatively estimated by WHO, using a linear multistage model, at one additional cancer per million people.

The guideline value has been set at the limit of determination because this is slightly less than the value derived using a risk assessment calculation, and provides an adequate degree of protection. This is consistent with the general approach adopted for genotoxic carcinogens (see Section 6.3.3).

The WHO guideline value of 0.0007 mg/L was based on an oral carcinogenicity study in mice and calculated using a 2-stage birth-death mutation model, and on carcinogenicity studies in mice following oral administration (WHO, 2004).

NOTE: Important general information is contained in PART II, Chapter 6

REFERENCES

ATSDR (Agency for toxic Substances and Disease Registry) (2008). Public Health Statement for Polycyclic Aromatic Hydrocarbons (PAHs). ATSDR.

CEPA (California Environmental Protection Agency) (2002). Air toxic hotspots program risk assessment guidelines. Part II. Technical support document for describing available cancer potency factors. Available from: https://oehha.ca.gov/media/downloads/crnr/tsdnov2002.pdf

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IARC (2010) *Monograph on the Evaluation of Carcinogenic Risks to Humans. Volume 92: Some non-heterocyclic, polycyclic aromatic hydrocarbons and some related exposures.* World Health Organization, International Agency for Research on Cancer, Lyon, France

Menzie CA, Potocki BB, Santodonato J (1992). Exposure to carcinogenic PAHs in the environment. *Environmental Science and Technology*, 26:1278-1284.

Neal J, Rigdon RH (1967). Gastric tumors in mice fed benzo(a)pyrene: a quantitative study. *Texas Reports on Biology and Medicine*, 25:553–557.

Nisbet ICT, Lagoy PK (1992). Toxic equivalency factors (TEF's) for polycyclic aromatic hydrocarbons (PAHs). *Regulatory and Toxicological Pharmacology,* 16:290-300.

Santodonato J, Howard P, Basu D (1981). Health and ecological assessment of polynuclear aromatic hydrocarbons. *Journal of Environmental Pathology and Toxicology*, 5:1-364.

USEPA (United States Environmental Protection Agency) (2008). Integrated Risk Information system (IRIS), Benzo[a]pyrene CASRN 50-32-8.

USEPA Draft Method 550 (1990). Determination of polycyclic aromatic hydrocarbons in drinking water by liquid–liquid extraction and HPLC with coupled ultraviolet and fluorescence detection. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

WHO (World Health Organization) (1996). *Guidelines for Drinking-Water Quality*, 2nd Edition, Vol. 2 – Health criteria and other supporting information. WHO, Geneva, Switzerland.

WHO (World Health Organization) (1998). *Guidelines for Drinking-Water Quality*, 2nd edition, Addendum to Volume. 2 – Health criteria and other supporting information. WHO, Geneva, Switzerland.

WHO (World Health Organization) (2004) *Guidelines for Drinking-Water Quality*, 3rd Edition, WHO, Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

Profenofos

(endorsed 2011)

GUIDELINE

Based on human health concerns, profenofos in drinking water should not exceed 0.0003 mg/L.

RELATED CHEMICALS

Profenofos (CAS 41198-08-7) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes temephos, fenthion, and methidathion (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, profenofos would not be a health concern unless the concentration exceeded 0.0003 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Users: Profenofos is used as an insecticide and acaricide (miticide) for the control of certain insects on cotton crops.

There are registered products containing profenofos in Australia. The products are intended for professional use and are applied as concentrated or diluted solutions by either ground boom spray or aerial application methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to profenfos is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of chemical may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of profenfos in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of profenfos in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Profenofos can be measured in drinking waters by gas chromatography–mass spectrometry, with a practical limit of detection of 0.1 µg/L (QHFSS 2008 pers comm).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for profenofos is 0.0001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.0072 mg/kg bw/day from a 6-month dog study. The NOEL is based on inhibition of plasma cholinesterase. The ADI incorporates a safety factor of 100, and was established in 1982.

The previous health value was 0.0003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Profenofos is rapidly absorbed in the gastro-intestinal tract and is completely metabolised to four metabolites, which are excreted mainly in urine.

Acute effects: Profenofos has a moderate oral and low dermal toxicity. Profenofos is a skin sensitiser. Clinical symptoms of toxicity were typical of cholinesterase inhibition and included tremors, prostration, coma, piloerection, ataxia, and salivation.

Short-term effects: Medium-term toxicity studies in rats (3 months) and dogs (6 months) reported decreased plasma, red blood cell and brain cholinesterase, with plasma cholinesterase the most sensitive, at dose levels above 0.3 mg/kg bw/day and 0.007 mg/kg bw/day, respectively.

Long-term effects: Long-term studies in mice and rats reported decreased cholinesterase as the most sensitive toxicity endpoint. Decreased plasma cholinesterase was noted at dose levels above 0.015 mg/kg bw/day in the rat.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for profenofos.

Genotoxicity: There is equivocal evidence of genotoxicity from *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a reproduction study in rats and developmental studies in rats and rabbits, there was no evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Profenofos is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.0003 mg/L for profenofos was determined as follows:

$$0.0003 \text{ mg/L} = \frac{0.0072 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.0072 mg/kg bw/day is the NOEL based on a medium-term (6-month) study in dogs.
- 70 kg is taken as the average weight of an adult
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult

NOTE: Important general information is contained in PART II, Chapter 6

- 100 is a safety factor applied to the NOEL from a study conducted in dogs. The safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) T*he Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

QHFSS (Queensland Health Forensic and Scientific Services) (2008). Personal communication.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Promecarb

(endorsed 2011)

GUIDELINE

The health concerns associated with promecarb have not been fully evaluated and therefore a health-based guideline value for promecarb in drinking water cannot be set.

RELATED CHEMICALS

Promecarb (CAS 2631-37-0) belongs to the carbamate class of chemicals. There are many other pesticides in this class, which includes aldicarb, carbaryl and methomyl (Tomlin 2006).

HUMAN RISK STATEMENT

There are currently insufficient data on which to base a human risk statement.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Promecarb is an insecticide formerly used to control lepidopterous pests, leaf miners of fruits, Colorado potato beetle and common rootworm, in agriculture and the home garden.

There are no registered products containing promecarb in Australia, but de-registered compounds may still be detected in water. Previously registered products were intended for both professional and home garden use.

Exposure sources: If used in the future, the main source of public exposure to promecarb and its metabolites would be residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of promecarb in the future may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No occurrence data on promecarb in Australian waters could be found.

TREATMENT OF DRINKING WATER

No information on efficiency of drinking water treatment to remove promecarb could be found.

MEASUREMENT

Promecarb can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 1 µg/L (Queensland Health, 2007).

HISTORY OF THE HEALTH VALUES

There is currently no acceptable daily intake (ADI) or acute reference dose (ARfD) value for promecarb.

The previous health value was 0.03 mg/L.

HEALTH CONSIDERATIONS

Metabolism: Promecarb is well absorbed from the gastrointestinal tract, extensively metabolised and rapidly excreted, mainly via the urine.

Acute effects: Promecarb has high acute oral toxicity and moderate acute dermal toxicity. It is unknown whether promecarb is a skin sensitiser. In rats, inhibition of plasma, brain and red blood cell cholinesterase was observed after a single oral dose of 10 mg/kg bw. Recovery was seen within 24 hours.

Short-term effects: In 3-month oral studies in mice, there was increased mortality, decreased bodyweight gain, severe hyperglycemia, decreased spleen and ovarian weights, and liver degeneration at 8.9 mg/kg bw/day and above.

In 3-month dietary studies in rats and dogs, no treatment-related effects were observed up to 20 mg/kg bw/day in rats and up to 5 mg/kg bw/day in dogs. These were the highest doses tested for each species.

Long-term effects: In an 18-month dietary study in rats, there were no clinical signs of toxicity at 20 mg/kg bw/day, the highest dose tested (cholinesterase activity was not measured).

Carcinogenicity: In an 18-month study in rats, there was no evidence of carcinogenicity for promecarb.

Genotoxicity: Only short-term *in vitro* studies are available; these report no evidence that promecarb is genotoxic.

Reproductive and developmental effects: There were no reproduction studies available. In a developmental study in rats, maternotoxicity and delayed ossification in the foetus occurred at 5 mg/kg bw/day.

Poisons Schedule: Promecarb was removed from Schedule 6 of the Standard for the Uniform Scheduling of Drugs and Poisons in August 1993 due to concerns over the lack of toxicity and residue data. Current versions of the Standard for the Uniform Scheduling of Medicines and Poisons (the Poisons Standard) (DoHA 2010) should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

There are currently insufficient data on which to establish a health-based guideline for promecarb in drinking water in Australia.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Queensland Health (2007). Organochlorine, organophosphorous and synthetic pyrethroid pesticide, urea and triazine herbicides and PCBs in water. QHFSS SOP 16315.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th edition, British Crop Production Council, UK.

Propachlor

(endorsed 2011)

GUIDELINE

Based on human health concerns, propachlor in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Propachlor (CAS 1918-16-7) belongs to the chloroacetamide class of chemicals. Other pesticides in this class include metolachlor and S-metolachlor (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, propachlor would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Propachlor is a herbicide for the control of annual grasses and certain broad-leaf weeds in sorghum and selected vegetable crops.

There is at least one registered product that contains propachlor in Australia. Propachlor products are intended for professional use, and are available as an aqueous concentrate to be diluted and applied as a surface spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to propachlor and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of propachlor may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of propachlor in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Propachlor can be effectively oxidised in drinking water by suitable dosing chemical oxidants such as ozone, or by photocatalytic advanced oxidation processes (Konstantinou *et al.* 2002, Liu *et al.* 2008).

MEASUREMENT

No suitable analytical methods have been identified for the analysis of propachlor in drinking waters. However, sensitive liquid chromatography–tandem mass spectrometry methods are available for the analysis of the major environmental degradation products of propachlor and other related herbicides in drinking waters (Fuhrman and Allan 2002, Shoemaker and Bassett 2006).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for propachlor is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.0 mg/kg bw/day established in two long-term studies (an 18-month study in mice and a 2-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, and was established in 1988.

Earlier ADIs established for propachlor were 0.1 and 0.002 mg/kg bw, set in 1972 and in 1987 respectively. The former ADI was based on a 90-day rat study in which the NOEL was 10 mg/kg bw/day; the latter was based on a NOEL of 3 mg/kg bw/day obtained in a 2-generation rat reproduction study. This NOEL was chosen in the absence of a NOEL derived from long-term toxicity studies.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Propachlor is absorbed readily and extensively in the gastrointestinal tract, with maximum blood concentration in 1 hour. It is metabolized rapidly and the major metabolites are excreted in the urine (68%) and faeces (19%). Biliary excretion followed by gut microflora metabolism and re-absorption is significant.

Acute effects: Propachlor has low acute oral and dermal toxicity. It is a skin sensitiser.

Short-term effects: Ninety-day dietary studies in mice, rats and dogs reported no clinical or pathological signs of toxicity at 930 mg/kg bw/day in mice, at 310 mg/kg bw/day in rats, or at 155 mg/kg bw/day in dogs.

Long-term effects: An 18-month dietary study in mice reported increases in liver weight at 7.5 mg/kg bw/day. A two-year dietary studies in rats reported increases in thyroid and parathyroid weights at 25 mg/kg bw/day. A 1-year dietary study in dogs reported a significant decrease in bodyweight in male dogs at 25 mg/kg bw/day. No clinical or pathological signs of toxicity were noted in any of these studies. The NOEL of 2 mg/kg bw/day from the long-term mouse and rat studies is the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for propachlor.

Genotoxicity: Propachlor is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a 2-generation reproduction study in rats and in a developmental study in rats, there was no evidence of reproductive or developmental effects. A developmental study in rabbits revealed post-implantation foetal losses and a subsequent decrease in the number of viable foetuses at 15 mg/kg bw/day, which was below the dose level causing maternal toxicity.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Propachlor is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for propachlor was determined as follows:

$$0.07 \text{ mg/L} = \frac{2.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.0 mg/kg bw/day is the NOEL based on long-term dietary studies in mice (18 months) and rats (2 years)
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Propanil

(endorsed 2011)

GUIDELINE

Based on human health concerns, propanil in drinking water should not exceed 0.7 mg/L.

RELATED CHEMICALS

Propanil (CAS 709-98-8) belongs to the anilide class of chemicals. Another chemical in this class is pentanochlor (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, propanil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Propanil is a herbicide for the post-emergent control of barnyard grass in rice.

There are registered products that contain propanil in Australia. The products are intended for professional use and are available as concentrated solutions to be applied in diluted form using boom, aerial and knapsack spray application methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to propanil and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of propanil on rice fields may lead to contamination of source waters through entry into groundwater and processes such as run-off and spray drift.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Propanil has been tested but not detected in the Ord River Irrigation Area, Western Australia (Oliver and Kookana 2005). It was detected in one of 53 finished drinking water samples collected at different sites in the USA at 0.7 µg/L (Li *et al.* 2006). Propanil has been detected in the drainage channels of the main rice cultivating countries in Europe. The highest concentration reported was 16.82 µg/L (Kuster *et al.* 2008).

TREATMENT OF DRINKING WATER

Propanil can be removed from drinking water by granular activated carbon (Ayranci and Hoda 2004) and reverse osmosis treatment.

MEASUREMENT

Propanil can be measured in water by online solid-phase extraction (SPE) liquid chromatography mass spectrometry (LC-MS) or direct injection on a triple quadrapole LC-MS instrument in multiple reaction monitoring mode. The method can achieve a limit of quantitation (LOQ) of 1 µg/L. SPE followed by high performance liquid chromatography using photochemically-induced fluorescence detection can achieve a LOQ in the range of 0.07 to 0.7 µg/L (de la Pena *et al.* 2003). Li *et al.* (2006) reported a propanil LOQ in drinking water of 0.02 µg/L using liquid chromatography–electrospray ionization–mass spectrometry.

Propanil can also be detected at very low concentrations in water. A fully automated method using on-line solid-phase extraction–liquid chromatography–electrospray-tandem mass spectrometry can achieve a LOQ of 0.5 ng/L (Kampioti *et al.* 2005). A solid-phase microextraction-gas chromatography-mass spectrometry method can achieve a LOQ of 2 ng/L (Natangelo *et al.* 1999) and on-line solid-phase extraction-liquid chromatography–electrospray–tandem mass spectrometry can achieve a LOQ of 0.4 ng/L (Kuster *et al.* 2008). Moreover, a method without any sample pre-treatment and without pre-concentration using a fully automated immunoassay for detection of propanil in aqueous samples can achieve a LOQ of 0.6 ng/L (Tschmelak *et al.* 2004).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for propanil is 0.2 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 20 mg/kg bw/day from a 2-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, and was established in 1981.

The previous health value was 0.5 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Propanil is readily and extensively absorbed via the gastrointestinal tract. It is metabolised and eliminated within 48 hours. The major metabolites are 3,4-dichloroaniline (DCA) and 3,3′,4,4′-tetrachloroazobenzene (TCAB) (WHO 2004). These metabolites in addition to tetrachloroazoxybenzene (TCAOB) have been reported as impurities of toxicological concern in propanil. The Australian Pesticides and Veterinary Medicines Authority have set impurity limits of 20 mg/kg for TCAB and 2 mg/kg for TCAOB in propanil active constituent.

Acute effects: Propanil has low oral and dermal acute toxicity. It is not a skin sensitiser.

Short-term effects: A short-term dietary study in rats reported an increase in number of abnormal red blood cells at doses of 25 mg/kg bw/day. At higher dose levels, effects reported included haemolytic anaemia, decreased bodyweight gain and increased mortality. In a 4-week dietary study in dogs, decreased bodyweight gain and food consumption was reported at 375 mg/kg bw/day.

Long-term effects: Long-term dietary studies with propanil in rats and dogs showed the main toxicological effect to be haemotoxicity. A 2-year dietary study in rats reported decreased bodyweight gain, decreased haemoglobin and haematocrit levels, and increased spleen, liver and testes weights at 80 mg/kg bw/day. In dogs, there was decreased bodyweight gain and decreased haemoglobin levels at 225 mg/kg bw/day and above. The lowest overall NOEL was 20 mg/kg bw/day in the rat study and this is the basis for the current ADI.

Carcinogenicity: Based on 2-year studies in rats and dogs, there is no evidence of carcinogenicity for propanil.

NOTE: Important general information is contained in PART II, Chapter 6

Genotoxicity: The genotoxicity of propanil has not been evaluated in Australia, but studies evaluated by the World Health Organization are reported as negative.

Reproductive and developmental effects: A 3-generation reproduction study in rats did not show any evidence of effects on reproductive parameters or foetal development. No specific developmental toxicity study was available.

Poisons Schedule: Propanil is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.7 mg/L for propanil was determined as follows:

$$0.7 \text{ mg/L} = \frac{20 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 20 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for propanil. The following reason is given: "Although a health-based value for propanil can be derived, this has not been done, because propanil 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 allow the derivation of a guideline value for them. Authorities should consider the possible presence in water of more toxic environmental metabolites." (WHO 2004).

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Propargite

(endorsed 2011)

GUIDELINE

Based on human health concerns, propargite in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Propargite (CAS 2312-35-8) is a sulfite ester acaricide. There are no other pesticides in this chemical class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, propargite would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Propargite is an acaricide (miticide), used on a wide variety of food crops, ornamentals and cotton for the control of mites.

There are registered products that contain propargite in Australia. The products are for professional use. Some are emulsifiable concentrates used on cotton, to be diluted and typically applied by ground rig. Others are a water-dispersible granule formulation used on various fruits and vegetable crops and ornamentals. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to propargite and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of propargite may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Propargite was detected in 2000 at Carole Creek, at Mungindi Road bridge, New South Wales, at a concentration of 1.10 µg/L (Muschal 2001).

TREATMENT OF DRINKING WATER

Measured removal of propargite by coagulation–flocculation during drinking water treatment ranged from less than 1% to 17% of the initial concentration (Ballard and Mackay 2005).

MEASUREMENT

Propargite can be extracted from water by liquid/liquid extraction with dichloromethane. The extract is then dried with sodium sulfate, concentrated, and analysed by gas chromatography–mass spectrometry (GC-MS) in selected ion monitoring mode (SIM). The method can achieve a limit of quantitation (LOQ) of 15 µg/L (Yu *et al*. 1997). Akhtar (1988) achieved a LOQ for propargite in groundwater of 0.1 µg/L using GC-MS-SIM. A multi-residue analysis of the pesticides involving extraction and clean-up using gel permeation chromatography and solid-phase extraction (SPE), and subsequent identification and quantification by GC-MS can achieve a LOQ of 2.5 µg/mL for propargite (Huang *et al*. 2007). SPE and gas chromatography ion-trap mass spectrometry can achieve a LOQ of 0.05 µg/L (Deger *et al*. 2000).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for propargite is 0.002 mg per kg of bodyweight (mg/kg bw), based on a NOEL of 2 mg/kg bw/day 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 1000. 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).

The first ADI of 0.2 mg/kg bw was set in 1988 and was based on a NOEL of 22.5 mg/kg bw/day in a long-term (2-year) dietary study in dogs. This ADI was revised in 1992 to 0.02 mg/kg bw, based on a NOEL of 2 mg/kg bw/day in a rabbit developmental study.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Propargite is partially absorbed from the gastrointestinal tract, extensively metabolised, and distributed evenly in the tissues. Excretion is approximately equal between urine and faeces, with biliary excretion contributing to the faecal excretion. Little unchanged propargite was found in the bile or plasma.

Acute effects: Propargite has low to moderate acute oral toxicity and low dermal toxicity. It is a skin sensitiser in guinea pigs.

Short-term effects: A 90-day dietary study in rats reported clinical signs of toxicity, reduced bodyweight gain and haematological and clinical chemistry changes at 50 mg/kg bw and above.

A 13-week dietary study in dogs reported decreased food consumption, reduced bodyweight gain, increased pigmentation in the reticuloendothelial cells in the liver and increased haemosiderin deposits in the spleen at 50 mg/kg bw/day and above.

Long-term effects: A 2-year dietary study in rats reported a moderate decrease in bodyweight gain, clinical chemistry changes and relative liver and kidney weight changes at 19 mg/kg bw/day. There was also a dose-related increase in undifferentiated sarcomas of the jejunum, often associated with ulceration, at a dose level of 3 mg/kg bw/day and above in females and 19 mg/kg bw/day and above in males. In some animals, there were metastases to the mesentery and lungs. A more detailed long-term study examining the changes in the jejunum in rats showed significant cell proliferation and increased jejunal mass at 14 mg/kg bw/day in males and 21 mg/kg bw/day in females. The NOEL for cell proliferation was 2 mg/kg bw/day and this is the basis of the ADI.

An 18-month study in mice reported no increase in jejunal tumours at the highest dose level of 150 mg/kg bw/day.

Carcinogenicity: There was evidence of carcinogenicity in rats but not mice. In rats, sarcomas of the

jejunum are likely to be the result of increased cell proliferation. This effect occurred at dose levels well in excess of the likely level of human exposure to propargite.

Genotoxicity: Propargite is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Propargite is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for propargite was determined as follows:

$$0.007 \text{ mg/L} = \frac{2.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 2.0 mg/kg bw/day is the NOEL based on a long-term (20-month) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation, 10 for intraspecies variation, and 10 for the narrow margin between the NOEL for cell proliferation (2 mg/kg bw/day) and the dose at which tumours occurred (3 mg/kg bw/day) in rats.

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NOTE: Important general information is contained in PART II, Chapter 6

Propazine

(endorsed 2011)

GUIDELINE

Based on human health concerns, propazine in drinking water should not exceed 0.05 mg/L.

RELATED CHEMICALS

Propazine (CAS 139-40-2) belongs to the triazine class of chemicals. There are many pesticides in this class, including atrazine, symazine and cyanazine (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, propazine would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Propazine is a herbicide used for the control of broad-leaf weeds in agricultural crops.

There are currently no products containing propazine registered in Australia, but de-registered conpounds may still be detected in water.

Exposure sources: The main source of public exposure to propazine and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of propazine may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of propazine in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

Relatively high removal rates of propazine have been achieved using conventional flocculation, adsorption onto activated carbon and ozonoation (Ormad *et al.* 2008). More research into the reliable removal of propazine is recommended. If propazine is detected, jar testing with a matrix of multiple oxidants, adsorbents, and coagulants is recommended.

MEASUREMENT

Analysis for propazine in drinking water now typically employs solvent extraction or solid phase extraction with gas chromatography-mass spectrometry determination (QHFSS, 2009 pers comm). Limits of detection are normally 10 ng/L using this methodology.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for propazine is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.5 mg/kg bw/day from a medium-term (90-day) dog study. The NOEL is based on reduced bodyweight gain. The ADI incorporates a safety factor of 100, and was established in 1986.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: No metabolism studies are available for propazine.

Acute effects: Propazine has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea pig.

Short-term effects: Medium-term (3-month) dietary studies have been conducted in rats and dogs. Decreased bodyweight gain and food consumption was observed in rats at doses of 14 mg/kg bw/day and above, and in dogs at doses of 6 mg/kg bw/day and above. At higher doses, effects on biochemical and haematological parameters as well as changes in urinalysis and histopathology, and increased mortality were reported in both rats and dogs. The lowest overall NOEL was 1.5 mg/kg bw/day based on decreased bodyweight gain in dogs, and this is the basis for the current ADI.

Long-term effects: In long-term studies in mice and rats, the most sensitive toxicological effect was decreased bodyweight gain and food consumption. A long-term dietary study in mice reported decreased food consumption and a slight increase in mortality at 480 mg/kg bw/day and above. In a 2-year rat study, decreased bodyweight gain and food consumption were observed at doses of 60 mg/kg bw/day and above. The NOEL for this study was 6 mg/kg bw/day.

Carcinogenicity: There was some evidence of carcinogenicity in rats; however, the mode of action is not considered relevant to humans at the normal levels of human exposure.

Genotoxicity: Only short-term *in vitro* studies are available; these report no evidence that propazine is genotoxic.

Reproductive and developmental effects: A 3-generation reproduction study in rats and developmental studies in rats did not produce any evidence of effects on reproductive parameters or on the developing foetus.

Poisons Schedule: Propazine is not included in the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.05 mg/L for propazine was determined as follows:

$$0.05 \text{ mg/L} = \frac{1.5 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 1.5 mg/kg bw/day is the NOEL based on a short-term (3-month) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Propiconazole

(endorsed 2011)

GUIDELINE

Based on human health concerns, propiconazole in drinking water should not exceed 0.1 mg/L.

RELATED CHEMICALS

Propiconazole (CAS 60207-90-1) is in the DMI: triazole class of chemicals. Other pesticides in this class include flutriafol, myclobutanil, paclobutrazol, and triadimefon (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, propiconazole would not be a health concern unless the concentration exceeded 0.1 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Propiconazole is a broad-spectrum fungicide used to control a variety of fungi in food crops, and as turf and timber treatments.

There are registered products containing propiconazole in Australia. The products are intended for professional use only and are available as emulsifiable concentrate formulations, to be diluted and applied using ground or aerial spray methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to propiconazole and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of propiconazole in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of propiconazole in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Propiconazole can be measured in drinking water by the use of high performance liquid chromatography–tandem mass spectrometry. The limit of detection for this approach has been reported as 0.05 ng/L (Van De Steene and Lambert 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for propiconazole is 0.04 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 4.0 mg/kg bw/day from a 2-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 and was established in 1983.

The previous guideline value was 0.0001 mg/L and previous health value was 0.1 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Propiconazole is rapidly and extensively absorbed via the gastrointestinal tract and widely distributed in various tissues. It is readily metabolised and excreted in faeces and urine within 144 hours (97%), and has low potential for bioaccumulation. The major metabolites of propiconazole are triazole derivatives of the parent compound and include 1,2,4-triazole, triazole alanine and triazole acetic acid.

Acute effects: Propiconazole has low oral and dermal acute toxicity. It is not a skin sensitiser.

Short-term effects: In medium-term dietary studies in rats, there was reduced bodyweight gain at 80 mg/kg bw/day. In medium-term studies in dogs, there were no adverse effects at dose levels up to 36 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice and rats. In mice, there were increased liver weights and associated changes in blood plasma enzymes at 50 mg/kg bw/day. In rats, there was reduced bodyweight gain at 20 mg/kg bw/day.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for propiconazole.

Genotoxicity: Propiconazole is not considered to be genotoxic, based on *in vitro* or *in vivo* short-term studies.

Reproduction and developmental effects: Two 3-generation reproduction studies in rats produced decreased bodyweight gain at high dose levels only. There was no evidence of effects on reproductive parameters. In developmental studies in rats and rabbits, there was no evidence of effects on foetal development in the absence of maternal toxicity.

Poisons Schedule: Propiconazole is included in Schedule 5 or 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.1 mg/L for propiconazole was determined as follows:

$$0.1 \text{ mg/L} = \frac{4 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 4 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Propyzamide

(endorsed 2011)

GUIDELINE

Based on human health concerns, propyzamide in drinking water should not exceed 0.07 mg/L.

RELATED CHEMICALS

Propyzamide (CAS 23950-58-5) belongs to the benzamide class of chemicals. Another herbicide in this class is isoxaben (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, propyzamide would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Propyzamide is a pre- and post-emergent herbicide for the control of certain grasses and broad-leaf weeds in sports turf and grazing pastures, home garden lawns, and agricultural legume and lettuce crops.

There are registered products that contain propyzamide in Australia. The products are intended for professional and home garden use, and are available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays to soil or established crops. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to propyzamide and its metabolites are residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of propyzamide may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of propyzamide in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of propyzamide in drinking water have been identified.

MEASUREMENT

Analysis of propyzamide in drinking water may be undertaken by high performance liquid chromatography–mass spectrometry (HPLC-MS). The analytical detection limit for this method is 8 ng/L (Di Corcia *et al.* 2000).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for propyzamide is 0.02 mg per kg bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.9 mg/kg bw/day from a long-term (2-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.

The previous health value was 0.3 mg/L (NHMRC NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Propyzamide is readily absorbed via the gastrointestinal tract and extensively metabolised. The major metabolite is chloromethylbutane. Excretion occurred evenly between faeces (as metabolites and unabsorbed compound) and urine (as metabolites) and is complete within 6 days.

Acute effects: Propyzamide has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 4-week dietary studies in rats and dogs, there was slight hepatocellular hypertrophy and increased absolute and relative liver weight at 37 mg/kg bw/day in rats and 62 mg/kg bw/day in dogs. Other changes observed in dogs were also indicative of liver damage.

In 3-month dietary studies in rats and dogs, increased absolute liver weights were seen at doses of 7.5 mg/kg bw/day and above in rats. Other effects, including reversible hormonal effects, indicative of thyroid toxicity, were observed 50 mg/kg bw/day in rats.

Long-term effects: Two-year dietary studies were conducted in mice, rats and dogs. In mice, there was increased liver weight, evidence of bile duct obstruction associated with necrosis, and an increased incidence of liver carcinomas at 10 mg/kg bw/day. In rats, there was an increased incidence of thyroid adenocarcinoma, testicular adenomas and ovarian hyperplasia at 50 mg/kg bw/day. In dogs, there was an increase in kidney and heart weights, and decreased spleen weights (all without histological changes) at 7.5 mg/kg bw/day, and liver hypertrophy at 35 mg/kg bw/day. The lowest NOEL was 1.9 mg/kg bw/day in mice, and this is the basis of the current ADI.

Carcinogenicity: Propyzamide is associated with an increased tumour incidence in rodents, however, the tumours are considered to be rodent-specific or resulting from regenerative hyperplasia or hormonal changes, and not relevant to humans at the likely levels of exposure to propyzamide.

Genotoxicity: Propyzamide is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Two- and 3-generation reproductive studies in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Endocrine effects: Special studies on thyroid function and endocrine regulation in the testes found tumour production was secondary to increased thyroxine turnover and perturbation of the pituitary-testicular endocrine axis, respectively.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Propyzamide is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.07 mg/L for propyzamide was determined as follows:

$$0.07 \text{ mg/L} = \frac{1.9 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.9 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in mice.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Pyrasulfotole

(endorsed 2011)

GUIDELINE

Based on human health concerns, pyrasulfotole in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

Pyrasulfotole (CAS 365400-11-9) belongs to the benzoylpyrazole class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pyrasulfotole would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pyrasulfotole is a herbicide used on cereal grains including wheat, barley, oats, rye and triticale.

There is at least one registered product containing pyrasulfotole in Australia. Pyrasulfotole products are intended for professional use only and is applied using ground boom apparatus. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to pyrasulfotole is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of pyrasulfotole may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of pyrasulfotole in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of pyrasulfotole in drinking water have been identified.

MEASUREMENT

No methods have been identified for the analysis of pyrasulfotole in drinking water.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pyrasulfotole is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1 mg/kg bw/day from a long-term (2-year) study in rats. This NOEL is based on corneal and retinal lesions, and centrilobular hepatocellular hypertrophy at 10 mg/kg bw/day. The ADI incorporates a safety factor of 100, and was established in 2007.

The acute reference dose (ARfD) of 0.2 mg/kg bw/day was established in 2007, based on a LOEL of 200 mg/kg bw/day for clinical signs of toxicity. The ARfD incorporates a safety factor of 1000.

A health value has not been previously established by NHMRC for pyrasulfotole.

HEALTH CONSIDERATIONS

Metabolism: Pyrasulfotole is readily absorbed via the gastrointestinal tract, and approximately 60% is excreted in the urine within 6 hours, mainly unchanged. There is also excretion in the faeces, partially via the bile. By 48 hours, there is <2% remaining in the body, indicating a low potential for bioaccumulation. The main metabolite is a desmethyl derivative.

Acute effects: Pyrasulfotole has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 28-day studies, there were histopathological changes in the urinary bladder at 961 mg/kg bw/day in mice, and increased serum triglyceride levels and elevated liver weights at 171 mg/kg bw/day in dogs. In a 90-day study in rats, increased liver weight, corneal effects and microscopic renal abnormalities were reported at 77 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. In mice, an increased incidence of gallstones was observed at 14 mg/kg bw/day. A 2-year study in rats reported corneal and retinal lesions, increased liver weight, centrilobular hepatocellular hypertrophy and elevated plasma cholesterol at 10 mg/kg bw/day. In dogs, tubular dilatation of the kidneys was seen at 101 mg/kg bw/day. The NOEL of 1 mg/kg bw/day in the rat study is the basis for the current ADI.

Carcinogenicity: Pyrasulfotole caused an increased incidence of neoplasms in the urinary tract of mice and in the eye of rats at high dose levels only. These dose levels were considered to be well in excess of the normal levels of human exposure.

Genotoxicity: Pyrasulfotole is not considered genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In multigeneration reproduction studies in rats, there was no evidence of effects on reproductive parameters. In developmental studies in rabbits, there was evidence of foetotoxicity in the absence of maternal toxicity at 10 mg/kg bw/day.

Poisons Schedule: Pyrasulfotole is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.04 mg/L for pyrasulfotole was determined as follows:

$$0.04 \text{ mg/L} = \frac{1 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1 mg/kg bw/day is the NOEL from a long-term (2-year) rat study.
- 70 kg is taken as the average weight of an adult.

NOTE: Important general information is contained in PART II, Chapter 6

- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Pyrazophos

(endorsed 2011)

GUIDELINE

Based on human health concerns, pyrazophos in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Pyrazophos (CAS 13457-18-6) belongs to the phosphorothiolate class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pyrazophos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pyrazophos is a fungicide for the control of powdery mildew in vegetable crops.

There are no registered products containing pyrazophos in Australia, but de-registered compounds may still be detected in water. When used previously, products containing pyrazophos were available as concentrated solutions and applied in diluted form using ground and aerial sprays.

Exposure sources: The main source of public exposure to pyrazophos, if used in the future, would be residues in food. Residue levels in food produced according to good agricultural practice are generally low.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on pyrazophos occurrence in Australian drinking water supplies were found.

TREATMENT OF DRINKING WATER

Activated carbon can be added in a powder form to the coagulation processes or in a granular form as part of the filtration process for the removal of pyrazophos. Effective removal of organophosphorous pesticides has also been observed with softening, disinfection, membrane treatments, and in some cases air-stripping (USEPA 2001).

MEASUREMENT

Pyrazophos can be extracted from the water by liquid/liquid extraction with dichloromethane. The extract is dried with sodium sulfate, concentrated, and analysed by gas chromatography coupled with a nitrogen phosphorus detector and flame photometric detector. The method can achieve a limit of quantitation (LOQ) of 0.05 µg/L. A fully automated at-line solid-phase extraction–gas chromatography procedure can achieve a LOQ of 0.05 µg/L (Hankemeier *et al*. 1996). Solid-phase microextraction with high resolution gas chromatography and mass spectrometry can achieve a LOQ of 10 ng/mL (Souza *et al*. 2003).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pyrazophos is 0.007 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.07 mg/kg bw/day 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, and was first established in 1991.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Pyrazophos is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, primarily through sulfoxidation to form organophosphate compounds. Excretion is rapid, being almost complete by 72 hours and proceeding through urine.

Acute effects: Pyrazophos has moderate acute oral toxicity and low acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: In a 28-day dietary study in rats, there was serum cholinesterase inhibition at 0.25 mg/kg bw/day, and erythrocyte cholinesterase inhibition at 0.75 mg/kg bw/day. In a 10-day oral study in humans, plasma cholinesterase activity was decreased at 0.15 mg/kg bw/day. The NOEL was 0.07 mg/kg bw/day and this is the basis of the ADI.

Three-month dietary studies were conducted in rats and dogs. In rats, there was decreased erythrocyte cholinesterase activity at 0.48 mg/kg bw/day and an increase in absolute adrenal and spleen weights at 8 mg/kg bw/day. In dogs, there was decreased erythrocyte and plasma cholinesterase activity at 0.25 mg/kg bw/day and decreased physical activity and anaemia at 16 mg/kg bw/day.

Long-term effects: Long-term dietary studies in mice, rats and dogs showed decreased plasma and erythrocyte cholinesterase activity at 0.7 mg/kg bw/day in mice, 1 mg/kg bw/day in rats, and 0.25 mg/kg bw/day in dogs.

Carcinogenicity: Based on a 2-year study in rats and an 18-month study in mice, there is no evidence of carcinogenicity for pyrazophos.

Genotoxicity: Pyrazophos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and development studies in rats and rabbits did not produce any evidence for effects on reproductive parameters or foetal development.

Neurotoxicity: A delayed neurotoxicity study in hens using doses up to 150 mg/kg bw found no evidence for delayed neurotoxicity from pyrazophos.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Pyrazophos is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for pyrazophos was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.07 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.07 mg/kg bw/day is the NOEL based on a short-term (10-day) oral dosing study in human volunteers.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from a study in humans, to allow for variation of response within the human population.

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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USEPA (United States Environmental Protection Agency) (2001). FIFRA Scientific Advisory Panel Meeting. Session VI- A Set of Scientific Issues Being Considered by the Environmental Protection Agency Regarding: Progress Report on Estimating Pesticide Concentrations in Drinking Water and Assessing Water Treatment Effects on Pesticide Removal and Transformation: A Consultation. Arlington, Virginia.

NOTE: Important general information is contained in PART II, Chapter 6

Pyroxsulam

(endorsed 2011)

GUIDELINE

Based on human health concerns, pyroxsulam in drinking water should not exceed 4 mg/L.

RELATED CHEMICALS

Pyroxsulam (CAS 422556-08-9) is in the triazolopyrimidine class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, pyroxsulam would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Pyroxsulam is a post-emergence herbicide used to control a wide range of grass and broad-leaf weeds in wheat.

There is at least one registered product containing pyroxsulam in Australia. Pyroxsulam products are for professional use and are available as an oil-dispersible liquid to be applied by ground boom spray for one post-emergent (early season) application to wheat. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to pyroxsulam is residues in food. Residue levels in food produced according to good agricultural practice are generally low

Agricultural use may potentially lead to residues in source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of pyroxsulam in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of pyroxsulam in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

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.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for pyroxsulam is 1.0 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 100 mg/kg bw/day from an 18-month dietary study in mice. The NOEL is based on effects on the liver. The ADI incorporates a safety factor of 100, and was established in 2008.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Pyroxsulam is rapidly absorbed from the gastrointestinal tract. It is rapidly eliminated, mainly in the urine, largely unchanged. It has low potential for bioaccumulation. The primary metabolite of pyroxsulam is 2'-demethyl-pyroxsulam.

Acute effects: Pyroxsulam has low to moderate oral acute toxicity, and low dermal toxicity. It is a skin sensitiser in guinea pigs.

Short-term effects: Medium-term dietary studies were conducted in mice, rats and dogs. The only effect observed was an increase in serum cholesterol levels at 1000 mg/kg bw/day; however, these returned to normal after cessation of treatment and were likely be adaptive and non-adverse.

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. In mice, there was an increase in liver weight at the highest dose, 1000 mg/kg bw/day. No adverse effects were observed in rat and dog studies.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for pyroxsulam.

Genotoxicity: Pyroxsulam is not considered to be genotoxic, based on *in vitro* or *in vivo* short-term studies.

Reproductive and developmental effects: In a 2-generation reproduction study in rats and developmental studies in rats and rabbits, there was no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Pyroxsulam is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 4 mg/L for pyroxsulam was determined as follows:

$$4 \text{ mg/L} = \frac{100 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 100 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in mice.
- 70 kg is taken as the average weight of an adult.

NOTE: Important general information is contained in PART II, Chapter 6

FACT SHEETS

- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

NOTE: Important general information is contained in PART II, Chapter 6

Quintozene

(endorsed 2011)

GUIDELINE

Based on human health concerns, quintozene in drinking water should not exceed 0.03 mg/L.

RELATED CHEMICALS

Quintozene (CAS 82-68-8) belongs to the nitroaniline class of chemicals. There are no other registered pesticides in this chemical class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, quintozene would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Quintozene is a soil fungicide for the control of pathogenic fungi on turf, ornamentals, cotton seedlings, peanuts, and vegetable agricultural crops.

There are registered products that contain quintozene in Australia. The products are intended for professional use and are available as concentrated solutions to be applied directly to soil in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to quintozene and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of quintozene may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of quintozene in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of quintozene in drinking water have been identified.

MEASUREMENT

No suitable techniques for the analysis of quintozene in drinking water have been identified. However, it is expected that a suitable method using high performance liquid chromatography–tandem mass spectrometry could be developed if required.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for quintozene is 0.007 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.7 mg/kg bw/day from a long-term (2-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, and was first established in 1987.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Quintozene is readily absorbed from the gastrointestinal tract of rats. The compound is extensively metabolised, mostly via nitrogen reduction to form acetyl pentachlorophenyl cysteine and pentachloroaniline. Excretion is rapid, occurring mostly via urine and being complete by three days, with small amounts of unabsorbed parent compound also excreted in faeces.

Acute effects: Quintozene has low acute oral and dermal toxicity. It is a skin sensitiser in humans.

Short-term effects: A 28-day dietary study in dogs reported increased relative liver weights at a dose of 64 mg/kg bw/day, but with no histological examination of the liver. Medium-term dietary studies in rats and dogs did not show any evidence of toxicity up to 100 mg/kg bw/day in rats and up to 25 mg/kg bw/day in dogs.

Long-term effects: In long-term studies in rats (2-year) and dogs (1- and 2-year), there was decreased bodyweight gain and increased liver and kidney weight in both species at 6 mg/kg bw/day. There was also evidence of liver toxicity in rats (necrosis) at this dose level. In dogs, there was increased serum alkaline phosphatase, serum cholesterol, hepatocyte size and granulosis at 40 mg/kg bw/day. The lowest overall NOEL was 0.7 mg/kg bw/day in dogs.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for quintozene.

Genotoxicity: Quintozene is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a 2-generation reproduction study in rats, and in developmental studies in rats, mice and rabbits, there was no evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Quintozene is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.03 mg/L for quintozene was determined as follows:

$$0.03 \text{ mg/L} = \frac{0.7 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.7 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has not established a health-based guideline value for quintozene and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th edition, British Crop Production Council, UK.

WHO (World Health Organization) (2004). *Guidelines for Drinking-water Quality*. 3rd Edition, WHO, Geneva, Switzerland.

Radionuclides, Specific Alpha and Beta Emitting

(updated 2022)

GUIDELINE

There are no specific reference levels set for specific alpha or beta emitting radionuclides.

Specific alpha or beta emitting radionuclides should be determined if the gross alpha screening value in drinking water exceeds 0.5 Bq/L, or if the gross beta screening value (with the contribution of potassium-40 subtracted) exceeds 0.5 Bq/L, or if there is a specific reason to analyse for individual radionuclides.

GENERAL DESCRIPTION

Alpha emitters:

Alpha emitters may be present in drinking water in low concentrations. Significant alpha emitters are naturally occurring radionuclides from the uranium and thorium decay chains. Depending on the source of the drinking water there may be areas with high activity concentrations for some of these alpha emitters. The most significant of these are radium-226, polonium-210 and uranium isotopes.

Radium-226, polonium-210 and the uranium isotopes have relatively long half-lives and may be present in drinking water. Radium-226 is commonly found in groundwater, whereas polonium concentrations are usually lower in concentration and uranium could be present in some groundwater (ARPANSA 2008, Kleinschmidt *et al*. 2011, Walsh *et al*. 2014).

Refer to the Radium fact sheet for more information on radium-226.

Beta emitters:

There are several radionuclides that are classified as beta emitters and may occasionally be present in drinking water. Long-lived radionuclides in this group are the naturally occurring isotopes potassium-40, lead-210 and radium-228 as well as the artificial radionuclides caesium-137 and strontium-90. Tritium, another radionuclide in this group, is present in the environment both from natural sources and as a result of nuclear fall-out and nuclear power generation.

Levels of strontium-90 and caesium-137 in the Australian environment have decreased substantially since atmospheric testing of nuclear weapons ceased, and these radionuclides are not detectable in drinking water. These radionuclides may be present as a result of transient contamination following an event such as a nuclear or radiological emergency.

Potassium-40 occurs naturally in a fixed ratio to stable potassium. Potassium is an essential element for humans and is absorbed mainly from the ingestion of food. Potassium-40 in the body is maintained at a constant level independent of intake.

Radium-228 is commonly found in groundwater supplies. Refer to the Radium fact sheet for more information on radium-228.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Limited data is available for anthropogenic (human-made) radionuclides such as strontium-90 and caesium-137. Levels can reasonably be expected to be negligible due to Australia's limited and regulated nuclear industry and protection measures for water supplies.

Knowledge of lead-210, polonium-210 and other naturally occurring thorium radioisotopes is also limited. However, they are expected to be at levels that are low due to their reactive nature and tendency to adsorb readily onto surfaces. Elevated concentrations of polonium-210 have been reported, which is suspected to be caused by the presence of scale causing a proximal source to the sampled water (Kleinschmidt *et al*. 2008).

Concentrations of radium-226 and radium-228 may be elevated and may exceed 0.5 Bq/L in some groundwater supplies (ARPANSA 2008, Kleinschmidt *et al*. 2011, Walsh *et al*. 2014).

TREATMENT OF DRINKING WATER

Treatment processes involving ion exchange or reverse osmosis will effectively remove radionuclides such as lead-210, strontium-90 and caesium-137. There is no suitable treatment to remove tritium.

ANALYSIS

For the initial screening analysis, gross alpha and gross beta activity and potassium-40 are determined as described in Information Sheet 2.2.

Table 1 provides some references to standard methods of analysis for specific alpha and beta radionuclides from the International Organization for Standardization (ISO) and the American Public Health Association (APHA). It is important to note that some of these radionuclides may also have gamma emissions and therefore gamma spectrometry techniques could also be considered.

The US Environmental Protection Agency (USEPA 2016) have compiled a list of approved methods for the analysis of radionuclides in drinking water. ASTM International (formerly known as American Society for Testing and Materials) Annual Book of ASTM Standards (2018) also provides some radionuclide specific standard methods.

Table 1 *Recommended standard method for the analysis of specific alpha and beta emitting radionuclides*

Method Reference	Sample preparation	Measurement technique
APHA 7120 B Gamma emitters (2017)	Direct measurement – no sample preparation required	High resolution gamma spectrometry
ISO 10703 Gamma emitters (2007)	Direct/evaporation/evaporation with iodine retention	High resolution gamma spectrometry
ISO 13161 Polonium-210 (2012)	Evaporation, autodeposition	Alpha spectrometry
APHA 7500-Cs B Radioactive caesium (2017)	Precipitation	Beta counting/gamma counting
ISO 13163 Lead-210 (2013)	Co-precipitation, separation using extraction chromatography	Liquid scintillation counting
APHA 7500-Sr A Radioactive strontium (2017)	Precipitation	Proportional counting
ISO 13160 Stronium-89/90 (2012)	Precipitation/liquid-liquid extraction/ extraction chromatography	Proportional counting/liquid scintillation counting
APHA 7500-3H Tritium (2017)	Distillation	Liquid scintillation counting
ISO 9698 Tritium (2010)	Distillation	Liquid scintillation counting

Note: the required detection limits should be considered when selecting an appropriate analytical method.

NOTE: Important general information is contained in PART II, Chapter 6

HEALTH CONSIDERATIONS

Once lead-210 has entered the body it will concentrate in bone where it remains for a long time. The radiation dose from lead-210 is due mainly to the emission of alpha particles from its progeny, polonium-210. In general, polonium in the blood stream will be deposited in the spleen, kidneys, liver and in bone where it remains for a short time. Immediate health risks from drinking water with low levels of lead-210 are very small.

In principle, lead-210 may increase the risk of bone cancers; however, no link has been demonstrated, either in animal studies or epidemiological studies.

Potassium-40 occurs naturally in the environment with stable potassium at the ratio of 27.6 Bq of potassium-40 per gram of stable potassium. The potassium content of the body is under strict control to sustain biological processes and it is not influenced by variations in environmental levels. While in the body, potassium-40 emits beta particle and gamma ray emissions. The dose due to this naturally occurring radionuclide in bodily tissues has been determined to be 0.165 and 0.185 mSv/year for adults and children, respectively (UNSCEAR 2000).

ESTIMATION OF DOSE

The dose from individual alpha or beta emitting radionuclides should be determined using the method described in Chapter 7, Section 7.6.2.

REFERENCES

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7120 B Gamma Spectroscopic Method.

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7500 B Radioactive Cesium-Precipitation Method.

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7500-Sr B Radioactive Strontium and Strontium-90 Precipitation Method.

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7500-3H B Tritium Liquid Scintillation Method.

ARPANSA (Australian Radiation Protection and Nuclear Safety Agency) (2008). The Radioactive Content of Some Australian Drinking Waters. Technical Report Series No 148.

ASTM (ASTM International) (2018) Annual Book of ASTM Standards. https://www.astm.org/Standard/standards-and-publications.html

ISO (International Organization for Standardization) (2007). Water quality – determination of the activity concentration of radionuclides – Method by high resolution gamma-ray spectrometry. ISO, International Standard ISO 10703:2007, Geneva, Switzerland.

ISO (International Organization for Standardization) (2010). Water quality – determination of tritium activity concentration – liquid scintillation counting method. ISO, International Standard ISO 9698:2010(E), Geneva, Switzerland.

ISO (International Organization for Standardization) (2011). Water quality – Measurement of Polonium 210 Activity Concentration in Water by Alpha Spectrometry. ISO, International Standard ISO 13161:2011, Geneva, Switzerland.

ISO (International Organization for Standardization) (2012). Water quality – strontium 90 and strontium 89 – Test methods using liquid scintillation counting or proportional counting. ISO, International Standard ISO 13160:2012 Geneva, Switzerland.

NOTE: Important general information is contained in PART II, Chapter 6

ISO (International Organization for Standardization) (2013). Water quality – Lead-210 – Test method using liquid scintillation counting. ISO, International Standard ISO 13163:2013, Geneva, Switzerland.

Kleinschmidt R, Black J, Akber R (2011). Mapping radioactivity in groundwater to identify elevated exposure in remote and rural communities. *Journal of Environmental Radioactivity*, 102: 235-243.

Kleinschmidt R, Akber R (2008). Naturally occurring radionuclides in materials derived from urban water treatment plants in southeast Queensland, Australia. *Journal of Environmental Radioactivity*, 99: 607-620.

UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) (2000). Sources, effects and risks of ionising radiation. UNSCEAR, report ISBN 92-1-142143-8, New York.

USEPA (United States Environmental Protection Agency) (2016). Approved Drinking Water Analytical Methods – Radionuclides https://www.epa.gov/dwanalyticalmethods/approved-drinking-water-analytical-methods.

Walsh M, Wallner G, Jennings P (2014). Radioactivity in drinking water supplies in Western Australia. *Journal of Environmental Radioactivity*, 130: 56-62.

NOTE: Important general information is contained in PART II, Chapter 6

Radium (radium-226 and radium-228)

(updated 2022)

GUIDELINE

Radium-226 and radium-228 should be determined if the gross alpha radioactivity in drinking water exceeds 0.5 Bq/L, or if the gross beta activity (with the contribution of potassium-40 subtracted) exceeds 0.5 Bq/L.

GENERAL DESCRIPTION

Radium isotopes are formed as a result of radioactive decay of isotopes from the natural uranium and thorium decay series. The two most significant isotopes in this process, in terms of radiological health, are radium-226 (uranium series) and radium-228 (thorium series), which have half-lives of 1620 years and 5.8 years, respectively. Radium-224 is generally not considered in assessments of radiological health effects due to its short half-life of 3.66 days and the minor contribution to radiation dose per unit of intake.

Drinking water sourced from groundwater can contain activity concentrations of radium at levels that may present a health concern (ARPANSA 2008, Kleinschmidt *et al.* 2011, Walsh *et al.* 2014). Concentrations in surface water are likely to be extremely low (ARPANSA 2008).

A number of chemical and physical processes contribute to the concentration of radium in groundwater. Physical processes of weathering, recoil[1] , decay, adsorption-desorption and precipitation during transport within aquifers will affect the radium content. Chemical processes are largely dependent on the chemical composition of the water. Generally, radium concentrations are considered to have a broad correlation with total dissolved solids (TDS) and salinity (IAEA 2014). Concentrations of radium isotopes in groundwater will also vary according to the mineralogy of the host rock for the aquifer (IAEA 2014a).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In supplies derived from groundwater sources, radium-226 and radium-228 concentrations vary considerably depending on the aquifer (Kleinschmidt 2011). Radium-226 concentrations in Australian surface water supplies are generally below 0.05 Bq/L. A small number of groundwater supplies exhibit concentrations up to, or exceeding, 0.5 Bq/L (ARPANSA 2008, Kleinschmidt *et al.* 2011, Walsh *et al.* 2014). These studies have shown that the values of radium in Australian drinking waters derived from groundwater supplies may be an order of magnitude higher than the reference values reported in the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR 2000).

ANALYSIS

Generally, analysis for radium isotopes is only required if either gross alpha or gross beta activities exceed 0.5 Bq/L (refer to Chapter 7 and Information Sheet 2.2).

Standard methods (or validated methods) should be used to determine concentrations of radium. Table 1 lists some recommended standard methods from the International Organization for Standardization (ISO) and the American Public Health Association (APHA). Sample analysis should be carried out as soon as possible and within 2-3 days of sample collection if a determination of radium-224 is required.

1 Nuclear recoil during the radioactive decay of naturally occurring radionuclides can create disequilibrium when the recoil liberates the nuclide from its mineral lattice.

Table 1 *Recommended standard method for the analysis of radium*

Method Reference	Sample preparation	Measurement technique	Radionuclide
ISO 13165 Radium-226 - Part 1(2013)	Precipitation	Liquid scintillation counting	Ra-226
ISO 13165 Radium-226 - Part 3 (2016)	Precipitation	Gamma counting	Ra-226
ISO 22908 Radium-226 and radium-228	Precipitation	Liquid scintillation counting	Ra-226 and Ra-228
APHA 7500-Ra B (2017)	Precipitation	Proportional counting or alpha scintillation counting	Alpha emitting radium isotopes
APHA 7500-Ra D (2017)	Sequential precipitation	Proportional counting and/or alpha scintillation counting	Ra-228 or Ra-226 and Ra-228
APHA 7500-Ra E (2017)	Precipitation	Gamma counting	Ra-224, Ra-226, Ra-228

Note: the required detection limits should be considered when selecting an appropriate analytical method. The method selected should take into account the determination of the annual dose, as described in Chapter 7, Section 7.6.2. It is recommended that the detection limit be 20% of the value required to meet the reference level.

HEALTH CONSIDERATIONS

The major evidence concerning radium exposure effects come from epidemiological studies of radium dial painters (Rowland *et al.* 1978). Exposure of the workers to large doses of radium indicated a positive dose response relationship in humans for bone and head and neck sarcomas. Once radium has entered the body, the metabolic behaviour of radium is similar to that of calcium and an appreciable fraction of ingested radium is deposited in bone tissue where it is retained for a long time. The internal radiation dose from radium-226 is due mainly to the emission of alpha particles. The internal radiation dose from radium-228 is due mainly to the emission of beta particles.

Epidemiological studies for low-level exposure to naturally occurring radionuclides in drinking water show no clearly demonstrated health effects (Guseva Canu *et al.* 2011, UNSCEAR 2018).

DERIVATION OF GUIDELINE

The dose from radium-226 and radium-228, and any other radioactive isotopes present in drinking water, should be estimated using the method described in Chapter 7, Section 7.6.2.

REFERENCES

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7500-Ra B Precipitation Method.

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7500-Ra D Sequential Precipitation Method.

APHA, AWWA, WEF (American Public Health Association, American Water Works Association, Water Environment Federation) (2017). 7500-Ra E Gamma Spectroscopy Method.

ARPANSA (Australian Radiation Protection and Nuclear Safety Agency) (2008). The Radioactive Content of Some Australian Drinking Waters. Technical Report Series No 148.

Guseva Canu I, Laurent O, Pires N, Laurier D, Dublineau I (2011). Health Effects of Naturally Radioactive Water Ingestion: The Need for Enhanced Studies. *Environmental Health Perspectives* 119(12): 1676-1680.

IAEA (International Atomic Energy Agency) (2014). The Environmental Behaviour of Radium: Revised Edition. Technical Report Series No. 476. ISBN 978–92–0–143310–7, Vienna.

NOTE: Important general information is contained in PART II, Chapter 6

IAEA (International Atomic Energy Agency) (2014a). Analytical Methodology for the Determination of Radium Isotopes in Environmental Samples. Analytical Quality in Nuclear Applications Series No. 19. ISSN 2074-7659, Vienna.

ICRP (International Commission on Radiological Protection) (2012). Compendium of Dose Coefficients based on ICRP Publication 60. ICRP Publication 119. Ann. ICRP 41(Suppl.).

ISO (International Organization for Standardization) (2014). Water quality - Radium-226 - Part 1: Test method using liquid scintillation counting ISO, International Standard ISO 13165-1:2013, Geneva, Switzerland.

ISO (International Organization for Standardization) (2016). Water quality - Radium-226 - Part 3: Test method using coprecipitation and gamma-spectrometry ISO, International Standard ISO 13165-3:2016, Geneva, Switzerland.

ISO (International Organization for Standardization) (2020). Water quality - Radium-226 and radium-228 - Test method using liquid scintillation counting ISO, International Standard ISO/ 22908:2020, Geneva, Switzerland.

Kleinschmidt R, Black J, Akber R (2011) Mapping radioactivity in groundwater to identify elevated exposure in remote and rural communities. *Journal of Environmental Radioactivity*, 102: 235-243.

Rowland RE, Stehney AF, Lucas HF (1978). Dose-response relationship for female radium dial workers. Radiation Research, 76: 368–383.

UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) (2000). Sources, effects and risks of ionising radiation. UNSCEAR, report ISBN 92-1-142143-8, New York.

UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation) (2018). Sources and Effects and risks of ionizing radiation. UNSCEAR 2017 Report to the General Assembly, Scientific Annexes A and B. ISBN: 978-92-1-142322-8, New York.

Walsh M, Wallner G, Jennings P (2014). Radioactivity in drinking water supplies in Western Australia. *Journal of Environmental Radioactivity*, 130: 56-52.

NOTE: Important general information is contained in PART II, Chapter 6

Radon-222

(updated 2022)

GUIDELINE

Based on the consideration of the potential health impact from radon released from tap water to the air inside a dwelling, the activity concentration of radon-222 in drinking water should not exceed 100 Bq/L.

The screening value applies to the concentration of radon at the point of use of the water, not at the source, because of the significant decrease in concentration which can occur due to radioactive decay and degassing during storage, treatment and reticulation.

Monitoring of radon activity concentrations in water is generally only warranted when groundwater is directly reticulated to an enclosed building.

GENERAL DESCRIPTION

Radon-222 is a radioactive gas produced from the decay of radium-226 in soil and minerals. It has a half-life of 3.8 days.

Radon concentrations in surface water supplies are very low due to the gas being rapidly lost to the atmosphere. Elevated concentrations of radon-222 may occur in drinking water derived from groundwater, due to the release of radon from aquifer rocks and minerals, particularly in granitic areas. Dissolved radon 222 in drinking water may be released to air during domestic use and contribute to indoor radon concentrations (WHO 2009).

SCREENING VALUE FOR RADON

The screening value was determined following consideration of these points:

- ingestion of radon in water does not pose a sufficient risk to health to warrant consideration of this pathway in setting a reference level based on ingestion (UNSCEAR 2000).
- the main sources of radon in indoor air are the subjacent ground and building materials, with radon in tap water being normally only a small contributor. The release of radon from tap water into household air will depend upon the volume and nature of water usage in the dwelling. The overall radon concentration in air will be influenced by factors such as the construction of the dwelling, ventilation rates and domestic practices.
- given the indirect nature of the exposure pathway and the number of assumptions that must be made to assess the dose to an individual arising from the inhalation of radon released to household air from tap water, it is not appropriate to use a level of dose as the basis for a screening value for radon in drinking water.
- the existing published data estimates that the transfer coefficient of radon from water to indoor air has an accepted value of 10^{-4} (UNSCEAR 2000), although the actual value is highly variable. On this basis, a concentration of radon in tap water of 100 Bq/L would give rise to a concentration in air of 10 Bq/m^3, which is 5% of the national reference level of 200 Bq/m^3 for radon in air in a dwelling (ARPANSA 2017). A screening value of 100 Bq/L would ensure that radon in drinking water would not be a significant contributor to indoor radon, even in the event the transfer coefficient was significantly higher than the accepted value.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

The data on the concentrations of radon-222 in Australian drinking water supplies are limited, but sufficient to indicate that radon may be significant in some rural groundwater supplies (Kleinschmidt *et al*. 2011).

TREATMENT OF DRINKING WATER

The most effective way of eliminating dissolved radon-222 from water is by aeration, either actively by processes such as spraying, or by passive processes such as open-air storage. It is important that radon released from the water during aeration is extracted to the outdoors. Radon concentrations will also decrease by radioactive decay in water stored before use.

ANALYSIS

The concentration of radon-222 in drinking water can be determined by liquid scintillation counting of a small volume of water (APHA 2017, ISO 2015, ASTM 2016). The limits of determination for these methods are approximately 1–2 Bq/L. Samples must be collected and transported in a way that avoids outgassing of radon, or delays in the analysis; thus coordination with the receiving laboratory is recommended. Jobbagy *et al*. (2017) provides an overview of laboratory methods for the measurement of radon in drinking water. On site determinations of radon concentration in water can be made using portable equipment described in ISO 13164-3 2015.

HEALTH CONSIDERATIONS

The main health risk from radon arises from inhalation of the gas, particularly when it accumulates inside dwellings. Radon-222 has several short-lived radioactive progeny that can give rise to an increased risk of lung cancer. Epidemiological studies have established a relationship between the incidence of lung cancer and exposure to radon in both occupational and residential settings (WHO 2009).

Radon is soluble in water. When a tap or shower is turned on, dissolved radon is released into indoor air. Therefore, controlling the inhalation pathway rather than the ingestion pathway is the most effective way to control doses from radon in drinking water.

No link has been demonstrated in either experimental or epidemiological studies between ingestion of radon in drinking water and increased cancer rates.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Selenium

(endorsed 1996)

GUIDELINE

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

GENERAL DESCRIPTION

Selenium and selenium salts are widespread in the environment. Selenium is released from natural and human-made sources, with the main source being the burning of coal. Selenium is also a by-product of the processing of sulfide ores, chiefly in the copper refining industry.

The major use of selenium is in the manufacture of electronic components. It is used in several other industries, and selenium compounds are used in some insecticides, in hair shampoos as an anti-dandruff agent, and as a nutritional feed additive for poultry and livestock.

Selenium concentrations in source waters are generally very low and depend on local geochemistry, pH and the presence of iron salts. Concentrations in drinking water supplies overseas are generally below 0.01 mg/L but groundwater concentrations as high as 6 mg/L have been reported in the United States.

Food is the major source of intake for Australians. Cereal and grain products contribute most to intake, while fish and liver contain the highest selenium concentrations. Average daily intakes for Australian adults are between 0.06 mg and 0.13 mg.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, selenium concentrations are less than 0.005 mg/L. Selenium concentrations in groundwater are not a problem in Australia, as they are in some overseas supplies.

TREATMENT OF DRINKING WATER

Selenium concentrations in drinking water can be reduced by coagulation with ferric chloride and by lime softening. Coagulation with alum is much less effective. Activated alumina absorption is the most effective means of treatment, but only at low pH.

MEASUREMENT

The selenium concentration in drinking water can be determined by hydride generation followed by atomic absorption spectroscopy (APHA Method 3500-Se Part C 1992). The limit of determination is 0.001 mg/L.

HEALTH CONSIDERATIONS

Selenium is an essential element for many species, including humans. Signs of selenium deficiency in humans are not well established but may include a chronic disorder of the heart muscle, other heart diseases and cancer. The Australian recommended dietary intake to maintain health is approximately 0.001 mg/kg body weight per day.

Most water-soluble selenium compounds are effectively absorbed by the gastrointestinal tract. Selenium is then distributed to most organs, with highest concentrations found in the kidney, liver and spleen.

The toxicity of selenium varies considerably among the different selenium compounds. Selenite and selenate are much more toxic than selenium sulfide.

An extensive review and summary of the human and animal toxicity data for selenium is available (IPCS 1987).

There have been a number of reports of ill effects attributed to short- and long-term exposure to selenium; most of these have resulted from occupational exposure or accidental poisoning; acute or chronic nutritional toxicity is comparatively rare. Intakes above about 1 mg/day over prolonged periods may produce nail deformities characteristic of selenosis. Other features of excess selenium intake include nonspecific symptoms such as gastrointestinal disturbances, dermatitis, dizziness, lassitude and a garlic odour to the breath.

A 2-year study on 140 people with an average selenium intake of 0.24 mg/day reported no effect associated with the level of selenium intake.

Domestic animals developed a symptom known as 'blind staggers' when fed plants that had accumulated selenium. The animals had impaired vision, depressed appetite and a tendency to wander in circles. This led to paralysis and death from respiratory failure.

Except for selenium sulfide, experiments with laboratory animals indicate that selenium compounds are not carcinogenic, with some selenium compounds displaying an anticarcinogenic effect. Results for selenium sulfide indicate that it causes liver and skin tumours in mice.

Tests for mutagenic activity using bacteria have reported both positive and negative results. Studies indicate that selenite can cause chromosome damage to mammalian cells.

The International Agency for Research on Cancer has concluded that selenium is not classifiable as to its carcinogenicity in humans (Group 3, inadequate evidence in humans and in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline value for selenium in drinking water was derived as follows:

$$0.01 \text{ mg/L} = \frac{0.24 \text{ mg/day} \times 0.1}{2 \text{ L/day}}$$

where:

- 0.24 mg per day is the acceptable daily intake (Longnecker *et al*. 1991).
- 0.1 is the proportion of daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Silica

(endorsed 2011)

GUIDELINE

To minimise an undesirable scale build up on surfaces, silica (SiO_2) within drinking waters should not exceed 80 mg/L.

GENERAL DESCRIPTION

Silica present in water is usually referred to as amorphous silica (i.e. lacking any crystalline structure). When silica is dissolved within water it forms monosilicic acid:

$$SiO_2 + 2H_2O \rightarrow Si(OH)_4$$

When the concentrations of monosilicic acid increase, polymerisation of the silica occurs, forming polysilicic acids followed by formation of colloidal silica. Monosilicic acid and polysilicic acids are the forms of silica analysed when determining dissolved silica content.

The deposition of silica from solutions can occur via various mechanisms. The deposition of silica that can cause the most problems for the water industry is via silica's ability to deposit on solid surfaces that have hydroxyl (OH) groups present. Surfaces that commonly have hydroxyl groups present are glass and metallic surfaces. For example, dissolved silica will react with the surfaces of glass and begin to form a white precipitate. The silica forms silicates on the surface, resulting in silica build-up. In cases where customer complaints occur due to scale build-up, water hardness and silica concentrations should be investigated to determine the cause.

Silica can be a problem in water treatment due to its ability to cause fouling of reverse osmosis (RO) membranes (Sheikholeslami and Tan, 1999, Ning 2002, Sahachaiyunta and Sheikholeslami 2002). This occurs when the dissolved silica of the concentrate becomes super-saturated, causing silicates to form in the presence of metals, and these deposit on the membrane surface. The silicate then dehydrates, forming hard layers on the membrane that reduce the effectiveness of the process.

Fouling of membranes can occur in two ways:

- precipitation fouling – monosilicic acid polymerises at the membrane surface forming a deposit similar to silica scale on glass surfaces;
- particulate fouling – accumulation of colloidal silica within the solution is then deposited on the membrane surface.

A suggested industry standard guideline is to limit the concentration of silica within the RO concentrate to ~ 120 mg/L at 25°C to limit fouling of RO membrane (Freeman and Majerle 1995).

Colloidal silica may affect ion-exchange processes in water treatment. The stability of colloidal silica as an un-ionised compound causes problems in removal using ion-exchange resins. High concentrations may also cause fouling of ion exchange units.

TYPICAL VALUES IN AUSTRALIAN RAW WATER

Dissolved silica from various source can range between 0.6 mg/L in some surface waters to 110 mg/L in ground waters.

MEASUREMENT

Silica can be determined by spectrophotometric techniques upon the addition of ammonium molybdate (EPA method 370.1, APHA Method 4500.F-SiO_2) (Clesceri *et a,* 1998).

TREATMENT OF WATER

The removal of silica from waters involves the use of cold lime softeners, hot process softeners, macroreticular anion resin, up-flow filters with chemical feed, cross-flow microfiltration with chemical feed, and nanofiltration.

Emerging processes in water treatment such as electrodialysis removal (EDR) and high efficiency reverse osmosis (HERO), as a by-product, have some success in silica removal. EDR is based on applying electrochemical separation processes within the water that allow for the removal of charged ions from the water. This process may offer some level of silica removal if the silica is in a charged form; however colloidal silica, which is likely to be present at large concentrations, will not be removed due to its stability as an un-ionised compound. HERO is based on normal RO processes; however pre-treatment removes divalent metals that form scale, and the operating pH has been increased to 11 to support the process. At this pH, silica is ionised, which increases its solubility and hence eliminates scaling of the membranes. It has also been reported that, at higher pH values, there is improved rejection of silica.

HEALTH CONSIDERATIONS

No health guideline has been set for silica as there are no data linking silica to adverse health outcomes.

DERIVATION OF GUIDELINES

The suggested guideline is based on the solubility of amorphous silica being between 100 and 140 mg/L at 25°C, so that, based on current date, limiting the value to below 80 mg/L should limit the formation of silica scaling.

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NOTE: Important general information is contained in PART II, Chapter 6

Silver

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of silver in drinking water should not exceed 0.1 mg/L.

GENERAL DESCRIPTION

Silver concentrations in natural source waters are generally very low, less than 0.0002 mg/L. In some countries silver and silver salts are used for disinfection and preservation of water, and this can result in higher silver concentrations.

Silver is a precious metal and is used in the production of tableware, jewellery and coins. It is also used in batteries, mirrors, as a chemical catalyst, and as an antiseptic agent.

Traces of silver can be found in most foods. The daily dietary intake has been estimated at between 0.03 mg and 0.09 mg.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for silver.

TREATMENT OF DRINKING WATER

Silver can be readily removed from drinking water by conventional coagulation or lime softening.

MEASUREMENT

The concentration of silver in drinking water can be determined by graphite furnace atomic absorption spectroscopy or inductively coupled plasma emission spectroscopy (APHA Method 3500-Ag Parts B or C 1992). The limits of determination are 0.001 mg/L and 0.01 mg/L respectively.

HEALTH CONSIDERATIONS

Although silver can be found in many biological substances, it is not considered an essential trace element for mammals.

It has been estimated that less than 10% of dietary silver is absorbed by the gastrointestinal tract. Silver is stored mainly in the liver and skin and is capable of binding to amino acids and proteins.

The best-known clinical condition of silver intoxication is argyria, which results in a bluish-grey metallic discolouration of the skin, hair, mucous membranes, mouth and eye. Most cases have been associated with self-administration of silver preparations, or occupational exposure to silver and silver compounds.

Experiments with laboratory rats and mice have reported similar results. Very high concentrations of silver in drinking water (over 600 mg/L) for a lifetime caused discolouration in the thyroid and adrenal glands, the choroids of the brain and eye, and the liver and kidney. Some hypoactive behaviour was also reported.

No data are available on the carcinogenicity of silver. Silver salts are not mutagenic in tests with bacteria, but can induce damage in mammalian DNA.

DERIVATION OF GUIDELINE

The guideline value for silver in drinking water was derived as follows:

$$0.1 \text{ mg/L} = \frac{0.4 \text{ mg/day} \times 0.5}{2 \text{ L/day}}$$

where:

- 0.4 mg/day is derived from a human lifetime no-effect level of 10 g (Hill and Pillsbury 1939).
- 0.5 is the proportion of total daily intake attributable to the consumption of drinking water.
- 2 L/day is the average amount of water consumed by an adult.

No additional safety factors were used, as the calculation was based on a human no-effect level.

It is unlikely that silver concentrations in drinking water would ever reach a concentration that could cause adverse effects. Silver or silver salts should not be used as antimicrobial agents unless no other disinfectants are available.

REFERENCES

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Simazine

(endorsed 2011)

GUIDELINE

Based on human health concerns, simazine in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Simazine (CAS 122-34-9) belongs to the triazine class of chemicals. There are many other pesticides in this class, including atrazine and cyanazine (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, simazine would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Simazine is a pre- and post-emergent herbicide for the control of annual grasses and broad-leaf weeds in a range of agricultural crops such as in citrus, pomefruits, grapes, chickpeas and canola crops. It is also used as an algicide in swimming pools.

There are registered products that contain simazine in Australia. The products are intended for professional and home garden use and are available as concentrated solutions to be applied in diluted form using ground and aerial sprays directly onto soil, or added to swimming pools. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to simazine are residues in food and use in swimming pools. Residue levels in food produced according to good agricultural practice are generally low. The concentrations in swimming pools, when the product is used correctly, are also low.

Agricultural use of simazine may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on occurrence of simazine in Australian drinking water could be found. Simazine has been reported at 0.04 µg/L in the Brisbane River (Bengston Nash *et al.* 2006) and at levels as high as 18 µg/L in an agricultural drainage channel in New South Wales (Tran *et al.* 2007).

Levels of 1-2 µg/L have been reported in groundwater in the USA (WHO 2003). Simazine has also been reported in private and public drinking water supplies in Canada, with a maximum concentration of 23 µg/L (Health Canada 1986).

TREATMENT OF DRINKING WATER

Chlorination, activated carbon or ozonation may be only partially effective at removing simazine from drinking waters, depending on precise operational conditions (Ormad *et al.* 2008).

MEASUREMENT

Simazine can be measured by routine gas chromatography–mass spectrometry analysis, with a limit of reporting of 0.01 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for simazine is 0.005 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.5 mg/kg bw/day from a long-term (2-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, and was established in 1990.

The previous ADI for simazine was set in 1985 at 0.003 mg/kg bw, based on a NOEL of 6 mg/kg bw/day from a 2-year study in rats and a safety factor of 2000.

The previous health value was 0.02 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Simazine is readily absorbed via the gastrointestinal tract, and is extensively metabolised via oxidative N-dealkylation to over 20 metabolites. The major metabolite is desethyl-desisopropyl-atrazine. Excretion in urine is rapid and almost complete within 24 hours.

Acute effects: Simazine has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In a 2-week dietary study in rats, there was a dose-dependant increase in oestrous cycle length, as well as an increase in the plasma levels of the hormones prolactin, estradiol, and corticosterone at 5 mg/kg bw/day and above. No other effects were seen up to the highest dose tested of 15 mg/kg bw/day. Thirteen-week dietary studies in dogs reported vomiting, tremors and decreased bodyweight gain at doses of 75 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. In mice, no toxic effects were observed up to 100 mg/kg bw/day. In rats, there was decreased survival, decreased bodyweight gain, and evidence of anaemia, as well as early onset of mammary growths symptomatic of premature reproductive senescence, at 5 mg/kg bw/day and above. In dogs, there was decreased bodyweight gain, increases in liver enzymes and increased thyroid weight at 37.5 mg/kg bw/day. The lowest overall NOEL was 0.5 mg/kg bw/day in rats. This NOEL is the basis for the current ADI.

Carcinogenicity: In long-term rat studies, growths in mammary tissue were observed, however these changes were not considered relevant to humans. Therefore, based on 2-year studies in mice and rats, there is no evidence of carcinogenicity in humans from simazine.

Genotoxicity: Simazine is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in rats and rabbits did not produce any evidence for effects on reproductive parameters or foetal development.

Special studies on endocrine effects: Simazine was found to bind weakly to the estrogen receptor of rat uterine cells *in vivo*, but only at levels well in excess of the likely levels of human exposure.

Poisons Schedule: Simazine is considered not to require control by scheduling due to its low toxicity and is therefore included in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for simazine was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.5mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a health-based guideline value of 0.002 mg/L for simazine, incorporating an additional safety factor of 10 for possible non-genotoxic carcinogenicity (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Sodium

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (taste), the concentration of sodium in drinking water should not exceed 180 mg/L.

No health-based guideline value is proposed for sodium. Medical practitioners treating people with severe hypertension or congestive heart failure should be aware if the sodium concentration in the patient's drinking water exceeds 20 mg/L.

GENERAL DESCRIPTION

The sodium ion is widespread in water due to the high solubility of sodium salts and the abundance of mineral deposits. Near coastal areas, windborne sea spray can make an important contribution either by fallout onto land surfaces where it can drain to drinking water sources, or from washout by rain. Apart from saline intrusion and natural contamination, water treatment chemicals, domestic water softeners and sewage effluent can contribute to the sodium content of drinking water.

Sodium salts are used in the paper, glass, soap, pharmaceutical and general chemical industries, and for a variety of other purposes. Sodium is also used in the food industry and for culinary purposes. Considerable amounts are excreted by humans and it is a common constituent of domestic sewage.

Sodium, as sodium salts such as sodium chloride or sodium sulfate, has a taste threshold of about 135 mg/L. The taste becomes appreciable when the sodium concentration exceeds 180 mg/L.

In most countries the majority of water supplies contain less than 20 mg/L but concentrations of up to 250 mg/L have been reported.

Food is the major contributor to sodium intake. In Australia the average dietary sodium intake has been estimated at about 4 g/day. Low-sodium diets may restrict this to less than 2 g/day.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, sodium concentrations vary from 3 mg/L to 300 mg/L, with a typical value of 50 mg/L. Concentrations can vary markedly with local conditions.

TREATMENT OF DRINKING WATER

Sodium salts cannot be easily removed from drinking water; however, any steps to reduce sodium concentrations are encouraged (such as the use of alternative salts in domestic water softeners). Processes such as reverse osmosis or distillation can be employed but are costly to operate.

MEASUREMENT

The sodium concentration in drinking water can be determined by flame atomic absorption spectroscopy, inductively coupled emission spectroscopy or flame emission spectroscopy (APHA Method 3500-Na Parts B, C or D 1992). The limits of determination are less than 0.1 mg/L.

HEALTH CONSIDERATIONS

Whether water is consumed directly or with food or beverages, virtually all of the sodium in it will be absorbed. Sodium is present in all body tissues and fluids and its concentration is maintained by the kidney; increases in the sodium concentration in plasma give rise to the sensation of thirst.

Sodium is essential to human life but there is no agreement on the minimum daily amount needed to maintain health. It has been estimated that a total daily intake of less than 200 mg/person is required to meet the needs of growing infants and children.

Excessive sodium intake, usually via diet, can severely aggravate chronic congestive heart failure.

While it is clear that reduced sodium intake can reduce the blood pressure of some individuals with hypertension, it is equally clear that this type of therapy is not effective in all cases. Health authorities are of the opinion, however, that reduced sodium intake is beneficial.

DERIVATION OF GUIDELINE

The guideline value for sodium in drinking water is based on the taste threshold for sodium in water of 180 mg/L.

While there is evidence linking excess sodium intake with cardiovascular disease, it must be recognised that sodium intake via the water supply makes only a modest contribution to total intake. Nevertheless, water authorities are strongly encouraged to keep sodium concentrations as low as possible.

People with severe hypertension or congestive heart failure may need to restrict their overall dietary intake of sodium further if the concentration in drinking water exceeds 20 mg/L. Medical practitioners treating people with these conditions should be aware of the sodium concentration in the patient's drinking water.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Spirotetramat

(endorsed 2011)

GUIDELINE

Based on human health concerns, spirotetramat in drinking water should not exceed 0.2 mg/L.

RELATED CHEMICALS

Spirotetramat (CAS 203313-25-1) belongs to the tetramic acid/cyclic ketoenol class of chemicals. There are no other pesticides in this class (Tomlin 2009).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, spirotetramat would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Spirotetramat is an insecticide for the control of aphids, whiteflies and mealybugs in citrus, grapes, pome fruit, stone fruit, tree nuts, hops, vegetables and potatoes.

While spirotetramat is approved as an active ingredient, there are currently no registered products containing spirotetramat in Australia. Spirotetramat is intended for professional use only, to be applied by spray, using open or enclosed cab tractor-mounted or drawn sprayer fitted with hydraulic nozzles.

Exposure sources: If there were registered products, the main source of public exposure to spirotetramat would be residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Future agricultural use of spirotetramat may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Monitoring studies for spirotetramat in raw and tap water are limited and few data appear to be available (USEPA 2008), Babczinski and Hellpointner 2008).

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of spirotetramat in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Spirotetramat in drinking water can be measured by high performance liquid chromatography (HPLC) with tandem mass spectrometry or HPLC with ultraviolet irradiation. The analytical method 00836 developed by Bayer CropScience has been validated (USEPA 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for spirotetramat is 0.05 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 5 mg/kg bw/day 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, and was established in 2008.

The acute reference dose (ARfD) of 1 mg/kg bw/day for spirotetramat was established in 2008, 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.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Spirotetramat is rapidly absorbed from the gastrointestinal tract. There is no evidence of bioaccumulation. Spirotetramat is completely metabolised in the rat and the majority is excreted via the urine and faeces within 24 hours. The primary metabolites are enols (66-100% of all metabolites) and ketohydroxy forms of spirotetramat.

Acute effects: Spirotetramat has low acute oral and dermal toxicity in animal studies. It exhibits skin sensitisation potential in animals and humans.

Short-term effects: Short-term dietary studies in dogs and rats reported effects on the thyroid and thymus gland in dogs and on the testes, lung and kidney in rats at dose levels above 5 mg/kg bw/day.

Long-term effects: Long-term dietary studies in rats and mice reported that the target organs in rats were the kidney in both sexes and the liver in females at dose levels of 169 mg/kg bw/day and above. There were no adverse effects reported in mice up to the highest dose tested. A one-year dietary study in dogs reported the thymus and thyroid as target organs of toxicity at dose levels of 20 mg/kg bw/day and above. The NOEL of 5 mg/kg bw/day in dogs is the basis for the ADI.

Carcinogenicity: Spirotetramat did not demonstrate any evidence of carcinogenicity in rats or mice.

Genotoxicity: Spirotetramat is not considered genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Reproduction studies in rats reported the presence of abnormal sperm cells, decreased sperm motility and decreased reproductive performance at 70 mg/kg bw/day. In developmental toxicity studies in rats and rabbits, there was an increased incidence of skeletal variations and malformations at the maternally toxic dose of 1000 mg/kg bw/day. Both reproductive and developmental effects occurred at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Spirotetramat is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.2 mg/L for spirotetramat was determined as follows:

$$0.2 \text{ mg/L} = \frac{5.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 5.0 mg/kg bw/day is the NOEL based on a long-term (1-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

Babczinski P, Hellpointner E (2008). Environmental fate of spirotetramat (Movento®). *Bayer CropScience Journal,* 61:181-202.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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USEPA (United States Environmental Protection Agency) (2008). Pesticide Fact Sheet: Spirotetramat. USEPA, Office of Prevention, Pesticides and Toxic Substances

Styrene (vinylbenzene)

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (odour), the concentration of styrene in drinking water should not exceed 0.004 mg/L.

Styrene would not be a health concern unless the concentration exceeded 0.03 mg/L.

GENERAL DESCRIPTION

Styrene may be present in drinking water as a result of contamination from industrial sources. It has occasionally been detected in water supplies in the United States and the Netherlands at concentrations of less than 0.001 mg/L.

The taste threshold of styrene in water at 40°C ranges from 0.02 mg/L to 2.6 mg/L, depending on individual sensitivities. At 60°C the odour threshold in water is 0.004 mg/L.

Styrene is used in the production of plastics and resins. It has been detected in food packaged in polystyrene containers. However, improvements in the use of polystyrene since 1980 have resulted in substantial decreases in the release of the monomer. The daily exposure to styrene has been estimated to be 0.04 mg per person, with smokers receiving a higher dose. Forest fires may contribute to atmospheric concentrations of styrene.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Styrene has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

Styrene can be removed from drinking water by reaction with ozone to form aldehydes, ketones and benzoic acid. It can also be adsorbed onto granular activated carbon.

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for analysis (USEPA Draft Method 503.1 1986). An inert gas is bubbled through the sample and styrene trapped on an adsorbent. The adsorbent is then heated and styrene analysed using gas chromatography with photoionisation detection. The limit of determination is less than 0.0001 mg/L.

HEALTH CONSIDERATIONS

Approximately 60–90% of styrene is absorbed following ingestion or inhalation. It is widely distributed in the body, with a preference for fatty tissues. It is metabolised by a number of tissues and organs to styrene-7,8-oxide.

An extensive review and summary of the human and animal toxicity data for styrene is available (IPCS 1983).

A number of studies have reported on occupational inhalation of styrene. High doses for long periods have resulted in irritation of the respiratory system and some neurotoxic effects on both central and peripheral nervous systems. Chromosomal aberrations in lymphocytes have been associated with high styrene exposures, but not with low concentrations, among workers in the glass fibre industry.

In a long-term study using rats, female body weights were depressed at high doses (250 mg/kg body weight per day). No other treatment-related effects were observed.

Most studies using rodents have not found any association between styrene intake and an increased incidence of tumours. Styrene is mutagenic in a variety of test microorganisms, but only after metabolic activation. It also induces gene mutations and chromosomal aberrations in mammalian cells. The mutagenic agent is probably styrene-7,8-oxide, the main metabolic by-product of styrene and a direct-acting mutagen. Two long-term gavage studies using rats have also reported that styrene-7,8-oxide significantly increased the incidence of fore-stomach tumours at a dose of 250 mg/kg body weight per day.

The International Agency for Research on Cancer has concluded that styrene-7,8-oxide is probably carcinogenic to humans (Group 2A, inadequate evidence in humans, sufficient evidence in experimental animals, and supporting mechanistic evidence) (IARC 1994).

DERIVATION OF GUIDELINE

The assessment of the toxicological data for styrene by the World Health Organization (WHO) has been used without review. The health-based guideline value of 0.03 mg/L was determined as follows:

$$0.03 \text{ mg/L} = \frac{7.7 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 7.7 mg/kg body weight per day is the no-effect level based on a 2-year drinking water study using rats (Beliles *et al*. 1985).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for carcinogenic and genotoxic effects).

This health-based value is greater than the odour threshold of 0.004 mg/L.

The WHO guideline value of 0.02 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

REFERENCES

Beliles RP, Butala JH, Stack CR, Makris S (1985). Chronic toxicity and three-generation reproduction study of styrene monomer in the drinking water of rats. *Fundamental and Applied Toxicology*, 5:855–868.

IARC (International Agency for Research on Cancer) (1994). IARC Monographs on the Evaluation of World Health. Carcinogenic Risks to Humans: Some Industrial Chemicals. World Health Organisation, IARC, 60, Lyons.

IPCS (International Programme on Chemical Safety) (1983). Styrene. Environmental Health Criteria, 26. World Health Organization, IPCS.

USEPA Draft Method 503.1 (1986). Volatile organic compounds in water by purge and trap gas chromatography. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Sulfate

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (taste), the concentration of sulfate in drinking water should not exceed 250 mg/L. Purgative effects may occur if the concentration exceeds 500 mg/L.

GENERAL DESCRIPTION

Sulfate occurs naturally in a number of minerals, and is used commercially in the manufacture of numerous products including chemicals, dyes, glass, paper, soaps, textiles, fungicides and insecticides. Sulfate, including sulfuric acid, is also used in mining, pulping, and the metal and plating industries. Barium sulfate is used as a lubricant in drilling rigs for groundwater supply.

In the water industry, aluminium sulfate (alum) is used as a flocculant in water treatment, and copper sulfate is used for the control of blue-green algae (cyanobacteria) in water storages.

The highest concentrations reported in drinking water overseas are from groundwater supplies where the presence of sulfate is due to natural leaching from rocks. Concentrations have been reported up to 2200 mg/L. In source waters, concentrations are typically less than 100 mg/L.

The taste threshold for sulfate is in the range 250–500 mg/L.

Under anoxic conditions, the reduction of sulfate to sulfide by sulfate-reducing bacteria can result in unpleasant taste and odour due to the release of hydrogen sulfide, and can increase corrosion in pipes.

Food is probably the major source of intake of sulfate. In areas where the concentration of sulfate in water is high, drinking water may constitute the principal source of intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, sulfate concentrations range from 1 mg/L to 240 mg/L, with a typical concentration of 20 mg/L. Sulfate concentrations can vary markedly in different parts of the country.

TREATMENT OF DRINKING WATER

Most sulfate salts are very soluble and cannot be removed from drinking water by conventional water treatment processes. Desalination methods such as reverse osmosis or distillation are required for sulfate removal.

MEASUREMENT

The sulfate concentration of drinking water can be determined by the methylthymol blue method (APHA 4500-SO_4^{2-} Part F 1992) or using ion chromatography (APHA Method 4500-SO_4^{2-} Part B 1992). Limits of determination are 0.1 mg/L and 1 mg/L respectively.

HEALTH CONSIDERATIONS

Sulfate is rapidly absorbed by the gastrointestinal tract but a number of factors, such as the accompanying cation, can influence the rate of absorption. Low doses are probably absorbed more effectively than high doses. Sulfate is found in all body tissue but is highest in the metabolically active areas of bone and tooth formation, and may be important in regulating bone development.

Sulfate is one of the least toxic anions. Ingestion of high doses can result in catharsis (loosening of the bowels) with dehydration as a possible side effect.

No harmful effects have been reported in studies with animals.

Sulfate can interfere with disinfection efficiency by scavenging residual chlorine. It can also increase corrosion of mild steel pipes.

DERIVATION OF GUIDELINE

The guideline value is based on the taste threshold of sulfate in drinking water of 250 mg/L.

REFERENCES

APHA Method 4500-SO_4^{2-} Part F (1992). Sulfate: Methylthymol blue method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

APHA Method 4500-SO_4^{2-} Part B (1989). Sulfate: Ion Chromatographic method. Standard Methods for the Examination of Water and Wastewater, 18th edition. American Public Health Association, Washington.

NOTE: Important general information is contained in PART II, Chapter 6

Sulprofos

(endorsed 2011)

GUIDELINE

Based on human health concerns, sulprofos in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Sulprofos (CAS 35400-43-2) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes fenthion, parathion, profenofos, and ethoprofos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, sulprofos would not be a health concern unless the concentration exceeded 0.01 mg/L. Excursions above this level even for a short period are of concern, as sulprofos causes cholinesterase inhibition even after relatively short periods of exposure.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Sulprofos is an insecticide for the control of whiteflies and other small plant-sucking pests on cotton, tomato and pepper crops.

There are no registered products containing sulprofos in Australia, but de-registered compounds may still be detected in water. Previously registered products were intended for professional use and were available as concentrated solutions to be applied in diluted form using ground or aerial sprays directly onto cotton or tomato foliage.

Exposure sources: The main source of public exposure to sulprofos and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of sulprofos in the future may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of sulprofos in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of sulprofos in drinking water have been identified.

MEASUREMENT

No suitable techniques for the analysis of sulprofos in drinking water have been identified. However, it is expected that a suitable method using high performance liquid chromatography with tandem mass spectrometry could be developed if required.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for sulprofos is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.3 mg/kg bw/day from long-term (2-year) dietary studies in rats and rabbits. The NOEL is based on decreased cholinesterase activity in plasma and red blood cells at doses of 3 mg/kg bw/day (dogs) and 4 mg/kg bw/day (rats) in dietary studies conducted over 2 years. The ADI incorporates a safety factor of 100, and was first established in 1979.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Sulprofos is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised via the organothiophosphate groups to form an organophosphate, and via sulfoxidation to form sulfoxides and sulfones. Excretion is mainly via urine and is complete within 72 hours.

Acute effects: Sulprofos has moderate acute oral and dermal toxicity. It is not a skin sensitiser. Clinical signs of acute poisoning were typical of cholinesterase inhibition and included hyperexcitability, salivation, bronchoconstriction, headache, vomiting and other behavioural changes.

Short-term effects: A 4-week oral study in rats reported decreased plasma and brain cholinesterase activity at doses of 1 mg/kg bw/day and above. No other effects were reported in this study.

Three-month dietary studies were conducted in rats and dogs. In rats, there was plasma cholinesterase inhibition and decreased bodyweight gain at doses of 0.6 mg/kg bw/day and above. In dogs, plasma cholinesterase was inhibited at doses of 0.7 mg/kg bw/day and clinical signs of cholinesterase inhibition were seen at higher doses. The NOEL in both studies was 0.3 mg/kg bw/day.

Long-term effects: Two-year dietary studies were conducted in mice, rats and dogs. There was cholinesterase inhibition in plasma and erythrocytes at doses of 4 mg/kg bw/day (mice and rats) and 3 mg/kg bw/day (dogs). Brain cholinesterase inhibition occurred in all three species at higher doses. The lowest overall NOEL was 0.3 mg/kg bw/day (rat, dog), and this is the basis for the current ADI.

Carcinogenicity: Based on 2-year studies in mice and rats, there is no evidence of carcinogenicity for sulprofos.

Genotoxicity: Sulprofos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation study in rats and developmental studies in rats and rabbits did not identify any adverse effects on reproductive parameters or foetal development.

Neurotoxicity: A 3-week dietary studies in hens using doses up to 50 mg/kg bw did not identify any clinical or histological signs of neurotoxicity.

Poisons Schedule: Sulprofos is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for sulprofos was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.3 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.3 mg/kg bw/day is the NOEL based on long-term (2-year) studies in rats and dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

NHMRC (National Health and Medical Research Council), NRMMC (Natural Resources Management Ministerial Council) (2004). *Australian Drinking Water Guidelines*. National Water Quality Management Strategy, Paper 6. NHMRC and NRMMC.

Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th edition, British Crop Production Council, UK.

Taste and Odour

(endorsed 2011)

GUIDELINE

The taste and odour of drinking water should not be offensive to most consumers

GENERAL DESCRIPTION

Taste and odour are two of the primary criteria consumers use to judge the quality and acceptability of drinking water. People's sense of taste and smell tends to vary, and so the acceptability of the same water can vary from person to person and from day to day for the same person. Similarly, one individual within a group may be more or less sensitive to a particular substance than the group as a whole. Whilst taste and odour present in water does not generally have a health impact, the presence of tastes and odours may raise consumer concern with regard to water quality.

SOURCES OF TASTE AND ODOUR

Taste and odour in drinking water can result from naturally occurring inorganic chemicals; from biological activity, either in the source, treatment process or distribution system; as a by-product of water treatment processes; or from chemical contamination at any point from source to tap.

Inorganic compounds are generally present in water in substantially higher concentrations than organic compounds. Taste thresholds for some commonly occurring inorganic ions are about 0.1 mg/L for manganese, 0.3 mg/L for iron, 3 mg/L for copper, 3 mg/L for zinc, 250 mg/L for chloride, and 250-500 mg/L for sulfate. Most of these ions have health guidelines at concentrations higher than their taste thresholds (except copper at 2 mg/L). In most cases the customer would reject the water for aesthetic reasons before it would be of health concern.

Contamination of source water from spills, discharges or leaks of organic compounds can result in unpleasant taste and odours. Diesel fuel, for example, has a taste and odour threshold of 0.0005 mg/L. Methyl tert-butyl ether (MTBE) is the most commonly used fuel oxygenate added to reduce atmospheric concentrations of carbon monoxide and other aromatics. MTBE has frequently been detected in samples of shallow groundwaters, particularly in the United States. It affects the taste/odour of water at concentrations below 0.030 mg/L (Young *et al.* 1996).

One of the most common odours in water is described as "earthy", "musty" or "woody". Compounds most often linked to these odours are geosmin and 2 methyl isoborneol (MIB), which have similar low odour threshold concentrations of 0.00001 mg/L (10 ng/L) (Young *et al.* 1996). Cyanobacteria that produce these compounds include taxa representing the genera *Anabaena, Aphanizomenon, Planktothrix, Oscillatoria* and *Phormidium* in either planktonic and benthic habitats. Actinomycetes grow preferably in terrestrial habitats such as exposed sediments and vegetative debris, and are considered to enter aquatic habitats mainly in run-off from the shoreline.

Production of odorous compounds has been reported for most of the major algal classes and other odours produced by particular algae have been described as sweet, aromatic, cucumber, flowery, geranium, nasturtium, violets, fishy, peaty, grassy, mouldy, and vegetable. These odours originate from a variety of odorous compounds produced by the algae including aldehydes, ketones, alkenes, alcohols, terpenes, sulfides, amines, hydrocarbons, fatty acids, esters, carbonyl and aromatics. Cell concentrations as low as 500 cells/mL for some cyanobacteria and for a range of other algae are sufficient to taint a water supply.

Disinfection chemicals can contribute taste or odour to water. The odour threshold for free chlorine varies with

pH, but is generally considered to be between 0.1 and 0.4 mg/L, whilst monochloramine and dichloramine odour thresholds are considered to be 0.5 mg/L and 0.15 mg/L respectively. A study by Piriou *et al.* (2004) has determined taste thresholds of 0.05 mg/L for free chlorine, 0.1 mg/L for monochloramine and 0.2 mg/L for chlorine dioxide using trained French panellists with flavour profile analysis. Untrained panellists were around 2-4 times less sensitive and the US consumer panel was 5-10 times less sensitive than the French consumer panel. This result can be linked to the different chlorination practices in the two countries (residuals are around 0.1-0.2 mg/L in France compared with 1.0-3.0 mg/L in the USA).

A number of organic compounds produced as by-products of disinfection, particularly chlorination, can cause tastes and odours. Some chlorinated phenols, for example, have an antiseptic smell and a very low taste and odour threshold, varying from 0.002 to 0.0001 mg/L, whilst some brominated phenols have a threshold as low as 0.0000005 mg/L (0.5 ng/L) (Mackey *et al.* 2004).

A range of chloroanisoles can result in earthy/musty odours (Young *et al.* 1996). For example 2,4,6-trichloroanisole (TCA) is produced from the action of biofilms in distribution systems on the disinfection by-product 2,4,6 trichlorophenol. TCA is detected at lower concentrations (typically <0.000001 mg/L [<1 ng/L]) than MIB or geosmin, but it is less frequently responsible for odour incidents.

Dimethyl di- and tri-sulfides (DMDS and DMTS) are responsible for septic/swampy odours. They have odour threshold concentrations at low ng/L concentrations. It has been suggested that these compounds may be produced by microorganisms in distribution systems (Franzmann *et al.* 2001, Heitz *et al.* 2000).

Taste and odour can also arise from impacts on the supplied water within the customer's property, such as contaminants in direct or indirect contact with water (e.g. contaminants from kettles, refrigerators, dishwashers or washing machine hoses). The compound 2,6-dibromophenol, identified as probably responsible for a "plastic" or "chemical" taste in water after it is boiled, has a taste threshold concentration of 0.0005 mg/L (Whitfield *et al.* 1992, Adams *et al.* 1999). Odours resembling kerosene and cat urine were found to be more intense and more diverse when chlorine dioxide (ClO_2) was used, and increased numbers of complaints about odours in domestic water supplies were associated with the presence of new carpets in customers' homes (Dietrich *et al.* 1992).

MEASUREMENT

Sensory analysis

Sensory methods provide a qualitative classification and a semi-quantitative determination of taste and odour intensity. Sensory techniques include flavour profile analysis and sensory gas chromatography.

A panel experienced in flavour profile analysis (Krasner 1995, McGuire 1995, Suffet *et al.* 1999) often represents the first step in coping efficiently with taste and odour episodes. The twenty-first edition of *Standard Methods for the Examination of Water and Wastewater* (APHA AWWA WEF Method 2170 - 2005) presents flavour profile analysis (FPA) as a technique for identifying taste and odour samples. FPA uses a group of four or five trained panellists to examine the sensory characteristics of samples. Flavour attributes are determined by tasting, odour attributes by sniffing the sample. Panellists must be able to detect and recognise various flavours present and quantify them according to standards. FPA requires well trained panellists and data interpreters, and reproducibility of results depends on the training and experience of panellists. These panels are useful for assessing complaints by consumers, potentially identifying the source of an adverse flavour; and for assessing the impact of a new or improved treatment process on taste and odour.

Sensory gas chromatography (GC) (Bruchet 1999, Suffet *et al.* 1999) is often used to complement chemical analysis when identifying odorous compounds. The effluent from the GC capillary column is directed to the nose of an operator through tubing and a sniffing funnel. This technique has been used for plastic odours detected from polyethylene pipes.

NOTE: Important general information is contained in PART II, Chapter 6

Chemical analysis

Chemical analysis during a taste and odour episode can identify the compound(s) responsible for the organoleptic characteristics of the sample and thus potentially ensure that the episode is not linked to a possible health threat. However, as the human nose is very sensitive, to obtain similar sensitivity from chemical analysis it is first necessary to concentrate the samples.

Closed loop stripping analysis (CLSA) (Bruchet 1999, Crozes *et al.* 1999, Khiari *et al.* 1999) and liquid-liquid extraction using methylene chloride (Khiari *et al.* 1999, Ventura *et al.* 1995) represent two methods of choice for the concentration of the most common odorous compounds. Solid phase micro extraction is an alternative technique to CLSA for the extraction of odorous compounds from water (Bao *et al.* 1999). Purge-and-trap and headspace methods can possibly be used as complementary sample preparation techniques for volatile compounds but these methods have limits of detection at or greater than 0.001 mg/L. Stir bar sorptive extraction (Twister extraction) is the most recent development in extraction techniques for taste and odour compounds (Benanou *et al.* 2004, Baltussen *et al.* 1999). A stir bar coated with polydimethyl siloxane is placed in the sample, which is stirred for 30-120 minutes. The compounds are extracted onto the stir bar surface through this procedure, and the bar is then placed into a thermal desorption unit, which is connected online to the gas chromatograph-mass spectrometer. The limit of detection for this method is reported to be <0.000001 mg/L (<1 ng/L) for both geosmin and MIB.

A gas chromatograph-mass spectrometer, for separation and detection of the off-flavours compounds, is a prerequisite for any laboratory wishing to identify taste and odour compounds.

TREATMENT OF DRINKING WATER

Inorganic compounds, which can cause taste and odour, can be removed by the use of appropriate treatment processes. For example iron and manganese can be removed during conventional treatment with pre-oxidation. High salinity water may require the use of reverse osmosis to make the water palatable.

Organic substances producing taste and odour are generally more common in source waters. Volatile compounds can sometimes be removed by aeration. However, the application of activated carbon, in powdered (PAC) or granular form (GAC), is often the most effective treatment for the removal of a range of odour compounds. In Australia, PAC is the chosen method for the treatment of cyanobacterial metabolites due to its ease of application and because it can be applied only when required (Newcombe 2006). However, this method is quite costly if continuously applied. In addition, high levels of PAC will increase the load on the sludge treatment facilities, and may result in additional wear and tear on mechanical equipment (pumps etc) resulting in higher maintenance costs. GAC has many other advantages over PAC, such as its long life, higher adsorptive capacity, the ease of process control, more efficient use of the carbon, and the ability to regenerate the carbon for reuse (Herzing *et al.* 1977). Unfortunately at present there are no GAC regeneration facilities in Australia, so the waste adsorbent must be disposed and replaced.

Oxidation can also reduce tastes and odours. The effectiveness of the process is dependent upon factors such as the type of oxidant used, the type of reaction (addition or substitution), the structure of the compound, contact time, and environmental factors (e.g. pH, temperature, the presence of interfering compounds). Chlorine, chloramine and chlorine dioxide are common oxidants/disinfectants used in drinking water treatment. They have been effective in treating a variety of tastes and odours. However, MIB and geosmin have been found to be virtually resistant to this form of oxidation due to their tertiary structures (Lalezary *et al.* 1986, Anselme *et al.* 1988, Glaze *et al.* 1990). Ozonation is more effective for MIB and geosmin; approximately 50% removal of these compounds has been recorded in the laboratory, and at pilot and full scale (Ho *et al.* 2002, Ho 2004). The combination of ozone and GAC (sometimes called biological activated carbon or BAC) can be very effective in removing a range of odour compounds.

When disinfection results in tastes and odours being formed within distribution systems, the removal of precursors such as natural organic matter during the treatment process, increased oxidation, or change of

oxidant can sometimes solve the problem.

Tastes and odours arising out of reaction with biofilms can be reduced by preventing or reducing biofilm growth. This is best accomplished by introducing treatment processes that reduce the food source for bacteria, the assimilable organic carbon, and hence reduce biofilm growth. The presence of a disinfectant residual will also reduce biofilm growth but care must be taken not to introduce disinfectant-related tastes and odours.

If materials used in distribution systems result in discernable tastes and odours, then replacement of the materials or *in situ* lining of the pipework is recommended. The use of non-return devices or back-flow prevention devices can eliminate taste and odour issues associated with the back-siphoning of water, including hoses attached to dishwashers and washing machines installed within close proximity to a draw-off point. The introduction of the Australian and New Zealand Standard AS/NZS 4020 (2005) to ensure materials used in contact with water comply with a range of tests, including the formation of taste under standard test conditions, should eventually eliminate taste and odour problems associated with materials in contact with drinking water. However the interaction of disinfected water with components such as plastics in customers' kettles or new plumbing can be more difficult to control.

HEALTH CONSIDERATIONS

Taste and/or odour in potable water may indicate pollution of the water, insufficient water treatment and/or inadequate maintenance of the distribution system. Odours of a biological origin can indicate increased biological activity, for example by algae. Some algae can produce toxins and the detection of these algae by odour provides a useful early warning of potential problems, although odour does not necessarily indicate the presence of toxins.

DERIVATION OF GUIDELINE

It is clearly unsatisfactory for a water authority to be supplying water that is objectionable in taste and odour to consumers. This will undermine consumer confidence and may lead to the use of water from sources that are aesthetically more acceptable, but potentially less safe. Such sources may include untreated private household supplies, bore water or water treated through poorly maintained domestic filters. It is also unrealistic to expect complete consumer satisfaction with aesthetic characteristics of a water supply; therefore an appropriate guideline should be that the taste and odour of drinking water not be offensive to most people. Due to the subjective nature and range of causes of taste and odour, it is not possible to set a quantitative guideline.

OPERATIONAL GUIDELINE FOR MIB/GEOSMIN

The major cause of taste and odour episodes in Australian water supplies is the presence of MIB and/or geosmin. Based on experience in water utilities, action based on concentrations of MIB/geosmin suggested below will help to minimise customer complaints.

At treatment plant inlet	Total MIB and/or geosmin >10 ng/L	Increase sampling to every 2 days at treatment plant inlet Start MIB/geosmin analysis on treatment plant outlet
At treatment plant outlet	Total MIB and/or geosmin >10 ng/L	Introduce powdered activated carbon dosing to treatment plant

Regular measurement and identification of algae should also be undertaken to complement MIB/geosmin analysis at the inlet to the water treatment plant. Depending on the species-specific relationship between cell numbers and MIB/geosmin concentrations, additional monitoring may be necessary at the treatment

NOTE: Important general information is contained in PART II, Chapter 6

plant inlet when algal organisms known to be producers of these compounds exceed approximately 1000 cells/mL.

GUIDELINES IN OTHER COUNTRIES

The 2004 World Health Organization (WHO) Guidelines require that taste and odour be acceptable to the consumer.

The 1998 European Economic Community Standard (Council Directive 98/83/EC), requires that taste and odour be acceptable to consumers and that there be no abnormal change.

The 2005 Canadian Guidelines stipulate that drinking water shall have an inoffensive taste and odour.

Since 1979 the United States Environmental Protection Agency has listed odour in the secondary drinking water contaminant standards and has listed a secondary maximum contaminant level for odour of 3 expressed as a Threshold Odour Number (TON). They also recommend a variety of reports for further information on identification and control of taste and odours.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Temephos

(endorsed 2011)

GUIDELINE

Based on human health concerns, temephos in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Temephos (CAS 3383-96-8) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, including fenthion, parathion, profenofos and ethoprophos (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, temephos would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Temephos is an insecticide for the control of skin parasites on farm and non-farm animals, and for the control of mosquito and midge larvae in breeding areas.

There are registered products containing temephos in Australia. The products are intended for professional use only. Use patterns include hand-held sprays, shower sprays, dip solution, and shampoo for control of fleas on farm and non-farm animals, and as a liquid concentrate for application to surface water for control of mosquito and midge larvae in public health settings. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to temephos and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The application of temephos to surface water in mosquito breeding areas may potentially lead to the contamination of drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of temephos in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of temephos in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Temephos can be measured in water by solvent extraction followed by high performance liquid chromatography (WHO 2008) or by on-line solid-phase extraction followed by thermospray liquid chromatography with mass spectrometry (Lacorte and Barcel 1995). The practical limit of quantitation is 0.04 μg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for temephos is 0.1 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1 mg/kg bw/day from a 4-week dietary study in humans. This NOEL is based on serum cholinesterase inhibition. The ADI incorporates a safety factor of 10, and was first established in 1988.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Temephos is only partially absorbed from the gastrointestinal tract, with wide, uniform tissue distribution in mammals. It is rapidly eliminated unchanged in the faeces or as temephos sulfoxide in urine. It has a low potential for bioaccumulation.

Acute effects: Temephos has low to moderate oral acute toxicity, and low dermal toxicity. It is not a skin sensitiser.

Short-term effects: Short-term dietary studies in rats and dogs reported symptoms indicative of nervous system toxicity. In a 5-day dietary study in humans, temephos had no effects on blood cholinesterase activity at 256 mg/kg bw/day. In a 4-week dietary study in humans, temephos had no effect on cholinesterase activity at 1 mg/kg bw/day. In medium-term dietary studies in rats and dogs, effects included red blood cell cholinesterase inhibition and increased liver weight at dose levels above 0.1 mg/kg bw/day in rats and above 0.45 mg/kg bw/day in dogs.

Long-term effects: Long-term dietary studies in rats and dogs reported symptoms indicative of nervous system toxicity. No toxicity was noted up to 15 mg/kg bw/day, but cholinesterase was not measured in these studies.

Carcinogenicity: Based on long-term toxicity studies in rats, there is no evidence of carcinogenicity for temephos.

Genotoxicity: Temephos is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In reproduction studies in rats and developmental studies in rats and rabbits, there was no evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Temephos is included in Schedule 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for temephos was determined as follows:

$$0.4 \text{ mg/L} = \frac{1.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 1.0 mg/kg bw/day is the NOEL based on a short-term (4-week) dietary study in humans.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from studies conducted in humans in order to take into account human variation.

Temephos is included in the WHO *Guidelines for Drinking Water Quality* list of pesticides excluded from guideline value derivation, as it is added to water supplies for control of mosquitoes and larvae (WHO 2006). The philosophy is that these pesticides play an important role in the control of disease, and guidelines that are unnecessarily stringent as to impede their use should be avoided if possible.

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NOTE: Important general information is contained in PART II, Chapter 6

Temperature

(endorsed 1996)

GUIDELINE

No guideline is set due to the impracticality of controlling water temperature.

Drinking water temperatures above 20°C may result in an increase in the number of complaints.

GENERAL DESCRIPTION

Temperature is primarily an aesthetic criterion for drinking water. Generally, cool water is more palatable than warm or cold water.

In general, consumers will react to a change in water temperature. Complaints are most frequent when the temperature suddenly increases.

The turbidity and colour of filtered water may be indirectly affected by temperature, as low water temperatures tend to decrease the efficiency of water treatment processes by, for instance, affecting floc formation rates and sedimentation efficiency.

Chemical reaction rates increase with temperature, and this can lead to greater corrosion of pipes and fittings in closed systems. Scale formation in hard waters will also be greater at higher temperatures.

MEASUREMENT

Temperature measurements should be made with a good quality, mercury-filled Celsius thermometer (APHA Method 2550B 1992).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Water temperatures in major Australian reticulated supplies range from 10°C to 30°C. In some long, above-ground pipelines, water temperatures up to 45°C may be experienced.

CONTROL IN DRINKING WATER SUPPLIES

Control of water temperature in reticulated supplies is seldom practical or effective. Selective withdrawal from deep reservoirs can be used but this may introduce other water quality problems. Aeration can also be used. In some situations it may be possible to place pipes underground to reduce water temperature fluctuations, or to vary the times water remains in pipes and storage tanks.

HEALTH CONSIDERATIONS

The effectiveness of chlorine as a disinfectant is influenced by the temperature of the water being dosed. Generally higher temperatures result in more effective disinfection at a particular chlorine dose, but this may be counterbalanced by a more rapid loss of chlorine to the atmosphere (AWWA 1990).

Chlorine reacts with organic matter in water to produce undesirable chlorinated organic by-products, and higher temperatures increase the rate of these reactions.

Temperature can directly affect the growth and survival of microorganisms. In general the survival time of infectious bacteria and parasites is reduced as the temperature of the contaminated water increases.

Naegleria fowleri, which can cause amoebic meningitis, grows between 18°C and 46°C and is likely to occur in nondisinfected water supplies that reach 30°C seasonally. *Legionella pneumophila* (which causes Legionnaires' disease) and related bacteria are found in hot and cold water systems, with colonisation occurring in stagnant water at temperatures between 20°C and 45°C. Increased temperatures can also promote the growth of taste- and odour-producing organisms in lakes and impoundments, and in distribution systems.

GUIDELINES IN OTHER COUNTRIES

The European Economic Community Standards have a guideline value of 12°C and a maximum of 25°C.

The Canadian Guidelines have a recommended value of 15°C.

The 1984 World Health Organization (WHO) Guidelines do not include a value for temperature as control is usually impractical. The 1993 WHO Guidelines require that temperature should be acceptable to avoid consumer complaints.

REFERENCES

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NOTE: Important general information is contained in PART II, Chapter 6

Terbacil

(endorsed 2011)

GUIDELINE

Based on human health concerns, terbacil in drinking water should not exceed 0.2 mg/L.

RELATED CHEMICALS

Terbacil (CAS 5902-51-2) belongs to the uracil class of chemicals. Other pesticides in this class include bromacil and butafenacil (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, terbacil would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Terbacil is a selective herbicide for the control of annual and perennial weeds in agricultural crops such as sugarcane, apples, peaches, citrus, and almond trees.

There are registered products that contain terbacil in Australia. The products are intended for professional use. Terbacil is available as concentrated solutions to be applied in diluted form using ground, aerial or hand-held sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to terbacil and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of terbacil may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of terbacil in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of terbacil by conventional drinking water treatment processes have been identified. However, advanced oxidation using ultraviolet radiation and hydrogen peroxide is effective under optimised conditions (Shemer *et al.* 2006, Elovitz *et al.* 2008).

MEASUREMENT

No suitable techniques for the analysis of terbacil in drinking water have been identified. However, it is expected that a suitable method using high performance liquid chromatography with tandem mass spectrometry could be developed if required.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for terbacil is 0.06 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 6.25 mg/kg bw/day from a long-term (2-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, and was first established in 1987.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Terbacil is readily and extensively absorbed via the gastrointestinal tract in mammals. It is not extensively metabolised, but the limited metabolic pathway proceeded by 6-methyluracil hydroxylation, sulfonation, and conjugation. Excretion was complete by 48 hours as metabolised compound in urine and minor amounts in faeces.

Acute effects: Terabacil has low acute oral and dermal toxicity. It is not a skin sensitiser in guinea-pig.

Short-term effects: A 3-month dietary studies in rats reported an increase in absolute and relative liver weights, associated with hepatocellular hypertrophy and vacuolation at doses of 250 mg/kg bw/day.

Long-term effects: Long-term dietary studies were conducted in mice, rats and dogs. In mice, there was decreased pituitary weight, and centrilobular hypertrophy at doses of 180 mg/kg bw/day. In rats, there were increased absolute and relative liver weights, associated with centrilobular hypertrophy and vacuolation, at doses of 125 mg/kg bw/day. In dogs, there was increased relative liver weight and elevated serum alkaline phosphatase, with no histological evidence of adverse effects, at the highest dose tested, 60 mg/kg bw/day. The next lowest dose and lowest overall NOEL was 6.25 mg/kg bw/day in this study, and this is the basis for the current ADI.

Carcinogenicity: Based on an 18-month study in mice, and a 2-year study in rats, there is no evidence of carcinogenicity for terbacil.

Genotoxicity: Terbacil is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats and a developmental study in rats did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Terbacil is considered not to require control by scheduling due to its low toxicity and is therefore in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.2 mg/L for terbacil was determined as follows:

$$0.2 \text{ mg/L} = \frac{6.25 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 6.25 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Terbufos

(endorsed 2011)

GUIDELINE

Based on human health concerns, terbufos in drinking water should not exceed 0.0009 mg/L.

RELATED CHEMICALS

Terbufos (CAS 13071-79-9) belongs to the organophosphate group of chemicals. There are many other pesticides in this class, which includes chlorpyrifos, dimethoate, ethoprophos and ethion (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population to terbufos is expected to be well below levels that may cause health concerns.

Terbufos is an acutely poisonous organophosphate pesticide. If it is detected in water as a result of spillage or misuse at levels above 0.0009mg/L, remedial action should be taken. Concentrations of terbufos greatly exceeding this guideline present an acute human health risk.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Terbufos is used as an insecticide and nematocide for the control of various above-ground insects, soil arthropods, and nematodes in agriculture, including food crops.

There are registered products containing terbufos in Australia. The products are granular formulations to be applied to the soil in agricultural settings**.** Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to terbufos and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of terbufos may potentially lead to contamination of source waters through processes such as run-off or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of terbufos in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of terbufos in drinking water have been identified.

MEASUREMENT

Terbufos can be measured in drinking water by solid phase extraction and capillary column gas chromatography–mass spectrometry (USEPA 2000). The practical limit of detection is 0.05 μg/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for terbufos is 0.0002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.0025 mg/kg bw/day from a short-term (6-month dietary) study. The NOEL is based on decreased serum cholinesterase activity in dogs. The ADI incorporates a safety factor of 10, and was established in 1992.

The previous ADI of 0.00003 mg/kg bw/day set in 1980 was based on the same study and endpoint. The use of a safety factor of 100 was reconsidered in 1992 following an evaluation by the WHO. The 1992 review affirmed the validity of cholinesterase inhibition as an endpoint of toxicity, but decreased the safety factor to 10.

The previous health value was 0.0005 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Terbufos is readily absorbed via the gastrointestinal tract and is widely distributed in tissues and blood. In rats, terbufos was slowly excreted as metabolites (within 7 days), mainly in the urine. The major metabolites were S-methylated metabolites, which are of similar or lower toxicity to terbufos.

Acute effects: Terbufos has high acute oral toxicity in rats and high acute dermal toxicity in rabbits. The skin sensitisation potential of terbufos is unknown. Clinical signs of acute poisoning were typical of cholinesterase inhibition and included hyperexcitability, salivation, bronchoconstriction, headache, vomiting and other behavioural changes.

Short-term effects: Short-term dietary studies in rats and dogs reported symptoms indicative of nervous system toxicity. In 28-day dietary studies, decreased cholinesterase activity was reported at doses above 0.0125 mg/kg bw/day in rats and above 0.01 mg/kg bw/day in dogs. In a 3-month dietary study in rats and a 6-month dietary study in dogs, cholinesterase inhibition occurred at doses above 0.05 mg/kg bw/day in rats and 0.0025 mg/kg bw/day in dogs. The NOEL of 0.0025 mg/kg bw/day in dogs is the basis for the current ADI.

Long-term effects: Long-term dietary studies in rats and dogs reported symptoms indicative of nervous system toxicity. A 1-year dietary study in dogs reported inhibition of cholinesterase at the lowest dose tested, 0.015 mg/kg bw/day.

Carcinogenicity: Based on long-term dietary studies in mice or rats, there is no evidence of carcinogenicity for terbufos.

Genotoxicity: Terbufos is not considered to be genotoxic, based on *in vitro* or *in vivo* short-term studies.

Reproductive and developmental effects: Reproduction studies and developmental studies in rats reported no effects on reproductive parameters or foetal development other than that resulting from maternal toxicity.

Neurotoxicity: There was no clinical evidence of delayed or residual neurotoxicity or demyelination in 21-day toxicity studies in hens.

Poisons Schedule: Terbufos is included in Schedule 7 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.0009 mg/L for terbufos was determined as follows:

$$0.0009 \text{ mg/L} = \frac{0.0025 \text{ mg/kg body weight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 10}$$

where:

- 0.0025 mg/kg bw/day is the NOEL based on a medium-term (6-month) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 10 is the safety factor applied to the NOEL derived from animal studies. The safety factor of 10 was considered to provide an adequate margin of safety, as despite being derived from animal studies, the end-point (inhibition of plasma cholinesterase) is considered to be a very sensitive indicator.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Terbuthylazine

(endorsed 2011)

GUIDELINE

Based on human health concerns, terbuthylazine in drinking water should not exceed 0.01 mg/L.

RELATED CHEMICALS

Terbuthylazine (CAS 5915-41-3) is in the triazine class of chemicals. Other pesticides in this class include ametryn, atrazine, simazine and terbutryn (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, terbuthylazine would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Terbuthylazine is a herbicide used to control pre- and post-emergent weeds in a variety of agricultural crops and in forestry. It is also used as an industrial algicide in water cooling systems, ponds and fountains, and is used as an algicide in swimming pools.

There are currently no registered products containing terbuthylazine in Australia, but de-registered compounds may still be detected in water. Terbuthylazine has been used previously by professionals and applied by boom spray to crops as well as being used in swimming pools. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to terbuthylazine, if used, would be residues in food.

If used in the future in agriculture, its use may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Values for terbuthylazine in Australian drinking water were not found. Levels in surface and bore waters in Europe and North America ranged from less than 0.1 µg/L to approximately 2 µg/L. Levels in Australian waters would normally be expected to be within this range.

TREATMENT OF DRINKING WATER

Relatively high removal rates of terbuthylazine have been achieved using conventional flocculation, adsorption onto activated carbon and ozonoation (Ormad *et al.* 2008). If terbuthylazine is detected, jar testing with a matrix of multiple oxidants, adsorbents, and coagulants is recommended.

MEASUREMENT

Measurement of residue levels in water can be undertaken by use of solid phase extraction and high performance liquid chromatography with either ultraviolet detection or tandem mass spectrometry.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for terbuthylazine is 0.003 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.35mg/kg bw/day 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, and was established in 2001.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Terbuthylazine is readily absorbed from the gastrointestinal tract (~ 90%) and distributed widely in tissues. It is extensively metabolised and excreted rapidly, mainly via the urine, within 7 days. There is no evidence of bioaccumulation.

Acute effects: Terbuthylazine has low acute oral and dermal toxicity. There is some evidence for skin sensitisation in guinea pigs.

Short-term effects: In dietary studies in rats, there was reduced bodyweight gain at 75 mg/kg bw/day in rats. There was no effect on organ weights or tissue histopathology at doses up to 5 mg/kg bw/day in rats.

Long-term effects: In long-term dietary studies in mice, rats and dogs, there was a decrease in bodyweight gain and food consumption in all species. There were no consistent changes in haematology, clinical chemistry or histopathological findings indicative of systemic toxicity. The lowest NOEL was 0.35 mg/kg/day in the 2-year rat study, based on reduced bodyweight gain and reduced food consumption. This NOEL is the basis for the ADI.

Carcinogenicity: Based on long-term studies in mice and rats, there is no evidence of carcinogenicity for terbuthylazine.

Genotoxicity: Terbuthylazine is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In a reproduction study in rats and developmental studies in rats and rabbits, terbuthylazine showed no evidence of effects on reproductive parameters or on foetal development.

Poisons Schedule: Terbuthylazine is included in Schedule 6 of the of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on the concentration and use. Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.01 mg/L for terbuthylazine was determined as follows:

$$0.01 \text{ mg/L} = \frac{0.35 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.35 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a guideline value of 0.007 mg/L for terbuthylazine (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Terbutryn

(endorsed 2011)

GUIDELINE

Based on human health concerns, terbutryn in drinking water should not exceed 0.4 mg/L.

RELATED CHEMICALS

Terbutryn (CAS 886-50-0) belongs to the triazene class of chemicals. There are many other pesticides in this class, which includes ametryn, propazine, prometon, and cyanazine (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.If present in drinking water as a result of a spillage or through misuse, terbutryn would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Terbutryn is a herbicide for the control of broad-leaf weeds in wheat, barley, triticale, peas, sugar cane and turf agricultural crops.

There are registered products that contain terbutryn in Australia. The products are intended for professional use. Terbutryn is available as concentrated solutions to be applied in diluted form using ground and aerial sprays. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to terbutryn and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of terbutryn may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No specific reports of terbutryn in Australian drinking waters have been identified. However, a study of four small river systems in Germany revealed maximum concentrations of up to 5.6 µg/L (Quednow and Puttmann 2007). Terbutryn has also been reported in ground water in the UK at concentrations up to 0.13 µg/L (Lapworth *et al.* 2006).

TREATMENT OF DRINKING WATER

Preoxidation of drinking water by chlorine is effective for the removal of terbutryn (Ormad *et al.* 2008). However, this approach will produce unidentified by-products, which will remain in the water. An alternative and equally effective approach is the preoxidation of terbutryn by ozone followed by activated carbon adsorption (Ormad *et al.* 2008).

MEASUREMENT

Numerous analytical methods are available for multiresidue analysis of triazene pesticides. For example, terbutryn may be measured in drinking waters by relatively common methods of solid phase extraction and gas chromatography–mass spectrometry, with a quantification limit of 30 ng/L (Ormad *et al.* 2008). More advanced methods, including gas chromatography coupled to high-resolution time-of-flight mass spectrometry, have also been reported (Hernandez *et al.* 2007). Terbutryn may also be measured in drinking waters along with other triazenes by ultra-performance liquid chromatography with tandem mass spectrometric detection. The limit of quantification for all analytes in this method was reported to be 5 ng/L (Drozdzynski and Folkman 2008).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for terbutryn is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 10 mg/kg bw/day from short-term dietary studies in rats (13-week) and dogs (6-months). The NOEL is based on clinical signs of toxicity in a 6-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, and was established in 1986. An ADI for terbutryn was not set in Australia before 1986.

The previous health value was 0.3 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Terbutryn is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, with the main metabolites in the form of polar metabolites and conjugates. It is excreted mainly in the urine and to a lesser extent in the faeces within 72 hours.

Acute effects: Terbutryn has low acute oral and dermal toxicity. It is a skin sensitiser in guinea pigs, although there are no reports of sensitisation in humans working with terbutryn.

Short-term effects: A 16-week dietary study in rats reported thyroid toxicity (follicular hypertrophy and follicular eosinophilic infiltration) and liver toxicity (increased serum alkaline phosphatase activity, cholesterol, alanine amino-transferase, and glucose) at doses of 50 mg/kg bw/day and above A 6-month dietary study in dogs reported clinical signs of toxicity (increased salivation, hyper-responsiveness to sound, and timid behaviour) and intestinal epithelial necrosis at doses of 25 mg/kg bw/day and above. The NOEL in both of these studies was 10 mg/kg bw/day, and this is the basis for the current ADI.

Long-term effects: In long-term dietary studies in mice, there was no evidence of toxicity up to doses of 150 mg/kg bw/day. In long-term dietary studies in rats, there was decreased bodyweight gain and food consumption, follicular hyperplasia, and liver adenomas at 150 mg/kg bw/day. The lowest NOEL was 15 mg/kg bw/day (rats) in these studies.

Carcinogenicity: There was evidence of carcinogenicity but only at dose levels well in excess of the likely level of human exposure.

Genotoxicity: Terbutryn is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 3-generation reproduction study in rats, and

developmental studies in rats and rabbits, did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Terbutryn is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.4 mg/L for terbutryn was determined as follows:

$$0.4 \text{ mg/L} = \frac{10 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 10 mg/kg bw/day is the NOEL based on a medium-term (13-week) dietary study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Tetrachloroethene (also known as tetrachloroethylene or perchloroethylene)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of tetrachloroethene in drinking water should not exceed 0.05 mg/L.

GENERAL DESCRIPTION

Tetrachloroethene is used as a solvent in the dry-cleaning industry. It may be present in drinking water through contamination of water sources by spills or discharges. In the United Kingdom and the United States it has occasionally been detected in drinking water at concentrations below 0.001 mg/L. It has been found at higher concentration in contaminated groundwater.

The odour threshold in water is 0.3 mg/L.

Tetrachloroethene is widespread in the environment through use in dry-cleaning and as a metal-degreasing fluid. It has been reported in trace amounts in food, water, aquatic organisms and human tissue.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Tetrachloroethene has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

Tetrachloroethene can be removed from drinking water by adsorption onto granular activated carbon or by aeration.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of tetrachloroethene (USEPA Draft Method 551 1990). Sodium chloride is added to the sample and tetrachloroethene extracted using methyl tert-butyl ether. The extract is then analysed using gas chromatography with an electron capture detector. The limit of determination is approximately 0.000004 mg/L (4 ng/L).

HEALTH CONSIDERATIONS

Tetrachloroethene is rapidly absorbed after ingestion or inhalation. It is eliminated primarily by the lungs. In the body it is slowly metabolised to trichloroacetic acid.

An extensive review and summary of the human and animal toxicity data for tetrachloroethene is available (IPCS 1984).

The most notable acute effect of short-term exposure is depression of the central nervous system. Short-term studies of up to 3 months using mice and rats reported weight loss, and found some evidence of liver and kidney toxicity at high doses (400 mg/kg body weight per day).

Inhalation exposure to impure tetrachloroethene at 100 ppm and above in air caused hepatocellular carcinomas in mice. Exposure at 200 ppm in air increased the incidence of leukaemia in rats.

Mutagenic activity was not observed in most tests with a number of strains of bacteria. No chromosome aberrations were observed using rat or mouse cells, or human lymphocytes.

The International Agency for Research on Cancer has concluded that tetrachloroethene is possibly carcinogenic to humans (Group 2B, inadequate human data but sufficient evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The guideline value of 0.05 mg/L for tetrachloroethene in drinking water was determined as follows:

$$0.05 \text{ mg/L} = \frac{14 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 14 mg/kg body weight per day is the no-effect level from a 90-day drinking water study using rats and mice (Buben and O'Flaherty 1985, Hayes *et al*. 1986).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 to account for possible carcinogenicity). An additional factor for the less than lifetime study was not applied as long-term carcinogenicity bioassays were available.

The World Health Organization guideline value of 0.04 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

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NOTE: Important general information is contained in PART II, Chapter 6

Thiobencarb

(endorsed 2011)

GUIDELINE

Based on human health concerns, thiobencarb in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

Thiobencarb (CAS 28249-77-6) belongs to the thiocarbamate class of chemicals. There are many other pesticides in this class, including EPTC, pebulate, and molinate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, thiobencarb would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Thiobencarb is a selective herbicide for the control of grass weeds in rice crops.

There is at least one registered product containing thiobencarb in Australia. Thiobencarb products are intended for professional use, and are available as a concentrated solution to be diluted and applied to water via ground and aerial spray. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to thiobencarb and its metabolites is residues in food and drinking water. Residue levels in food produced according to good agricultural practice are generally low, and maximum residue limits are at the level of detection.

The agricultural use of thiobencarb involves direct application into irrigation water, which may then enter source waters for drinking water.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of thiobencarb in Australian drinking waters have been identified. However, thiobencarb has been reported in run-off from Australian rice fields (Quayle *et al*. 2006), indicating the potential for drinking water contamination in rice-growing regions.

TREATMENT OF DRINKING WATER

During chlorination of drinking water, thiobencarb has been shown to be quickly degraded, producing chlorobenzyl alcohol, chlorotoluene, chlorobenzyl chloride, chlorobenzoic acid and chlorobenzyl aldehyde as chlorination by-products (Magara *et al*. 1994).

MEASUREMENT

No suitable techniques for the analysis of thiobencarb in drinking water have been identified. However, thiobencarb has commonly been measured in soils and run-off from rice growing operations using high performance liquid chromatography–tandem mass spectrometry, and such methods could be adapted if required.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for thiobencarb is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1.0 mg/kg bw/day from long-term dietary studies in dogs (1-year) and rats (2-year). The NOEL is based on decreased plasma cholinesterase activity, reduced bodyweight gain, and evidence of anaemia at doses of 5 mg/kg bw/day and above. The ADI incorporates a safety factor of 100, and was established in 1989.

The previous ADI of 0.007 mg/kg bw was set in 1977, based on a NOEL of 0.75 mg/kg bw/day. The basis for this NOEL is not available.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Thiobencarb is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised by oxidation and hydrolysis to the major metabolites, 4-chlorohippuric acid and 4-chlorobenzoic acid. Excretion was via urine and to lesser extent faeces, and was almost complete within 72 hours.

Acute effects: Thiobencarb has moderate acute oral toxicity and low acute dermal toxicity. It is not a skin sensitiser.

Short-term effects: A three-month oral study in rats reported increased liver weight and serum alkaline phospatase activity at dose levels of 33 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies in rats (2-year) and dogs (1-year) reported decreased plasma cholinesterase activity, reduced bodyweight gain, and evidence of anaemia at doses of 5 mg/kg bw/day and above. In a long-term dietary study in mice, liver discolouration was the only effect seen at high dose levels. The lowest overall NOEL was 1 mg/kg bw/day (in both rats and dogs). This NOEL is the basis for the current ADI.

Carcinogenicity: Based on 18-month studies in mice and a 2-year study in rats, there is no evidence of carcinogenicity for thiobencarb.

Genotoxicity: Thiobencarb is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats, and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Poisons Schedule: Thiobencarb is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.04 mg/L for thiobencarb was determined as follows:

$$0.04 \text{ mg/L} = \frac{1.0 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1.0 mg/kg bw/day is the NOEL based on a long-term dietary studies in dogs (1 year) and rats (2 years).
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Thiometon

(endorsed 2011)

GUIDELINE

Based on human health concerns, thiometon in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Thiometon (CAS 640-15-3) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes chlorpyrifos, terbufos, azinphos methyl (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, chemical would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Thiometon is an insecticide and acaricide used to control lice, mites and sawflies on a wide variety of agricultural crops.

There are currently no products containing thiometon registered for use in Australia, but de-registered compounds may still be detected in water. After a review, the toxicological database was considered inadequate to support continued registration of products containing thiometon.

Exposure sources: If used in the future, the main source of public exposure to thiometon and its metabolites would be residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of any thiometon products in the future may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of thiometon in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of thiometon in drinking water have been identified.

MEASUREMENT

The National Measurement Institute reports that gas chromatography with mass spectrometry can achieve a limit of reporting of 0.0001 mg/L for thiometon.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for thiometon is 0.001 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.12 and 0.15 mg/kg bw/day from long-term (2-year) dietary studies in rats and dogs, respectively. The NOEL is based on decreased erythrocyte cholinesterase activity. The ADI incorporates a safety factor of 100, and was first established in 1989.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Thiometon is readily and extensively absorbed via the gastrointestinal tract in rats. It is extensively metabolised, primarily through sulfoxidation pathways to form sulfoxides and sulfones. These metabolites are rapidly excreted in urine as sulfates, glucoronides, and glutathione conjugates, almost completely within 24 hours.

Acute effects: Thiometon has moderate acute oral and dermal toxicity. Skin sensitisation studies are unavailable, but it has not been associated with sensitisation during occupational exposure. Clinical signs of acute poisoning were typical of cholinesterase inhibition and included hyperexcitability, salivation, bronchoconstriction, headache, vomiting and other behavioural changes.

Short-term effects: In 90-day dietary studies in rats and dogs, cholinesterase inhibition was seen at doses of 1.5 mg/kg bw/day (rats) and 0.6 mg/kg bw/day (dogs). No other effects were seen up to the highest doses tested, 4.5 mg/kg bw/day in rats and 1.2 mg/kg bw/day in dogs.

Long-term effects: In 1- and 2-year dietary studies in dogs and rats, respectively, erythrocyte cholinesterase inhibition was seen at doses of 0.3 mg/kg bw/day (dogs) and 1.5 mg/kg bw/day (rats) in 1- and 2-year dietary studies. Plasma cholinesterase inhibition was the only other effect seen up to the highest dose tested, 1.2 mg/kg bw/day, in dogs. In rats, increased serum alkaline phosphatase activity, and decreased serum cholesterol, protein, and glucose, and brain cholinesterase activity was seen at the highest dose tested, 14.4 mg/kg bw/day. The NOELs were 0.12 mg/kg bw/day (rats) and 0.15 mg/kg bw/day (dogs), and these are the basis for the current ADI of 0.001 mg/kg bw/day.

Carcinogenicity: Based on a 2-year study in rats, there is no evidence of carcinogenicity for thiometon.

Genotoxicity: Thiometon is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Three-generation reproduction studies in rats, and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: No delayed developmental toxicity was seen in a 21-day dietary study in chickens up to the highest dose tested, 4 mg/kg bw/day.

Poisons Schedule: Thiometon is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

NOTE: Important general information is contained in PART II, Chapter 6

The health-based guideline of 0.004 mg/L for thiometon was determined as follows:

$$0.004 \text{ mg/L} = \frac{0.12 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.12 mg/kg bw/day is the NOEL based on a long-term (2-year) dietary study in rats. This NOEL is closely supported by a NOEL of 0.15 mg/kg bw/day from a long-term (2-year) dietary study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

DoHA (2010) *The Poisons Standard; Schedule 1-Standard for the Uniform Scheduling of Medicines and Poisons*, Department of Health and Ageing, Commonwealth of Australia, Canberra.

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Thiram

(endorsed 2011)

GUIDELINE

Based on human health concerns, thiram in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Thiram (CAS 137-26-8) belongs to the dimethyldithiocarbamate class of chemicals. Another pesticide in this class is ziram (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, thiram would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Thiram is used as a fungicide for the control of disease in turf, ornamentals, vines and agricultural crops or as an antifouling agent on industrial equipment and boats.

There are registered products that contain thiram in Australia. The products are intended for professional and/or home garden use and are available as concentrated solutions. They are applied diluted as a seed dressing prior to sowing, as a drench to seedbeds, or as a spray using hand-held or ground boom equipment. They are also applied as concentrated paint using brushes, rollers or air spray equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to thiram and its metabolites are the use of home garden products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of thiram may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No data on the occurrence of thiram in Australian waters could be found. Thiram adsorbs strongly to soils. In the USA, thiram is predicted at concentrations of approximately 4.3 and 0.84 µg/L in surface water and groundwater, respectively (USEPA 2004).

TREATMENT OF DRINKING WATER

No information on the efficiency of drinking water treatment processes to remove thiram could be found.

MEASUREMENT

Thiram in water can be analysed by a variety of methods (Sharma *et al*. 2003). Using high-performance liquid chromatography coupled with enrichment with a minicolumn allows determination of thiram to 0.5 µg/L (Suzuki *et al*. 1993).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for thiram is 0.004 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.4 mg/kg bw/day from a long-term (2-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, and was established in 1995.

The previous ADI for thiram was 0.001 mg/kg bw. It was amended in 1995 following the evaluation of new studies that addressed the inadequacies of the toxicological database.

The previous health value was 0.003 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Thiram is well absorbed via the gastrointestinal tract and is widely distributed in tissues and blood. It is extensively metabolised and excreted mainly in expired air and urine, with smaller amounts detected in the faeces. The majority of the dose is eliminated within 48 hours in rats.

Acute effects: Thiram has low to moderate acute oral toxicity and low acute dermal toxicity. It is a skin sensitizer in guinea pigs and is associated with allergic dermatitis in humans following occupational use.

Short-term effects: Short-term dietary studies were conducted in mice, rats and dogs. In both mice and rats, there was reduced food consumption and reduced bodyweight gain at 25 mg/kg bw/day and above. In rats, there was also evidence of anaemia and changes in clinical chemistry parameters indicative of liver/kidney damage. Histopathological changes in the stomach at 25 mg/kg bw/day and degenerative changes in the testes at 90 mg/kg bw/day were also observed. In dogs, there were reduced erythrocyte counts at 2.3 mg/kg bw/day as well as other haematological and clinical chemistry changes at higher dose levels.

Long-term effects: Long-term dietary studies have been conducted in mice, rats and dogs. In mice, there was reduced bodyweight gain, evidence of anaemia and irritation of the stomach at 57 mg/kg bw/day and above. In rats, there was pancreatic atrophy, bile duct hyperplasia, and extramedullary haematopoiesis in the liver and spleen at 1.5 mg/kg bw/day and above. At higher doses, there was evidence of neurotoxicity, anaemia, and benign neoplastic lesions in the liver and thyroid. In dogs, there were clinical chemistry changes indicative of liver effects at 2.6 mg/kg bw/day. Histopathological changes in the liver, as well as anaemia and clinical signs of neurotoxicity, were reported at 4 mg/kg bw/day. At the highest dose of 40 mg/kg bw/day, clonic convulsions, severe anaemia and ophthalmological effects were reported. The NOEL for neurological, anaemic and liver effects in the dog was 0.4 mg/kg bw/day, and is the basis for the current ADI.

Carcinogenicity: Long-term dietary studies in rats reported benign neoplastic lesions in the liver, thyroid and retina. These effects occurred at doses well in excess of the likely level of human exposure.

Genotoxicity: Thiram produced both positive and negative results in *in vitro* and *in vivo* short-term assays. The weight of evidence indicates that it is weakly genotoxic.

NOTE: Important general information is contained in PART II, Chapter 6

Reproductive and developmental effects: A two-generation reproduction study in rats and developmental toxicity studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: Short-term dietary studies in chicks and long-term dietary studies in rats and dogs reported symptoms indicative of nervous system toxicity, but only at dose levels well in excess of the likely level of human exposure.

Poisons Schedule: Thiram is included in Schedule 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.007 mg/L for thiram was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.4 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 200}$$

where:

- 0.4 mg/kg bw/day is the NOEL based on a long-term (2-year) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 200 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation. With an additional safety factor of 2 to address the additional uncertainty in relation to the carcinogenicity of thiram.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Tin

(endorsed 2011)

GUIDELINE

No guideline value is considered necessary for tin in drinking water, as concentrations are likely to be considerably lower than the level that can cause health effects.

GENERAL DESCRIPTION

Tin is mainly used for plating. Tin coatings are used in the manufacture of food containers and in food processing equipment. Tin is also used in alloys such as solders, bronzes and pewters. Inorganic tin compounds are used as pigments in the ceramic and textile industries. Organic tin compounds are used as biocides (see Fact Sheet on organotins).

The concentration of tin in rivers, estuaries and oceans is generally less than 0.000005 mg/L (5 ng/L), but in some instances has been measured up to 0.002 mg/L. The use of organotin biocides can produce significantly higher concentrations in environmental waters. Levels of <0.042–0.3 mg/L were found in 37 different bottled mineral waters. A mean range of 0.001– 0.002 mg/L (maximum 0.030 mg/L) was found in a survey of water supplies in the United States; values greater than 0.002 mg/L are exceptional (WHO 2004, IPCS 2005).

Food, and particularly canned food, is the major source of human exposure to tin. Intake from this source can vary widely and estimates range from 0.1 mg per day up to 100 mg per day, with a median of 0.2 mg per day.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Australian drinking water supplies have not been routinely monitored for tin. Based on measurements made overseas, it is likely that concentrations would be extremely low.

TREATMENT OF DRINKING WATER

Treatment of drinking water to reduce the concentration of inorganic tin is unlikely to be required.

MEASUREMENT

The concentration of tin in drinking water can be determined using graphite furnace atomic absorption spectroscopy (APHA Method 3500-Sn part B 1992). The limit of determination is 0.01 mg/L.

HEALTH CONSIDERATIONS

Tin is thought to be an essential element in animals. It is not known whether it is essential for humans.

Tin, or tin salts, are poorly absorbed from the gastrointestinal tract. Most studies indicate that less than 5% is absorbed. Highest concentrations of tin occur in the bone, kidney and liver. Biological half-lives range from 1 to 4 months, and tin is excreted primarily via the kidneys and bile.

Extensive reviews and summaries of the human and animal toxicity data for tin are available (JECFA 2000, WHO 2004, IPCS 2005, ATSDR 2005).

There is no evidence of adverse effects in humans associated with long-term exposure to tin. The main effects, due to consumption of canned food with high tin concentrations (over 150 mg/kg), are gastric irritation resulting in vomiting, diarrhoea, fatigue and headache.

In animals, long-term ingestion studies over 2 years using rats and mice reported no significant adverse effects.

Inorganic tin in the form of stannous chloride was found not to be mutagenic in tests with bacteria; however, in mammalian cells *in vitro*, inorganic tin has induced DNA and chromosomal aberrations.

DERIVATION OF GUIDELINE

The low toxicity of tin and inorganic tin compounds is due largely to low absorption, low tissue accumulation and rapid excretion. A guideline value of approximately 0.7 mg/L could be derived from a 2-year feeding study with rats (WHO 1982), but this value is approximately three orders of magnitude higher than tin concentrations in drinking water. Therefore, the presence of tin in drinking water does not represent a hazard to human health and the establishment of a guideline value is not deemed necessary.

REFERENCES

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ATSDR (Agency for Toxic Substances and Disease Registry) (2005). Toxicological Profile for Tin and Tin Compounds. ATSDR, US Department Of Health and Human Services Public Health Service. PB2006-100006

IPCS (International Programme on Chemical Safety) (2005). Concise International Chemical Assessment Document 65. Tin and Inorganic Tin Compounds. IPCS, World Health Organization Geneva, Switzerland.

JECFA (Joint Expert Committee on Food Additives) (2000). Who Food Additives Series 46:Tin (Addendum). JECFA, World Health Organization.

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NOTE: Important general information is contained in PART II, Chapter 6

Toltrazuril

(endorsed 2011)

GUIDELINE

Based on human health concerns, toltrazuril in drinking water should not exceed 0.004 mg/L.

RELATED CHEMICALS

Toltrazuril (CAS 69004-03-1) belongs to the triazinetrione class of chemicals. There are no other pesticides in this class (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, toltrazuril would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Toltrazuril is a coccidiostat for the control of protozoa infection (coccidiosis) in poultry, young cattle and piglets.

There are registered products that contain toltrazuril in Australia. The products are intended for professional use and are available as concentrated formulations to be applied to drinking water and feed provided to animals. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to toltrazuril is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

The veterinary use of toltrazuril provides some potential for contamination of drinking water through the washing of equipment near dams, streams or watercourses.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on toltrazuril occurrence in Australian drinking water supplies were found. However, there is an identified risk that toltrazuril may reach groundwater after spreading of contaminated poultry manure on agricultural land. (EMEA 2008).

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of toltrazuril in drinking water, but it is expected that advanced treatment methodologies such as ozonation, reverse osmosis and advanced oxidation would be effective.

MEASUREMENT

Toltrazuril is a veterinary product and the majority of analytical methods have been developed to determine residue concentrations in animal tissues. A high performance liquid chromatography (HPLC) analytical method based on fluorescence detection has been used to determine toltrazuril concentrations in tissues and plasma (EMEA 2008). Determination of toltrazuril in eggs by HPLC with ultraviolet detection or HPLC with tandem mass spectrometric detection can achieve a limit of quantitation of 30 µg/kg and 1 µg/kg respectively (Mulder *et al*. 2004). No published reports on methods for analysis of toltrazuril in drinking water were found.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for toltrazuril is 0.01 mg per kg of bodyweight (mg/kg bw), based on a lowest-observed-effect level (LOEL) of 1 mg/kg bw/day from a 2-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, and was first established in 1993.

A health value has not been previously established by NHMRC.

HEALTH CONSIDERATIONS

Metabolism: Toltrazuril is rapidly and moderately well absorbed via the gastrointestinal tract. It is extensively metabolised by sulfoxidation of the trifluoromethyl-thio group to form sulfoxide and sulfones. Excretion is in faeces and urine, and is almost complete within 7 days.

Acute effects: Toltrazuril has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 3-month dietary studies in rats and dogs, there was anaemia and organ weight changes (testes, liver and kidney) at 4.2 mg/kg bw/day in rats and dogs; decreased prostate weights at 13.5 mg/kg bw/day in dogs; and decreased bodyweight gain and effects on the liver at 16.6 mg/kg bw/day in rats.

Long-term effects: Long-term dietary studies were conducted in mice and rats. In rats, there was an increased incidence of pre-neoplastic nodular changes in the uterus at 1 mg/kg bw/day and decreased bodyweight gain and increased uterine fluid and distension of the uterus at 3 mg/kg bw/day. In mice, anaemia was seen at 41 mg/kg bw/day. No other effects were seen. The LOEL of 1 mg/kg bw/day is the basis for the current ADI.

Carcinogenicity: There was an increase in pre-neoplastic lesions in the rat uterus at the lowest dose tested of 1 mg/kg bw/day and above. This dose level is well in excess of the likely level of human exposure. Uterine adenomas were observed at the next highest dose tested of 3 mg/kg bw/day and above.

Genotoxicity: Toltrazuril is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats reported evidence of maternotoxicity (decreased bodyweight gain) and pup toxicity (increased pup mortality and decreased bodyweight gain) at 4 mg/kg bw/day. A developmental toxicity study in rabbits reported maternotoxicity, and increased foetal death and abortion rates at 3 mg/kg bw/day, but no evidence of teratogenicity.

Poisons Schedule: Toltrazuril is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

NOTE: Important general information is contained in PART II, Chapter 6

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.004 mg/L for toltrazuril was determined as follows:

$$0.004 \text{ mg/L} = \frac{1 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 1 mg/kg bw/day is the LOEL based on a long-term (2-year) dietary study in rats, and is the NOEL from the reproduction study in rats and the developmental toxicity study in rabbits.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 1000 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation, with an additional safety factor of 10 to account for the uncertainty in the ADI, which is based on a LOEL for pre-neoplastic uterine lesions.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Tomlin CD (ed) (2006). *The Pesticide Manual: a world compendium*, 14th Edition, British Crop Production Council, UK.

Toluene [CASRN 108-88-3]

(endorsed 2013)

GUIDELINE

Based on aesthetic considerations (taste and odour), the concentration of toluene in drinking water should not exceed 0.025 mg/L.

Based on health considerations the concentration of toluene should not exceed 0.8 mg/L.

GENERAL DESCRIPTION

Toluene is a colourless liquid, which occurs naturally as a component of crude oil and is present in petrol. It constitutes approximately 5-8% of unleaded gasoline by volume. It can enter water sources through atmospheric deposition, by leaching from synthetic coatings used to protect storage tanks, and by point-source pollution.

Toluene, also known as methylbenzene is produced in large quantities during petroleum refining and is a byproduct in the manufacture of styrene and coke-oven preparations. Toluene is also used as solvent in paints adhesives and nail polish. It also occurs in natural gas and emissions from volcanoes, forest fires, and cigarettes.

Toluene has a taste and odour threshold at 0.025mg/L.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Toluene has only rarely been identified in Australian drinking waters. Natural concentrations in most water sources are usually very low. Toluene can occur naturally in groundwater as a result of proximity to, or contact with, coal seams, petroleum and gas deposits, and shales. It may be mobilised by extraction activities (Lesage *et al.*, 1997; Leusch and Bartkow, 2011; Volk *et al*, 2011). However, contamination can occur, usually via exposure to petrochemicals in surface waters or groundwaters. Known sources of groundwater contamination include leakage from sub-surface fuel storage tanks (do Rego & Netto, 2007). Emissions of fuel components from boating use is a known source of contamination of multiple-use lakes and reservoirs (Schmidt *et al.*, 2004). Toluene was reported in 19% of samples from an extensive groundwater survey undertaken in Denmark with the highest concentration being 0.002 mg/L (Juhler & Felding, 2003). Toluene has been detected in well water at 0.005 to 0.1 mg/L in the USA (IPCS, 1985). Groundwater from contaminated wells in the USA contained up to 3.5 mg/L of toluene (ATSDR, 2000). Toluene has been reported at up to 0.001 mg/L in municipal drinking water in Croatia (Karaconji *et al.*, 2006), up to 0.027 mg/L in Canada (average 0.002 mg/L; IPCS, 1985), up to 0.063 mg/L in municipal drinking water in Taiwan (Kuo *et al.*, 1997) and is occasionally detected in drinking waters in the USA (Williams *et al.*, 2004) up to 0.011 mg/L (IPCS, 1985).

TREATMENT OF DRINKING WATER

Volatile organic chemicals such as toluene are most commonly treated in drinking water by aeration stripping and/or adsorption to granular activated carbon (GAC). A conventional biologically active sand filter has been shown to be highly effective for the removal of toluene from contaminated water, under suitable conditions (Arvin *et al.*, 2004). Effective bioremediation of highly contaminated groundwaters has also been demonstrated (Sedran *et al.*, 2004; Zein *et al.*, 2006).

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for the analysis of toluene (APHA, AWWA & WEF, 2012). An inert gas is bubbled through the sample and toluene is trapped on an adsorbent. The adsorbent is then heated and toluene analysed using gas chromatography with mass spectrometric (GC-MS) detection (Method 6200 B) or photoionisation (PI) detection (Method 6200 C) (APHA, AWWA & WEF, 2012). The method detection limit is 47 ng/L for GC-MS and 23 ng/L for GC-PI (APHA, AWWA & WEF, 2012).

HEALTH CONSIDERATIONS

In humans, toluene is readily absorbed from the gastrointestinal tract after ingestion, and is distributed preferentially in adipose tissue, then the kidneys, liver and brain. It is rapidly metabolised by the liver to benzyl alcohol, benzoic acid, and to a lesser extent, phenols.

Data on human health effects come mainly from inhalation studies. The predominant effects of acute exposure were impairment of the central nervous system and irritation of the mucous membranes, with fatigue and drowsiness being the most obvious symptoms (ATSDR, 2000).

Rats exposed to toluene vapour for 2 years exhibited decreased blood haematocrit values at high toluene concentrations (380 ppm in air). No data are available on long term oral toxicity; however, a 13 week gavage study using rats and mice reported increased liver weights at doses from 625 mg/kg body weight per day (NTP 1990).

Toluene generally did not exhibit genotoxic activity in tests on bacteria, yeast cells, and mammalian cells in vitro.

The International Agency for Research on Cancer has concluded that toluene is not classifiable as to its carcinogenicity in humans (Group 3, inadequate evidence in humans and in animals) (IARC, 1989).

DERIVATION OF GUIDELINE

The USEPA (2009) has set a drinking water guideline of 1.0 mg/L for toluene, while the WHO (2011) proposes a guideline of 0.7 mg/L.

The health-based guideline value of 0.8 mg/L for toluene in drinking water was determined as follows:

$$0.8 \text{ mg/L} = \frac{312 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000} \times \frac{5}{7}$$

where:

- 312 mg/kg body weight per day is the no effect level based on a 13-week oral study using rats (NTP 1990)
- 70 kg is the average weight of an adult
- 0.1 is the proportion of total daily intake attributable to the consumption of water
- 2 L/day is the average amount of water consumed by an adult
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 because a less than lifetime study was used)
- 5/7 is used to convert data based on a 5 day per week gavage study to a 7-day week equivalent.

This health-based guideline value exceeds the taste threshold of toluene in water of 0.025 mg/L.

The WHO guideline value of 0.7 mg/L is based on an adult body weight of 60 kg. The difference in guideline values is not significant.

NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

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Total dissolved solids

(endorsed 2011)

GUIDELINE

No specific health guideline value is provided for total dissolved solids (TDS), as there are no health effects directly attributable to TDS. However for good palatability total dissolved solids in drinking water should not exceed 600 mg/L.

GENERAL DESCRIPTION

Total dissolved solids (TDS) consist of inorganic salts and small amounts of organic matter that are dissolved in water. Clay particles, colloidal iron and manganese oxides and silica, fine enough to pass through a 0.45 micron filter membrane can also contribute to total dissolved solids.

Total dissolved solids comprise: sodium, potassium, calcium, magnesium, chloride, sulfate, bicarbonate, carbonate, silica, organic matter, fluoride, iron, manganese, nitrate, nitrite and phosphates.

The palatability of drinking water can be rated according to TDS concentrations and a breakdown is provided below, based on World Health Organization guidelines (WHO 2004):

TDS (mg/L)	Palatability
0 – 600	good
600 – 900	fair
900 – 1200	poor
> 1200	unacceptable (unpalatable)

Precisely what level of TDS an individual water supply system decides to accept is a function of community acceptance, available water resources, and the cost and practicality of effecting any change to natural TDS levels.

High TDS values may be associated with excessive scaling in pipes, fittings and household appliances. Water with very high or very low TDS may also be corrosive.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian cities, TDS values can range from below 100 mg/L to more than 750 mg/L; regional supplies can have TDS values up to 1000 mg/L and some rural and remote communities may have TDS in excess of 1000 mg/L, owing mainly to groundwater characteristics.

MEASUREMENT

Three methods can be used to determine to determine TDS. The most accurate entails a complete analysis of the sample and summation of the concentration of all the anions and cations. The most common and least expensive method is to convert electrical conductivity measurements to TDS values by multiplication by a factor that varies with the type of water (APHA Method 2510A 1992). Gravimetric measurement (i.e. by evaporation and weighing) can also be used (APHA Method 2540C 1992). As a rough guide, electrical conductivity, measured in micro Siemens per cm ($\mu S.cm^{-1}$, also known as EC, or electroconductivity units), is multiplied by 0.64 to estimate TDS. The relationship, however, is dependant

on both chemistry and temperature, and factors of between 0.50 and 0.64 are used across Australia. The factor is also likely to vary between raw and treated water. Inferring a TDS value therefore has to be based on local circumstances.

TREATMENT OF DRINKING WATER

It is difficult to remove dissolved solids from drinking water. Suitable technologies include reverse osmosis, ion exchange, and distillation, but all of these require considerable energy input and can be expensive to operate. Lime softening may also be effective where high TDS is mainly due to hardness.

HEALTH CONSIDERATIONS

No health effects have been associated specifically with high TDS concentrations. The health effects of individual components of TDS are discussed separately in the discussions on inorganic chemicals (Section 6.3.1 and relevant Fact Sheets). Indirectly, high TDS water, being less palatable than that with a low TDS, might discourage consumers from drinking tap water, leading to use of potentially less healthy water (from alternative sources, natural or manufactured) and/or other less healthy drinks.

GUIDELINES IN OTHER COUNTRIES

The 2004 World Health Organization guidelines do not specify a value for TDS but do describe values according to palatability.

The European Communities (1998) Directive 98/83/EC nominates a conductivity value of 2500 $\mu S.cm^{-1}$ at 20ºC and, in a footnote, requires that the water not be aggressive. An online converter function (Lenntech 2010) converts that value to 1600 mg/L of TDS (the standard for EC is intended to be at 25ºC).

The United States Environmental Protection Agency nominates a TDS level of 500 mg/L in its list of National Secondary Drinking Water Regulations (USEPA 2009) and explains the category as follows:

> *National Secondary Drinking Water Regulations (NSDWRs or secondary standards) are non-enforceable guidelines regulating contaminants that may cause cosmetic effects (such as skin or tooth discoloration) or aesthetic effects (such as taste, odor, or color) in drinking water. EPA recommends secondary standards to water systems but does not require systems to comply. However, states may choose to adopt them as enforceable standards.*

The Federal-Provincial-Territorial Committee on Drinking Water of the Federal-Provincial-Territorial Committee on Health and the Environment (2008) provides Guidelines for Canadian Drinking Water Quality, and a TDS level of 500 mg/L is nominated as an “aesthetic objective”.

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NOTE: Important general information is contained in PART II, Chapter 6

Triadimefon

(endorsed 2011)

GUIDELINE

Based on human health concerns, triadimefon in drinking water should not exceed 0.09 mg/L.

RELATED CHEMICALS

Triadimefon (CAS 43121-43-3) belongs to the triazole class of chemicals. Another pesticide in this class is amitrole (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, triadimefon would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Triadimefon is a fungicide for the control of powdery mildews, rusts and other fungal diseases in turf and agricultural crops.

There are registered products that contain triadimefon in Australia. The products are intended for professional use and are available as wettable powders or concentrated solutions, to be applied as a diluted or concentrated spray using ground rig or aerial application, or added to fertilizer and applied using truck mounted equipment. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to triadimefon and its metabolites is residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of triadimefon may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of triadimefon in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

No specific data on the treatment of triadimefon in drinking water have been identified.

NOTE: Important general information is contained in PART II, Chapter 6

MEASUREMENT

Triadimefon can be measured in water using high performance liquid chromatography with tandem mass spectrometry (Schermerhorn *et al*. 2005). The limit of quantitation for this technique is 0.5 ng/L.

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for triadimefon is 0.03 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.5 mg/kg bw/day from a long-term rat dietary study. The NOEL is based on haematological effects. The ADI incorporates a safety factor of 100, and was established in 1987.

The previous health value was 0.002 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Triadimefon is readily and extensively absorbed via the gastrointestinal tract of mice and rats. It undergoes some metabolism in rats, and 80% is excreted in the urine and faeces in 7 days. Triadimenol was the major metabolite recovered.

Acute effects: Triadimefon has low to moderate acute oral toxicity and low dermal toxicity. It is not a skin sensitiser.

Short-term effects: A 1-month oral study in rats reported increased relative and absolute liver weights with no associated liver pathology at dose levels of 10 mg/kg bw/day and above.

Medium-term studies conducted in rats and dogs reported no toxicological effects up to doses of 100 mg/kg bw/day in rats, and hepatic enzyme induction at doses of 15 mg/kg bw/day and above in dogs. Pathological effects in the liver were not observed.

Long-term effects: Long-term dietary studies conducted in mice, rats and dogs reported liver toxicity and effects on haematological parameters to be the main toxicological effects. In mice, there was an increase in erythrocyte counts, haemoglobin and haematocrit concentrations, liver weights, and hyperplastic liver nodules (indicative of liver toxicity) at 90 mg/kg bw/day. In rats, decreased body weight gain and reduced erythrocyte counts and haemoglobin levels were observed at doses of 25 mg/kg bw/day and above. The NOEL of 2.5 mg/kg bw/day from this study forms the basis for the current ADI.

A 2-year dietary study in dogs reported reduced bodyweight gain and microsomal enzyme induction in the liver at doses of 25 mg/kg bw/day and above, with no pathological changes.

Carcinogenicity: Based on 2-year studies in mice, rats and dogs there is no evidence of carcinogenicity for triadimefon.

Genotoxicity: Only *in vitro* short-term studies were available, and these show no evidence of genotoxicity. No *in vivo* studies were conducted.

Reproductive and developmental effects: In 2- and 3-generation reproduction studies in rats, there was evidence of maternotoxicity and effects on reproductive parameters, but only at doses well in excess of the likely level of human exposure. Developmental studies in rats and rabbits did not produce any evidence of effects on foetal development.

Neurotoxicity: Neurological studies conducted in mice and rats reported no adverse effects up to doses of 3 mg/kg bw/day.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Triadimefon is included in Schedule 5 and 6 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010), depending on its concentration and use. Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.09 mg/L for triadimefon was determined as follows:

$$0.09 \text{ mg/L} = \frac{2.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.5 mg/kg bw/day is the NOEL based on a long-term (2-year) study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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Trichlorfon

(endorsed 2011)

GUIDELINE

Based on human health concerns, trichlorfon in drinking water should not exceed 0.007 mg/L.

RELATED CHEMICALS

Trichlorfon (CAS 52-68-6) belongs to the organophosphate class of chemicals. There are many other pesticides in this class, which includes dichlorvos, diazinon, and phorate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, trichlorfon would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Trichlorfon is used as an insecticide for the control of insect pests in home garden lawns, sports fields and agricultural crops, and as an acaricide for the control of parasites in livestock, and household and commercial aquariums.

There are registered products that contain trichlorfon in Australia. The products are intended for professional and home garden use. They are available as concentrated solutions to be diluted and applied by aerial and ground sprays to crops as an insecticide. When used as an acaricide, trichlorfon is supplied as pellets for addition to aquarium water, and as pellets or paste for oral drenching of livestock. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The potential sources of public exposure to trichlorfon and its metabolites are the use of home garden and aquarium products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of chemical may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater. When trichlorfon is added to water, it degrades to dichlorvos.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No reports of trichlorfon in Australian drinking waters have been identified.

TREATMENT OF DRINKING WATER

There is insufficient information on the treatment of trichlorfon in drinking water, but it is expected that advanced treatment methodologies such as ozonation and advanced oxidation would be effective.

MEASUREMENT

Several methods have been reported for the analysis of trichlorfon in water, including high performance liquid chromatography with ultraviolet detection, with a limit of detection (LOD) of 2.0 µg/L (Zhu *et al*. 2008); liquid chromatography with mass spectrometry-mass spectrometry, LOD 10 µg/L (Geiss *et al*. 2006); liquid chromatography with ionspray mass spectrometry, LOD 0.2 µg/L (Molina *et al*. 1996); and gas chromatography with mass spectrometry, LOD 0.73 µg/L (Molto *et al*. 1991).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for trichlorfon is 0.002 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.2 mg/kg bw/day 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, and was established in 1986.

The previous health value was 0.005 mg/L (NHMRC and NRMMC, 2004).

HEALTH CONSIDERATIONS

Metabolism: Triclorfon is extensively and rapidly absorbed from the gastrointestinal tract and distributed widely in the body. Under normal alkaline physiological conditions, it is converted to dichlorvos by a non-enzymatic process. Following metabolism, excretion is rapid, primarily via the urine, with a half-life of about 80 minutes.

Acute effects: Triclorfon has moderate acute oral toxicity and low acute dermal toxicity. It is a skin sensitiser in guinea pigs. Clinical symptoms of toxicity were typical of cholinesterase inhibition and included tremors, prostration, coma, piloerection, ataxia, and salivation.

Short-term effects: In short-term oral studies (12-26 weeks) in rats, dogs and monkeys, the most significant effect was on the nervous system, with cholinesterase depression reported at 10 mg/kg bw/day in rats and 1.25 mg/kg bw/day in dogs. A 12-week oral study in humans reported clinical signs of toxicity and cholinesterase depression at 0.2 mg/kg bw/day.

Long-term effects: In long-term dietary studies in rats, dogs and monkeys, the most significant effect was on the nervous system, with monkeys the most sensitive to cholinesterase depression, at 1 mg/kg bw/day. The NOEL was 0.2 mg/kg bw/day, and this is the basis of the ADI.

Carcinogenicity: Based on long-term studies in rats, there is no evidence of carcinogenicity for trichlorfon.

Genotoxicity: While positive in *in vitro* assays, the weight of evidence indicates that trichlorfon is not genotoxic *in vivo*.

Reproductive and developmental effects: Reproduction studies in rats and developmental studies in mice and rats did not show any evidence of effects on reproductive parameters or foetal development.

Neurotoxicity: There was no evidence of delayed neuropathy in chickens. Short-term neurotoxicity studies in rats, hens and monkeys, conducted with oral doses up to 200 mg/kg bw/day, confirmed that trichlorfon has an effect on the nervous system, with effects such as increased locomotor activity and decreased learning ability and nerve conduction velocity, impaired nerve conduction, demyelination of nerves and axonal degeneration observed at high doses.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Trichlorfon is included in Schedule 6 and in Schedule 4 (as metrifonate, for human therapeutic use) of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline value of 0.007 mg/L for trichlorfon was determined as follows:

$$0.007 \text{ mg/L} = \frac{0.2 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.2 mg/kg bw/day is the NOEL based on a long-term (10-year) dietary study in monkeys.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is a safety factor derived from a long-term study in monkeys. The safety factor of 100 incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variations..

The World Health Organization has not established a health-based guideline value for trichlorfon and it is excluded from the list of agricultural chemicals guideline value derivation because it is "unlikely to occur in drinking water" (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

Trichlorobenzenes
1,2,3-trichlorobenzene (1,2,3-TCB)
1,2,4-trichlorobenzene (1,2,4-TCB)
1,3,5-trichlorobenzene (1,3,5-TCB)

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (taste and odour), the concentration of trichlorobenzenes in drinking water, either individually or in total, should not exceed 0.005 mg/L.

Trichlorobenzenes would not be a health concern unless the concentration exceeded 0.03 mg/L.

GENERAL DESCRIPTION

Trichlorobenzenes are present in the environment mainly as a result of a variety of industrial processes. They have only occasionally been found in drinking water supplies overseas, and rarely above 0.001 mg/L. Food and air are the primary routes of exposure.

Taste and odour thresholds vary from 0.005 mg/L to 0.03 mg/L, depending on individual sensitivities and water temperature.

Industrial-grade TCB is more than 90% 1,2,4-TCB with the remainder 1,2,3-TCB. The compound has a wide variety of uses. It is used as a solvent for high-melting products, an electrical coolant, a lubricant and an insecticide, and in polyester dyeing and termiticide preparations.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

TCBs have not been found in Australian drinking waters. They are included here to provide guidance in the unlikely event of contamination, and because they have been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

The concentration of TCBs in drinking water can be reduced by adsorption onto granular activated carbon.

MEASUREMENT

TCBs can be analysed using a solvent extraction procedure (USEPA Method 612 1984). The TCBs are extracted using dichloromethane and analysed using gas chromatography with electron capture detection. The limit of determination for 1,2,4-TCB is 0.00005 mg/L (50 ng/L). The purge and trap method can also be used (USEPA Draft Method 502.1 1986).

HEALTH CONSIDERATIONS

The TCBs are readily absorbed from the gastrointestinal tract and distributed in fat, skin and the liver. In rats and rabbits the TCBs are metabolised into trichlorophenols and mercapturic acids.

An extensive review and summary of the human and animal toxicity data for chlorobenzenes is available (IPCS 1991).

There are very few studies on the effects of human exposure. TCBs have caused marked irritation of the

mucous membranes following inhalation over short periods of exposure. No data are available on the effects of long-term exposure.

Animal studies are of short-term duration. A 13-week study using rats reported that toxic effects of the three isomers were similar: low doses produced no adverse effects, but higher doses (77 mg/kg body weight per day) caused changes to the liver and thyroid.

No increase in the incidence of tumours was observed in longer-term animal studies. TCBs did not exhibit mutagenic activity in tests with bacteria.

DERIVATION OF GUIDELINE

As the three TCBs have similar toxic effects, the guideline value can be based on the total concentration of all the TCBs rather than on the individual compounds. The health-based guideline value for total TCBs in drinking water was determined as follows:

$$0.03 \text{ mg/L} = \frac{7.7 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 7.7 mg/kg body weight per day is the no-effect level from a 13-week dietary study using rats (Côté *et al*. 1988).
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for a less than lifetime study).

This health-based guideline value exceeds the taste and odour threshold of 0.005 mg/L.

The World Health Organization guideline value of 0.02 mg/L was based on an adult body weight of 60 kg. The difference in guideline values is not significant.

REFERENCES

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1,1,1-Trichloroethane

(endorsed 1996)

GUIDELINE

Data are inadequate to set a guideline value for 1,1,1-trichloroethane in drinking water.

GENERAL DESCRIPTION

1,1,1-Trichloroethane may be present in drinking water as a result of contamination from industrial discharges and spills. In the United States, 1,1,1-trichloroethane has occasionally been found in water supplies at concentrations ranging from 0.0002 mg/L to 0.02 mg/L.

It is widely used as a cleaning solvent, and is used to clean electrical equipment, motors, electronic components, printed circuit boards, photographic film, and various metal and plastic parts. It is also used as a lubricant in metal-cutting oils and as a component in inks, correction fluid and drain cleaners.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

1,1,1-Trichloroethane has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

1,1,1-Trichloroethane can be removed from drinking water by adsorption onto granular activated carbon, by aeration and by boiling. If aeration is used for removal, consideration should be given to effects associated with inhalation.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of 1,1,1-trichloroethane (USEPA Draft Method 551 1990). Sodium chloride is added to the sample and 1,1,1-trichloroethane extracted using methyl tert-butyl ether. The extract is then analysed using gas chromatography with an electron capture detector. The limit of determination is approximately 0.000008 mg/L (8 ng/L).

HEALTH CONSIDERATIONS

1,1,1-Trichloroethane is absorbed rapidly and efficiently from the human gastrointestinal tract and the lungs. It is metabolised to a very limited extent (probably less than 6%) by both humans and animals.

An extensive review and summary of the human and animal toxicity data for 1,1,1-trichloroethane is available (IPCS 1992).

Inhalation of high concentrations of 1,1,1-trichloroethane has proved fatal, causing acute congestion of the lungs, fluid build-up and fatty deposits in the liver.

In animals, long-term studies have reported diminished body-weight gains at high doses (above 350 mg/kg body weight) but data were insufficient to determine no-effect levels. Liver tumours were observed in mice, but not in rats, fed 1,1,1-trichloroethane for 2 years; however, the study reported a high number of accidental deaths in both the control and study groups, and the results may not be significant.

Mutagenic activity has been reported in tests with some strains of bacteria, but not others.

The International Agency for Research on Cancer has concluded that 1,1,1-trichloroethane is not classifiable as to its carcinogenicity in humans (Group 3, no adequate data in humans, inadequate evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The World Health Organization health-based guideline value of 2 mg/L was based on a short-term inhalation study. The data were not considered to be sufficient to set an Australian guideline.

REFERENCE

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NOTE: Important general information is contained in PART II, Chapter 6

Trichloroethylene (TCE)

(endorsed 1996)

GUIDELINE

Data are inadequate to set a guideline value for trichloroethylene in drinking water.

GENERAL DESCRIPTION

TCE may be present in drinking water as a result of direct contamination of water sources, or from atmospheric contamination of rainfall. In the United States, TCE has been detected in the water supplies of about 20% of cities tested, with mean concentrations of 0.02 mg/L or less.

TCE is used in cleaning fluids, as an industrial solvent and as a degreaser for metal components. The most significant route of exposure to humans is inhalation, particularly from use as a cleaning fluid.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

TCE has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

TCE can be removed from drinking water by aeration, or by adsorption onto granular activated carbon.

MEASUREMENT

A solvent extraction procedure is suitable for the analysis of TCE (USEPA Draft Method 551 1990). Sodium chloride is added to the sample and TCE extracted using methyl tert-butyl ether. The extract is then analysed using gas chromatography with an electron capture detector. The limit of determination is approximately 0.000002 mg/L (2 ng/L).

HEALTH CONSIDERATIONS

TCE is readily absorbed by all routes of exposure and distributed to all tissues. It is metabolised to reactive epoxides and the trichloro derivatives of acetaldehyde, ethanol and acetic acid.

An extensive review and summary of the human and animal toxicity data for trichloroethylene is available (IPCS 1985).

In humans, TCE is a known central nervous system depressant and has been used as a general anaesthetic. Liver damage has been reported in people occupationally exposed to high concentrations.

There is some evidence that TCE induces liver and lung tumours in various strains of mice. In an inhalation study, TCE produced a dose-related increase in malignant lymphomas in female mice exposed to 100 ppm or above in air. TCE is a weakly acting mutagen in bacteria and yeast.

The International Agency for Research on Cancer has concluded that TCE is not classifiable as to its carcinogenicity in humans (Group 3, inadequate evidence in humans and limited evidence in animals) (IARC 1987).

DERIVATION OF GUIDELINE

The World Health Organization health-based guideline value of 0.07 mg/L was based on a 6-week feeding study using mice which identified a low-effect level but not a no-effect level. No long-term studies are available to establish a no-effect level. The data were not considered to be sufficient to set an Australian guideline.

REFERENCES

IARC (International Agency for Research on Cancer) (1987). IARC Monographs on the Evaluation of Carcinogenic Risks to Humans: Overall Evaluations of Carcinogenicity. An updating of IARC monographs volumes 1 to 42. World Health Organization, IARC, Supplement 7.

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USEPA Draft Method 551 (1990). Determination of chlorination disinfection by-products and chlorinated solvents in drinking water by liquid–liquid extraction and gas chromatography with electron capture detection. United States Environmental Protection Agency, Environmental Monitoring and Support Laboratory (EMSL), Cincinnati, Ohio.

NOTE: Important general information is contained in PART II, Chapter 6

Triclopyr

(endorsed 2011)

GUIDELINE

Based on human health concerns, triclopyr in drinking water should not exceed 0.02 mg/L.

RELATED CHEMICALS

Triclopyr (CAS 55335-06-3) belongs to the pyridinecarboxylic acid class of chemicals. Other pesticides in this class include chlopyralid, fluroxypyr and picloram (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, triclopyr would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Triclopyr is a post-emergence herbicide for the control of woody and broad-leaf weeds in commercial and industrial areas, native pastures, right of ways, forests, fence lines and in the home garden.

There are registered products that contain triclopyr, its triethylamine salt or butoxyethyl ester in Australia. The products are intended for professional and/or home garden use. Products are available as a concentrated solution to be applied directly to weeds as a dilute spray by hand-held, mistblower, boom and aerial application methods. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main source of public exposure to triclopyr and its metabolites is the use of home garden products. A further possible source of exposure is residues in food from livestock grazing in treated areas. Residue levels in food produced according to good agricultural practice are generally low.

Commercial use of triclopyr may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

REPORTED VALUES IN AUSTRALIAN WATERS

No data on occurrence of triclopyr in Australian waters could be found. In the USA, the United States Environmental Protection Agency predicts that triclopyr will not reach high concentrations in groundwater, and concludes that it is not a concern in drinking water that is derived from groundwater. Triclopyr is also not expected to be present in significant concentrations in surface water due to its quick degradation (USEPA 1998).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No information could be found on the efficiency of drinking water treatment processes in removing triclopyr.

MEASUREMENT

Triclopyr can be measured by routine gas chromatography with mass spectrometry analysis, with a limit of reporting of 0.01 µg/L (Queensland Health 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for triclopyr is 0.005 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 0.5 mg/kg bw/day 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 and was established in 1986.

The previous health value was 0.01 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Triclopyr is readily and extensively absorbed via the gastrointestinal tract in animals and humans. It is not extensively metabolised, and the majority of the dose is excreted unchanged in the urine within 72 hours.

Acute effects: Triclopyr has moderate acute oral toxicity and low acute dermal toxicity. It is a skin sensitiser.

Short-term effects: Short-term dietary studies conducted in mice, rats and dogs reported the kidney to be the most sensitive target organ. Studies in mice and rats reported changes in relative kidney weights together with histopathological changes in the kidney at doses of 20 mg/kg bw/day and above. At 70 mg/kg bw/day in rats, there was an increase in relative liver weights and decreased bodyweight gain, as well as some evidence of necrosis of hepatocytes. In dogs, there was evidence of decreased renal function at doses of 2.5 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies conducted in mice, rats and dogs reported the liver and kidneys to be the main target organs. A 2-year study in mice reported decreased bodyweight gain, and clinical chemistry changes indicative of kidney and liver damage, together with histopathological effects in the bladder, liver and kidneys, at doses of 25.5 mg/kg bw/day and above.

A 2-year study in rats reported increased absolute and relative kidney weights and histopathological effects in the kidney at doses of 12 mg/kg bw/day and above.

A 1-year dog study reported evidence of decreased renal function together with histopathological changes in the kidney at doses of 2.5 mg/kg bw/day and above. The NOEL from this study was 0.5 mg/kg bw/day and this is the basis of the current ADI.

Carcinogenicity: Based on long-term studies in mice, rats and dogs, there is no evidence of carcinogenicity for triclopyr.

Genotoxicity: Triclopyr is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: Two and three-generation reproductive studies in rats and developmental studies in rats and rabbits did not produce any evidence of effects on reproductive parameters or foetal development, other than maternal toxicity at high dose levels that were well in excess of the likely level of human exposure.

Poisons Schedule: Triclopyr is included in Schedule 6 of the *Standard for the Uniform Scheduling of*

NOTE: Important general information is contained in PART II, Chapter 6

Medicines and Poisons No.1, 2010 (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.02 mg/L for triclopyr was determined as follows:

$$0.02 \text{ mg/L} = \frac{0.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 0.5 mg/kg bw/day is the NOEL based on a long-term (1-year) study in dogs.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

Trifluralin

(endorsed 2011)

GUIDELINE

Based on human health concerns, trifluralin in drinking water should not exceed 0.09 mg/L.

RELATED CHEMICALS

Trifluralin (trifluraline)(CAS 1582-09-8) belongs to the dinitroaniline class of chemicals. Other pesticides in this class include oryzalin and pendimethalin (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, trifluralin would not be a health concern unless the concentration exceeded 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.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Trifluralin is a pre-emergent herbicide for the control of ryegrass, wireweed, and yellow burr weeds in cereal, legume, herb, and vegetable crops, and for the control of garden weeds in domestic settings.

There are registered products containing trifluralin in Australia. The products are intended for professional and home garden use. Use patterns include application to soil by ground boom spray in agricultural settings and by hand-held spray for home gardens. Data on currently registered products are available from the Australian Pesticides and Veterinary Medicines Authority.

Exposure sources: The main sources of public exposure to trifluralin and its metabolites are the use of home garden weedkiller products, and residues in food. Residue levels in food produced according to good agricultural practice are generally low.

Agricultural use of trifluralin may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Trifluralin has low solubility in water and generally is not detected in surface water. It is unlikely to leach into groundwater supplies, given its low solubility and strong soil adsorption (Health Canada 1989). Trifluralin has been detected very occasionally in drinking water supplies in Australia at concentrations well below the health-based guideline value. It was reported above 1 µg/L in 0.2% of the samples taken in the Murray-Darling Basin (NSW 1998/99 data) (NSW Department of Primary Industries 2005).

In the USA, trifluralin was found in 172 of 2047 surface water samples and in 1 of 507 groundwater samples analysed, but was not found in 229 drinking-water supplies analysed in Italy (WHO 1996). It was detected at low concentrations (ng/L) in raw drinking water samples and in 1 of 91 groundwater samples (41 µg/L) in Canada (Health Canada 1989).

TREATMENT OF DRINKING WATER

Trifluralin is efficiently removed (100% effectiveness) by conventional treatment using alum, sedimentation and filtration. In addition, it may be removed from drinking water by reverse osmosis, granular activated carbon and air stripping (Health Canada 1989, Ormad *et al.* 2008).

MEASUREMENT

Trifluralin can be analysed in water by solvent extraction or by solid phase extraction. Quantification is performed by gas chromatography with electron capture detection (GC-ECD); gas chromatography with mass spectrometry (GC-MS) or liquid chromatography (LC) with ultraviolet detection. The limit of detection (LOD) is 0.01µg/L (Van Hoof *et al.* 2001, Carabias-Martinez *et al.* 2003). Direct injection liquid chromatography–mass spectrometry or online solid phase microextraction liquid chromatography with mass spectrometry can achieve a lower LOD. The GC-ECD-GCMS United States Environmental Protection Agency method 3510/8080 can achieve a LOD of 0.1 µg/L (Queensland Government 2007).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for trifluralin is 0.02 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 2.5 mg/kg bw/day from a 2-generation study in rats. The NOEL is based on decreased foetal and parental weights. The ADI incorporates a safety factor of 100, and was established in 1991.

The previous health value was 0.05 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Trifluralin is poorly absorbed via the gastrointestinal tract and the majority is excreted unchanged in the faeces. Absorbed trifluralin is eliminated as metabolites in urine within three days. The primary metabolites are dealkylated and hydrogenated compounds.

Acute effects: Trifluralin has low acute oral and dermal toxicity. It has some potential for skin sensitisation.

Short-term effects: In a 3-month dietary study in rats born from mothers pre-treated with oral doses of trifluralin, bodyweights were decreased and relative liver weights were increased at 100 mg/kg bw/day. In a 4-month dietary study in rats, effects on the kidney were seen at the lowest dose, 20 mg/kg bw/day and above.

Long-term effects: Long-term dietary studies in rats reported liver weight changes and tissue irritation in the kidney at 33.5 mg/kg bw/day.

Carcinogenicity: Kidney tumours were noted in rats at high dose levels as a result of persistent tissue irritation. This effect was not considered relevant to humans at the normal low levels of exposure.

Genotoxicity: Trifluralin is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: In three reproduction studies in rats (2-3 generations), there was reduced fertility and reduced neonatal viability at dose levels above 2.5 mg/kg bw/day. In developmental studies in rats and rabbits, there was no evidence of effects on foetal development. The NOEL of 2.5 mg/kg bw/day is the basis for the ADI.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Trifluralin is considered not to require control by scheduling due to its low toxicity and is therefore in Appendix B of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.09 mg/L for trifluralin was determined as follows:

$$0.09 \text{ mg/L} = \frac{2.5 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 2.5 mg/kg bw/day is the NOEL based on a 2-generation reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the conservative assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

The World Health Organization has a Guideline value of 0.02 mg/L for trifluralin (WHO 2004).

REFERENCES

NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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Trihalomethanes (THMs)
trichloromethane (chloroform)
bromodichloromethane
dibromochloromethane
tribromomethane (bromoform)

(endorsed 1996)

GUIDELINE

Based on health considerations, the concentration of trihalomethanes, either individually or in total, in drinking water should not exceed 0.25 mg/L.

Trihalomethane concentrations fluctuating occasionally (for a day or two annually) up to 1 mg/L are unlikely to pose a significant health risk.

Action to reduce THMs is encouraged, but must not compromise disinfection, as nondisinfected water poses significantly greater risk than THMs.

GENERAL DESCRIPTION

In Australia, trihalomethanes are present in drinking water principally as the result of disinfection using chlorination or, to a much lesser extent, chloramination. Chlorine, which produces hypochlorous acid when added to water, can react with naturally occurring organic material, such as humic and fulvic acids, to produce trihalomethanes. The brominated trihalomethanes are produced by the oxidation of bromide present in water to form hypobromous acid, which can then react with organic matter in a similar way.

High trihalomethane concentrations may indicate the presence of other chlorination by-products.

Chloroform is produced commercially and is an important solvent. It is used in the manufacture of refrigerants, and as an ingredient in pharmaceutical and cosmetic preparations. Brominated trihalomethanes are also produced industrially, but less commonly than chloroform.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies concentrations of total trihalomethanes range up to 0.6 mg/L.

LIMITING PRESENCE IN DRINKING WATER

The concentration of trihalomethanes can be minimised by removing precursors, by removing trihalomethanes after formation, or by using alternative disinfectants. Precursors can be removed by activated carbon, by coagulation followed with filtration, or by oxidation with ozone or potassium permanganate. Once produced, trihalomethanes can be removed with air stripping or adsorption onto granular activated carbon. Alternative disinfection agents to chlorine, such as chloramines, ozone and chlorine dioxide, can substantially reduce trihalomethane concentrations, but may produce other by-products.

MEASUREMENT

There are a number of methods available for the analysis of trihalomethanes, including head-space analysis, solvent extraction, purge and trap, and direct collection on resins. The solvent extraction procedure is relatively simple to use (USEPA Draft Method 551 1990). Sodium chloride is added to the sample and the trihalomethanes extracted using methyl tert-butyl ether. The extracts are then analysed

using gas chromatography with electron capture detection. Limits of determination are 0.00002 mg/L (20 ng/L) or less.

HEALTH CONSIDERATIONS

The trihalomethanes are rapidly and efficiently absorbed following ingestion. They are metabolised primarily to carbon dioxide and/or carbon monoxide, and rapidly exhaled. They are fat soluble, and accumulate in tissues with the highest lipid content (such as adipose tissue, brain, kidney and blood).

In animals, the trihalomethanes are central nervous system depressants and liver and kidney toxicants. Chloroform and bromoform are also known to cause central nervous system depression in humans.

Some epidemiological studies have reported associations between the ingestion of chlorinated drinking water (which typically contains THMs) and increased cancer mortality rates. The International Agency for Research on Cancer has concluded that the available data for chlorinated water provide inadequate evidence of carcinogenicity in humans (Group 3, inadequate evidence in humans and limited evidence in animals) (IARC 1991).

Long-term carcinogenicity bioassays with animals have shown that trihalomethanes can produce tumours in rats and mice, but only at doses that are toxic to the animals. Chloroform increased the incidence of liver tumours in mice when administered in food at doses from 25 mg/kg body weight per day, but not in drinking water at the same doses, and has induced kidney tumours in male rats at doses from 263 mg/kg body weight per day. Dibromochloromethane, given by gavage 5 days per week, clearly induced liver tumours in female mice at 100 mg/kg body weight per day, and possibly in male mice, but not in rats. Bromodichloromethane, given by gavage 5 days per week, induced kidney tumours in rats at 100 mg/kg body weight, and in male mice at 50 mg/kg body weight; a rare tumour of the large intestine in male rats at doses of 50 and 100 mg/kg body weight; and liver tumours in female mice at 75 and 150 mg/kg body weight. Bromoform induced a small increase in relatively rare tumours of the large intestine in rats at a gavage dose of 200 mg/kg body weight per day, but not in mice.

Results of studies on the genotoxicity of trihalomethanes in bacteria have been inconsistent, with most reporting negative results. Trihalomethanes have, however, induced chromosomal aberrations in human lymphocyte cells *in vitro*, and in mouse bone-marrow cells *in vivo*.

Available studies indicate that THMs can produce maternal and foetal toxicity at high doses, but not teratogenicity.

The International Agency for Research on Cancer has concluded that chloroform and bromodichloromethane are possibly carcinogenic to humans (Group 2B, inadequate evidence in humans but sufficient evidence in animals); and that bromoform and dibromochloromethane are not classifiable as to their carcinogenicity to humans (Group 3, inadequate evidence in humans and limited evidence in animals)(IARC 1991).

DERIVATION OF GUIDELINE

The guideline value for trihalomethanes in drinking water was determined as follows:

$$0.25 \text{ mg/L} = \frac{7 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 7 mg/kg body weight per day is the no-effect level based on a 90-day study using rats (Chu *et al*. 1982). The use of this value was recommended by the NHMRC Standing Committee on Toxicity following a review of the available toxicity data for THMs.
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water. A higher value was not used because exposure to chloroform from other sources may be significant.
- 2 L/day is the average amount of water consumed by an adult.
- 100 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations and 10 for intraspecies variations). An additional safety factor for the less than lifetime study was not applied as long-term studies have reported the same effects, and no other forms of toxicity were observed. In addition, the changes observed to the liver at higher doses were mild in nature and disappeared when exposure stopped. The use of this safety factor was recommended by the NHMRC Standing Committee on Toxicity.

Separate guideline values were not derived for each compound as the no-effect levels were similar (ranging from 6.5 to 7.8 mg/kg body weight per day), and the compounds are metabolised in the body in similar ways. The guideline value should therefore apply to the concentration of each compound, or the sum of any combination of individual THM concentrations.

The World Health Organization (WHO) has derived separate guideline values for each compound, but in doing so recognises that the compounds have similar toxicological action.

The WHO guideline values for chloroform (0.2 mg/L) and bromodichloromethane (0.06 mg/L) were based on calculations that estimated additional lifetime risks of one fatal cancer per 100,000 people. The use of this approach is questionable because there is evidence that tumours do not occur at low concentrations.

The WHO guideline values for bromoform (0.1 mg/L) and dibromochloromethane (0.1 mg/L) were based on different studies and safety factors from those recommended by the NHMRC Standing Committee on Toxicity, although toxicological effects were similar.

It is recommended that future reviews of the Guidelines consider the various THMs individually, as data are emerging that suggest the different THMs have different toxic effects. Data were not sufficient at the time of this review to justify individual assessments

In view of the safety factors used in the derivation of the guideline value, it is unlikely that short-term consumption of water containing significantly higher concentrations of trihalomethanes would pose a health risk.

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NOTE: Important general information is contained in PART II, Chapter 6

NOTE: Important general information is contained in PART II, Chapter 6

Turbidity

(endorsed 2011)

GUIDELINE

Chlorine-resistant pathogen reduction: Where filtration alone is used as the water treatment process to address identified risks from Cryptosporidium and Giardia, it is essential that filtration is optimised and consequently the target for the turbidity of water leaving individual filters should be less than 0.2 NTU, and should not exceed 0.5 NTU at any time

Disinfection: A turbidity of less than 1 NTU is desirable at the time of disinfection with chlorine unless a higher value can be validated in a specific context.

Aesthetic: Based on aesthetic considerations, the turbidity should not exceed 5 NTU at the consumer's tap.

GENERAL DESCRIPTION

Turbidity is a measure of the light-scattering property of water caused by the presence of fine suspended matter such as clay, silt, plankton and other microscopic organisms. The degree of scattering depends on the amount, size and composition of the suspended matter. At low levels, turbidity can only be detected by instruments, but at higher levels the water has a "muddy" or "milky" appearance clearly visible to the naked eye. As a guide, water with a turbidity of 5 Nephelometric Turbidity Units (NTU) appears slightly muddy or milky in a glass, while at >60 NTU, it is not possible to see through the water. "Crystal-clear" water usually has a turbidity of less than 1 NTU.

There are three distinct aspects to turbidity to be considered within the catchment-to-consumer risk management framework:

- the use of turbidity as a measure to provide assurance of the optimal operation of filter performance, where filtration is used to address identified risks associated with chlorine-resistant pathogens in the source water;
- the impact of turbidity on the efficiency of disinfection processes;
- the effect that turbidity has on the aesthetics of the treated water.

MEASUREMENT

For laboratory-based analyses, the ration-recording nephelometroc turbidity meter is the preferred method for turbidity meanreument, as it can compensate for the effect of dissolved colour. Results are expressed in NTU and are calibrated against a prepared formazin standard (APHA 2130B, 2005). The detection limit is about 0.1 NTU.

When using turbidity for accurate monitoring of filter performance (i.e. where filtration is the only water treatment process to remove chlorine-resistant pathogens), it is recommended that on-line, continuously reading turbidity meters be installed on the outlet of each individual filter in addition to any on-line turbidity meter that is installed on the combined filter outlet. It is prudent to have the turbidity meter outputs linked into plant SCADA and/or alarm systems, to ensure that immediate action is taken in response to the detection of filtered water turbidity above the set target. This intensity or operational monitoring is strongly recommended to ensure that any performance issues related to individual filters are detected and addressed proactively (USEPA 2004, Mosse 2009). Particle counting facilities are used for the same purpose of filter optimisation but the results are too dependent on the actual equipment used and their mode of operation to provide general guidance in the same context as for tubidity.

While real-time monitoring of the turbidity trends generated from the on-line instruments is crucial in determining the instantaneous performance of the plant, and therefore the safety of the water, longer-term monitoring is beneficial to demonstrate the need for continuous improvement and maintenance activities such as filter inspections, optimised backwash and other process procedures.

TREATMENT OF DRINKING WATER

Pathogen reduction

Chlorine-based disinfection is only effective against bacterial and most viral, pathogens. At the doses typically applied in water treatment, chlorine is not effective against the protozoan pathogen *Cryptosporidium* and only has a limited effect on *Giardia* in the absence of large filtered water storages to provide adequate contact time for effective disinfection. *Cryptosporidium* oocysts are quite small (4-6 µm) and will pass readily through a conventional media filter in the absence of effective coagulation and flocculation. Filtration combined with effective coagulation, flocculation and clarification can be used as a barrier for *Cryptosporidium* and other protozoan pathogens. In many cases, coagulation-assisted clarification and filtration may be the only existing treatment barrier to protozoan pathogens.

In the absence of reliable real-time pathogen detection methodologies, continuous turbidity monitoring is considered the best available surrogate for assessing filter performance.

Many studies have investigated the relationship between pre-treatment turbidity, turbidity reduction (or particle removal) via filtration, and pathogen reduction. It has been demonstrated in pilot scale trials that a change in filter effluent turbidity from 1.0 through 0.5 to 0.3 NTU would not significantly improve the reliability of pathogen control. However, by setting filter effluent turbidity goals below 0.2 NTU, significant improvements in microbial quality could be obtained (Xagoraraki *et al.* 2004). The USEPA identified that turbidity limits of 0.15 NTU from individual filters with an upper limit of 0.3 NTU provided a substantial improvement in removal of *Cryptosporidium* compared to its previous limits of 0.3 NTU, with an upper limit of 1 NTU (USEPA 2006).

Targets for filtered water turbidity should be based on the pathogen risks in the raw water; for example, surface run-off from a catchment with significant sewage inputs or dairy farms would have tighter turbidity targets than a catchment without such impacts. Therefore, when setting turbidity targets for filtered water, raw water quality and treatment capabilities need to be aligned to manage any potential health risks. The United States Environmental Protection *Agency Long Term 2 Enhanced Surface Water Treatment Rule* (USEPA 2006) and the *Drinking-water Standards for New Zealand* (NZ-MOH 2008) directly relate raw water quality to the setting of filtered water turbidity targets.

Where a given water supply system risk assessment identifies a significant risk associated with protozoan pathogens, and a high level of operational monitoring of turbidity and any associated adjustment or maintenance of coagulation, flocculation, clarification and filtration processes or facilities are not considered practical, then alternative processes (e.g. ultraviolet radiation disinfection) may need to be applied to ensure the identified risk is adequately addressed.

Catchment management and source protection can be good enough to obviate the need for water treatment to remove and/or inactive protozoan pathogens. Exclusion of contamination from humans and domesticated animals in run-off from catchments and source areas generally leads to only minimal risk from protozoan pathogens in the Australian context, and specific treatment to remove protozoa is not required. In many cases, however, catchments and sources are not sufficiently managed and protected to ensure safe drinking water without additional treatment.

NOTE: Important general information is contained in PART II, Chapter 6

Where water is harvested from partly protected catchments and sources with a relatively low level of contamination, protozoan pathogens can be removed adequately by conventional treatment alone. Conventional treatment involves the addition of coagulants, removal of solids using clarifiers such as sedimentation, solids contact or dissolved air floatation, and removal of the remaining solids in clarified water in media filters, followed by chlorine-based disinfection. Such treatment is widely used and technically capable of reducing turbidity to below 0.2 NTU but requires close operator attention and continuous monitoring as discussed above.

Where water is harvested from sources with significant risks of contamination with protozoan pathogens, filtration to 0.2 NTU alone may not reduce the risk from protozoan pathogens to acceptable levels. Other treatment, such as membrane filtration, or disinfection by ultraviolet radiation or ozonation, may be needed.

In most cases, the turbidity of the filtered water during ripening periods after filter backwash, may exceed 0.3 NTU. It is considered best practice to limit these short spikes in turbidity to no longer than 15 minutes. Spikes above 0.3 NTU represent periods of increased risk, and appropriate risk management practices should be employed, such as rejecting ripening water to waste or optimising filter backwash processes.

Turbidity added after treatment can arise from the use of lime to raise the final pH of the water. This turbidity is unlikely to have an associated pathogen risk.

Disinfection

High turbidity has been shown to shield microorganisms from the action of disinfectants (Katz 1986). Low turbidity, however, is no guarantee that water is free from pathogenic microorganisms.

If the turbidity in a water supply exceeds 1 NTU, adequate disinfection may be more difficult to maintain, but may nevertheless be achievable.

Where water that is to be disinfected has not been previously filtered, it is desirable that the turbidity be less than 1 NTU at the time of disinfection, subject to the type of disinfectant being used. For example, disinfection using ultraviolet light is likely to remain effective at turbidities above 1 NTU, providing transmission is maintained, whereas the effectiveness of chlorine-based disinfectant can be affected above 1 NTU.

If water of a higher turbidity is to be disinfected, then validation work should be undertaken to demonstrate that disinfection of water under such conditions is effective.

Disinfection is discussed in more detail in Information Sheet 1 Disinfection of drinking water.

Aesthetics

Turbidity has an impact on the aesthetic acceptability of water. Many consumers relate the appearance of water to its safety, and turbid or coloured water is interpreted as being unsafe to drink. Turbidity must therefore be maintained as low as possible to the point of supply to customers.

Passage of water through a distribution system can also lead to an increase in turbidity, generally as a result of the resuspension of fine sediments settled over a long period of time, or from the breakdown of pipe materials or biofilms lining the walls of the pipes. While the associated health risk is generally minimal, it may be significant in poorly maintained systems, as some biofilms are known to harbour living microorganisms. Therefore turbidity in the distribution system can be also used as an indicator of good distribution management practices.

NOTE: Important general information is contained in PART II, Chapter 6

HEALTH CONSIDERATIONS

Consumption of highly turbid waters is not necessarily a health hazard, but may constitute a health risk if the suspended particles harbour pathogenic microorganisms capable of causing disease in humans, or if the particles have adsorbed toxic organic or inorganic compounds.

For a treatment system designed for chlorine-resistant pathogen reduction via filtration only, detection of increases in the turbidity of filtered water above 0.5 NTU should trigger investigative action. Major filtration failures should referred to the relevant health authority or regulator to assess the potential health risk.

Turbidity can have a significant impact on the microbiological quality of drinking water. High turbidity interferes with both the detection and the disinfection of pathogens, by adsorbing them into the particulate matter and thus shielding them. Some turbidity may also promote bacterial growth if they provide a source of nutrients.

It is important to recognise the sources of suspended or particulate matter in water, and the potential associated risks to human health. Particulate matter from multi-use surface catchments often contains human pathogens. The poor management of turbid water events is a significant factor in many waterborne disease outbreaks (Hrudey and Hrudey 2004).

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NOTE: Important general information is contained in PART II, Chapter 6

Uranium

(updated 2022)

GUIDELINE

Based on health considerations, the concentration of uranium in drinking water should not exceed the health-based guideline value of 0.02 mg/L. This health-based guideline value is based on chemical toxicity. The chemical toxicity of uranium is more restrictive than its radiological toxicity.

GENERAL DESCRIPTION

Uranium may be present in the environment as a result of leaching from soils, rocks and natural deposits. It can be released from mining and mill tailings, from the combustion of coal and other fuels, and from the production or use of phosphate fertilizers (which can contain as much as 150 mg/kg uranium). Naturally occurring uranium is a mixture of three radionuclides: uranium-238, uranium-234 and uranium-235. Uranium-238 and uranium-234 decay predominantly by alpha particle emission, whereas uranium-235 emits both gamma rays and alpha particles. Natural uranium consists almost entirely of the uranium-238 isotope. The other two isotopes are less than 1% abundant.

Studies overseas have reported uranium concentrations in drinking water of generally less than 0.001 mg/L; however, concentrations as high as 0.7 mg/L have been reported in some private water supplies in Canada (Moss *et al.* 1983).

Food is the major source of uranium intake and the highest concentrations are typically found in shellfish (UNSCEAR 2000). Dietary intake of uranium through food is estimated between 0.001 and 0.004 mg/day (WHO 2004). Intake through drinking water is normally low; however, drinking water can contribute the majority of daily intake in circumstances where uranium is present at higher concentrations in drinking water (WHO 2004).

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In most Australian drinking water supplies uranium concentrations are well below 0.02 mg /L. However, concentrations up to 0.12 mg/L have been recorded in some groundwater supplies in remote areas.

Studies of Australian drinking water supplies have shown that generally uranium levels are below 50 mBq/L (0.004 mg/L). However, for some groundwater samples levels may be close to 1 Bq/L (0.08 mg/L) (ARPANSA 2008, Kleinschmidt *et al.* 2011, Walsh *et al.* 2014).

TREATMENT OF DRINKING WATER

Conventional treatment processes are not effective in removing uranium from water supplies. Some laboratory or pilot scale studies have found that coagulation using ferric sulfate at optimal pH dosages can achieve 80–95% removal of uranium, whereas at least 99% removal can be achieved using lime softening, anion exchange resin or reverse osmosis processes (WHO 2004).

MEASUREMENT

The concentration of uranium in water can be determined using solid fluorimetry with laser excitation (Blanchard *et al.* 1985), or inductively coupled plasma mass spectrometry (Boomer *et al.* 1987). The limit of determination is about 0.0001 mg/L.

The isotopes of uranium can be determined by radiochemical techniques using high resolution alpha spectrometry to measure their activity (APHA 2017, ISO 2014). The limit of determination is approximately 0.5 mBq/L (equivalent to approximately 0.00004 mg/L uranium).

HEALTH CONSIDERATIONS

The toxicity of uranium has been reviewed by the World Health Organization (WHO 2004), the Swedish National Food Administration (Svensson *et al.* 2005), the United Kingdom Committee on Toxicity (COT 2006) and Health Canada (Health Canada 2001).

Average absorption of dietary uranium by the gastrointestinal tract is 1-2%, but may be as low as 0.1% or as high as 5-6% depending on the solubility of the uranium compound ingested. Uranium rapidly appears in the bloodstream and is primarily associated with red blood cells. Uranyl compounds readily combine with proteins and nucleotides to form stable complexes. Clearance of uranium from the blood is rapid but it accumulates in the kidney and bone, with little in the liver. Once equilibrium in the skeleton has occurred, uranium is excreted in the urine and faeces. The half-life of uranium in rat and rabbit kidney is of the order of 5–15 days, but in bone it is 100–300 days (Health Canada 2001).

In humans and experimental animals, the main toxic effect of short-term exposure to high concentrations of uranium is inflammation of the kidney. Little information is available on the effects of long-term exposure to low concentrations. Epidemiological studies report increases in urinary markers of possible kidney proximal tubule damage at drinking water concentrations between 0.1 and 1 mg/L, but not at lower concentrations (Moss *et al.* 1983, Mao *et al.* 1995, Zamora *et al.* 1998, Kurttio *et al.* 2002, Kurttio *et al.* 2006, Seldén *et al.* 2009, Magdo *et al.* 2007).

A tolerable daily intake (TDI) of 0.0006 mg per kg bodyweight (mg/kg bw) has been derived by WHO (2004) and Health Canada (2001). This is based on a lowest-observed-adverse-effect level (LOAEL) of between 0.06 (males) and 0.09 (females) mg/kg bw/day in a 91-day rat drinking water study (Gilman *et al.* 1998) and application of an uncertainty factor of 100 (10 for interspecies extrapolation and 10 for intraspecies variation). The critical effect was degenerative kidney lesions, noted by the authors as not being severe. Although these represented a clear adverse effect, they were not dose-related. In addition, because the effects were minimal, it is considered that the dose at which they occurred may be close to the no-observed-adverse-effect level (NOAEL) (WHO 2004, COT 2006, Health Canada 2001). Thus an uncertainty factor to extrapolate from a LOAEL to a NOAEL was not applied in the derivation of the TDI.

No data are available on chemically induced mutagenic effects in relation to uranium.

Studies have shown high specific activity uranium isotopes to be carcinogenic in animals, causing malignant tumours in mice and bone sarcomas in rats. Similar studies using natural uranium (uranium-238) have not shown similar effects, possibly due to the lower radiation doses involved. Epidemiological data are inadequate to show whether exposure to uranium in drinking water will lead to an increased risk of cancer.

DERIVATION OF GUIDELINE

i) From chemical toxicity data:

The health-based guideline value for uranium in drinking water of 0.02 mg/L was set from chemical toxicity data as follows:

$$0.02 \text{ mg/L} = \frac{0.0006 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.8}{2 \text{ L/day}}$$

NOTE: Important general information is contained in PART II, Chapter 6

where:

- 0.0006 mg/kg bodyweight/day is the TDI (WHO 2004, Health Canada 2001).
- 70 kg is taken as the average weight of an adult.
- 0.8 is a proportionality factor based on a conservative assumption that 80% of total daily intake may be attributable to the consumption of water (WHO 2004).
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- The calculated value of 0.0168 mg/L is rounded to a final health-based guideline value of 0.02 mg/L as per the rounding conventions described in Chapter 6. The difference is not significant.

ii) From radiological data:

$$3.0 \text{ Bq/L} = \frac{0.1 \text{ mSv /year}}{730 \text{ L/year} \times 4.5 \times 10^{-5} \text{ mSv/Bq}}$$

where:

- 0.1 mSv/year is one tenth of the reference level for dose of 1 mSv/year.
- 730 L/year is the estimated maximum amount of water consumed by an adult (2 L/day x 365 days).
- 4.5×10^{-5} mSv/Bq is the committed effective dose received per unit intake of uranium-238 activity (Bq) (ICRP 2012).

iii) Comparing the chemical and radiological data:

The health-based guideline value of 0.02 mg/L is equivalent to an activity concentration of 0.2Bq/L. This indicates that the health-based guideline value based on chemical toxicity is considerably more restrictive than one based on radiological data. If uranium needs to be considered with regard to radiological dose, refer to Chapter 7, Section 7.6.2 for information on the calculation of dose.

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NOTE: Important general information is contained in PART II, Chapter 6

Vernolate

(endorsed 2011)

GUIDELINE

Based on human health concerns, vernolate in drinking water should not exceed 0.04 mg/L.

RELATED CHEMICALS

Vernolate (CAS 1929-77-7) belongs to the thiocarbamate class of chemicals. Other pesticides in this class include EPTC, molinate, and pebulate (Tomlin 2006).

HUMAN RISK STATEMENT

With good water quality management practices, the exposure of the general population is expected to be well below levels that may cause health concerns.

If present in drinking water as a result of a spillage or through misuse, vernolate would not be a health concern unless the concentration exceeded 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 medium- to long-term effects.

With good water quality management practices, pesticides should not be detected in source waters used for drinking water supplies. Persistent detection of pesticides may indicate inappropriate use or accidental spillage, and investigation is required in line with established procedures in the risk management plan for the particular water source.

GENERAL DESCRIPTION

Uses: Vernolate is a selective herbicide for the control of grasses and broad-leaf weeds in food-producing agricultural crops including soybeans, peanuts and potatoes.

There are currently no registered products that contain vernolate in Australia, but de-registered compounds may still be detected in water. Previously, products containing vernolate were intended for professional use and were available as concentrated solutions to be applied directly to soils in diluted form using ground, aerial or hand-held sprays.

Exposure sources: If used in the future, the main source of public exposure to vernolate and its metabolites would be residues in food. Residue levels in food produced according to good agricultural practice are generally be low.

Agricultural use of any vernolate in the future may potentially lead to contamination of source waters through processes such as run-off, spray drift or entry into groundwater.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

No published reports on vernolate occurrence in Australian drinking water supplies were found.

TREATMENT OF DRINKING WATER

No specific data on the treatment of vernolate in drinking water have been identified.

MEASUREMENT

United States Environmental Protection Agency (USEPA) method 525.2 for the determination of organic compounds in drinking water by liquid-solid extraction and capillary column gas chromatography with mass spectrometry (GC-MS) can achieve a limit of quantitation (LOQ) of 0.047 µg/L to 0.14 µg/L for vernolate (USEPA 1995). Vernolate can be extracted from water by liquid-liquid extraction with dichloromethane and analysed by GC/MS in selected ion monitoring mode, with a LOQ of 0.5 µg/L. USEPA method 634 for the determination of thiocarbamate pesticides in industrial and municipal wastewaters by gas chromatography is also approved for the analysis of vernolate in water (USEPA 1993). USEPA method 507 for the determination of nitrogen and phosphorus containing pesticides in water by gas chromatography with a nitrogen-phosphorus detector can achieve a LOQ of 0.13 µg/L (Munch 1995). Solid-phase microextraction (SPME), followed by gas-liquid chromatography (GC) employing a nitrogen-phosphorus detector can achieve a LOQ of 0.1 µg/L, and SPME-GC employing mass spectrometry can achieve a LOQ of 0.02 µg/L (Choudhury *et al.* 1996).

HISTORY OF THE HEALTH VALUES

The current acceptable daily intake (ADI) for vernolate is 0.01 mg per kg of bodyweight (mg/kg bw), based on a no-observed-effect level (NOEL) of 1 mg/kg bw/day from a reproduction study in rats. The NOEL is based on decreased bodyweight gain and food intake. The ADI incorporates a safety factor of 100 and it was first established in 1989.

The previous health value was 0.03 mg/L (NHMRC and NRMMC 2004).

HEALTH CONSIDERATIONS

Metabolism: Vernolate is rapidly absorbed via the gastrointestinal tract in rats. Metabolism is extensive, and proceeds through sulfoxidation. Excretion is primarily through urine in the form of conjugates and is complete by 7 days.

Acute effects: Vernolate has low acute oral and dermal toxicity. It is not a skin sensitiser.

Short-term effects: In 14-week dietary studies in rats and dogs, no effects were seen up to the highest doses tested, namely, 45 mg/kg bw/day in rats and 32 mg/kg bw/day in dogs.

Long-term effects: Long-term dietary studies were conducted in mice and rats. In mice, the only effects were changes in relative weights of kidney and liver at the highest dose tested, 100 mg/kg bw/day, and these were of doubtful toxicological significance. In rats, there was an increase in macrophage infiltration in lungs, and decreased bodyweight gain at the highest dose tested, 13 mg/kg bw/day. The lowest overall NOEL was 3.3 mg/kg bw/day in rats.

Carcinogenicity: Based on 2-year dietary studies in mice and rats, there is no evidence of carcinogenicity for vernolate.

Genotoxicity: Vernolate is not considered to be genotoxic, based on *in vitro* and *in vivo* short-term studies.

Reproductive and developmental effects: A 2-generation reproduction study in rats and developmental studies in mice and rabbits found no evidence of effects on reproductive parameters or foetal development. In the rat reproduction study, there was a decrease in parental food intake and an associated decrease in bodyweight gain at doses of 5 mg/kg bw/day and above in first generation parent animals. The NOEL of 1 mg/kg bw/day is the basis for the current ADI.

Neurotoxicity: A 35-day neurotoxicity study in hens found no evidence of delayed neurotoxicity at oral doses of 10 mg/kg bw.

NOTE: Important general information is contained in PART II, Chapter 6

Poisons Schedule: Vernolate is included in Schedule 5 of the *Standard for the Uniform Scheduling of Medicines and Poisons No.1, 2010* (the Poisons Standard)(DoHA 2010). Current versions of the Poisons Standard should be consulted for further information.

DERIVATION OF THE HEALTH-BASED GUIDELINE

The health-based guideline of 0.04 mg/L for vernolate was determined as follows:

$$0.04 \text{ mg/L} = \frac{1 \text{ mg/kg bodyweight/day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 100}$$

where:

- 1 mg/kg bw/day is the NOEL based on a 2-generation reproduction study in rats.
- 70 kg is taken as the average weight of an adult.
- 0.1 is a proportionality factor based on the assumption that 10% of the ADI will arise from the consumption of drinking water.
- 2 L/day is the estimated maximum amount of water consumed by an adult.
- 100 is the safety factor applied to the NOEL derived from animal studies. This safety factor incorporates a factor of 10 for interspecies extrapolation and 10 for intraspecies variation.

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NOTE: The toxicological information used in developing this fact sheet is from reports and data held by the Department of Health, Office of Chemical Safety.

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NOTE: Important general information is contained in PART II, Chapter 6

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Vinyl chloride

(endorsed 1996)

GUIDELINE

No safe concentration for vinyl chloride in drinking water can be confidently set. However, for practical purposes, the concentration should be less than 0.0003 mg/L, which is the limit of determination.

GENERAL DESCRIPTION

Vinyl chloride is used industrially in the production of poly vinyl chloride (PVC), which has wide application in the plastics, rubber, paper and glass industries.

Vinyl chloride may be present in drinking water through pollution of water sources by chemical spills. Water bottled and stored for long periods in PVC containers may contain very low concentrations of vinyl chloride. It has occasionally been detected in drinking water supplies that use PVC pipes in the United States and Germany, with a maximum reported concentration of 0.01 mg/L. In Australia there are stringent requirements on the maximum permissible residual vinyl chloride concentrations in PVC pipes and fittings.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Vinyl chloride has not been found in Australian drinking waters. It is included here to provide guidance in the unlikely event of contamination, and because it has been detected occasionally in drinking water supplies overseas.

TREATMENT OF DRINKING WATER

There are no published reports on methods for the removal of vinyl chloride from drinking water.

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for the analysis of vinyl chloride (USEPA Draft Method 502.1 1986). An inert gas is bubbled through the sample and vinyl chloride trapped on an adsorbent. The adsorbent is then heated and vinyl chloride analysed using gas chromatography with electron capture detection. The limit of determination is 0.0003 mg/L.

HEALTH CONSIDERATIONS

Vinyl chloride is readily absorbed following ingestion. It is metabolised to chloroethylene oxide, which can rearrange spontaneously to chloroacetaldehyde. Both substances are highly reactive and mutagenic.

In humans, vinyl chloride is a narcotic agent, and occupational exposure to high doses causes a number of symptoms including Raynaud's phenomenon, a painful disorder of the hands. This is not a concern for environmental exposure.

Vinyl chloride is a well-documented human carcinogen, with inhalation of high concentrations causing tumours in the liver, particularly angiosarcoma. Tumours in the brain and lung and malignancies of the lymphatic and haematopoietic tissues have also been reported.

No data are available on oral exposure in humans.

Vinyl chloride is also carcinogenic to animals. When administered by inhalation at doses above 100 ppm in air, it induced tumours of the liver and of some other organs in rats, mice and hamsters. Oral administration resulted in dose-related tumours of the liver at a dose of 14 mg/kg body weight per day. Some tumours were also observed in other organs, including the lungs and mammary glands.

Vinyl chloride has exhibited mutagenic activity in a variety of tests on bacteria and mammalian cells.

The International Agency for Research on Cancer has concluded that vinyl chloride is carcinogenic to humans (Group 1, sufficient evidence of carcinogenicity in humans) (IARC 1987).

DERIVATION OF GUIDELINE

Vinyl chloride is a genotoxic human carcinogen, and there is no safe or acceptable concentration for vinyl chloride in drinking water. The guideline of less than 0.0003 mg/L is based on a consideration of health effects in relation to the limit of determination.

i) The excess risk of lifetime consumption of drinking water with a vinyl chloride concentration of 0.0005 mg/L was conservatively estimated by the World Health Organization (WHO), using a linear multistage model, at one additional cancer per million people.

ii) A value of 0.0005 mg/L can also be derived as follows:

$$0.0005 \text{ mg/L} = \frac{0.13 \text{ mg/kg body weight per day} \times 70 \text{ kg} \times 0.1}{2 \text{ L/day} \times 1000}$$

where:

- 0.13 mg/kg body weight per day is the no-effect level from lifetime studies using rats (Feron *et al.* 1981, Til *et al.* 1991). Tumours were reported at higher doses.
- 70 kg is the average weight of an adult.
- 0.1 is the proportion of total daily intake attributable to the consumption of water.
- 2 L/day is the average amount of water consumed by an adult.
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for evidence of carcinogenicity).

The limit of determination is slightly less than the values derived from health considerations, and provides an adequate degree of protection. This is consistent with the general approach adopted for genotoxic human carcinogens (see Section 6.3.4).

The WHO guideline value of 0.005 mg/L was based on a calculation that estimated an additional lifetime risk of one fatal cancer per 100,000 people.

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NOTE: Important general information is contained in PART II, Chapter 6

Xylenes [CASRN 1330-20-7]

(endorsed 2013)

GUIDELINE

Based on aesthetic considerations (taste and odour), the concentration of xylenes in drinking water should not exceed 0.02 mg/L.

Based on health considerations the concentration of xylenes should not exceed 0.6 mg/L.

GENERAL DESCRIPTION

The term 'xylenes' encompasses three isomers of dimethylbenzene. The isomers are distinguished by the designations ortho- (o-) [CASRN 95-47-6], meta- (m-) [CASRN 108-38-3], and para- (p-) [CASRN 106-42-3], which specify to which carbon atoms of the benzene ring the two methyl groups are attached. o-Xylene is also known as 1,2-dimethylbenzene, m-xylene is also known as 1,3-dimethylbenzene, and p-xylene is also known as 1,4-dimethylbenzene. The mixture is a slightly greasy, colourless liquid commonly encountered as a solvent.

Xylenes occurs naturally in petroleum and coal tar and represent about 0.5–1% of crude oil, depending on the source (hence xylenes are found in small amounts in petrol and aviation fuels). Xylenes can also be formed naturally during forest fires (ATSDR, 2007). It is mainly produced from reformate, but is also obtained from coal carbonisation derived from coke ovens.

Xylenes have a taste and odour threshold of 0.02 mg/L.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

Xylenes have only rarely been identified in Australian drinking waters. Natural concentrations in most water sources are usually very low. Xylenes can occur naturally in groundwater as a result of proximity to, or contact with, coal seams, petroleum and gas deposits, and shales. It may be mobilised by extraction activities (Lesage *et al.*, 1997; Leusch and Bartkow, 2011; Volk *et al*, 2011). However, contamination can occur, usually via exposure to petrochemicals in surface waters or groundwater. Known sources of groundwater contamination include leakage from sub-surface fuel storage tanks (do Rego & Netto, 2007) and nearby hydrocarbon deposits (IPCS, 1997). Emissions of fuel components from boating use is a known source of contamination of multiple-use lakes and reservoirs (Schmidt *et al.*, 2004). Xylenes were reported in 3% of samples from an extensive groundwater survey undertaken in Denmark with the highest concentration being 0.000 03 mg/L (Juhler & Felding, 2003). Concentrations in groundwater in the USA were generally <0.001 mg/L, but were as high as 1 mg/L in contaminated areas (IPCS, 1997; ATSDR, 2007). Xylenes have been reported at up to 0.000 5 mg/L in municipal drinking water in Croatia (Karaconji *et al.*, 2006), and are occasionally detected in drinking waters in the USA (Williams *et al.*, 2004), up to a maximum of 0.012 mg/L (IPCS, 1997).

TREATMENT OF DRINKING WATER

Volatile organic chemicals such as xylenes are most commonly treated in drinking water by aeration stripping and/or adsorption to granular activated carbon (GAC). A conventional biologically active sand filter has been shown to be highly effective for the removal of xylenes from contaminated water, under suitable conditions (Arvin *et al.*, 2004). Effective bioremediation of highly contaminated groundwaters has also been demonstrated (Sedran *et al.*, 2004; Zein *et al.*, 2006).

MEASUREMENT

A purge and trap gas chromatographic procedure can be used for the analysis of xylenes (APHA, AWWA & WEF, 2012). An inert gas is bubbled through the sample and xylenes are trapped on an adsorbent. The adsorbent is then heated and xylenes analysed using gas chromatography with mass spectrometric (GC-MS) detection (Method 6200 B) or photoionisation (PI) detection (Method 6200 C) (APHA, AWWA & WEF, 2012). The method detection limit is 38 ng/L for GC-MS and 24 ng/L for GC-PI (APHA, AWWA & WEF, 2012).

HEALTH CONSIDERATIONS

Xylenes are readily absorbed after inhalation and metabolised almost completely to methyl benzoic acid. They can cross the placenta. No data are available on human absorption after ingestion, or on health effects of oral exposure in humans.

A 2-year gavage study using rats and mice reported decreased growth at high doses (500 mg/kg body weight per day) but no xylene-related lesions (NTP 1986). There was no evidence of carcinogenicity in oral and skin administration studies using rats and mice, and xylenes were not mutagenic in tests using bacteria and mammalian cells.

The International Agency for Research on Cancer has concluded that xylenes are not classifiable as to their carcinogenicity in humans (Group 3, inadequate evidence in humans and in animals) (IARC 1989).

DERIVATION OF GUIDELINE

The USEPA (2009) has set a drinking water guideline of 10 mg/L for total xylenes, while the WHO (2011) proposes a guideline of 0.5 mg/L.

The health-based guideline value for xylenes in drinking water was determined as follows:

$$0.6\ \text{mg/L} = \frac{250\ \text{mg/kg body weight per day} \times 70\ \text{kg} \times 0.1}{2\ \text{L/day} \times 1000} \times \frac{5}{7}$$

where:

- 250 mg/kg body weight per day is the no effect level based on a 2-year gavage study using rats (NTP 1986).
- 70 kg is the average weight of an adult
- 0.1 is the proportion of total daily intake attributable to the consumption of water
- 2 L/day is the average amount of water consumed by an adult
- 1000 is the safety factor in using the results of an animal study as a basis for human exposure (10 for interspecies variations, 10 for intraspecies variations and 10 for the limited toxicological end point)
- 5/7 is used to convert data based on a 5 day per week feeding study to a 7-day week equivalent.

The WHO guideline value of 0.5 mg/L is based on an adult body weight of 60 kg. The difference in guideline values is not significant.

The health-based guideline value exceeds the taste and odour threshold of xylenes in water of 0.02 mg/L.

NOTE: Important general information is contained in PART II, Chapter 6

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NOTE: Important general information is contained in PART II, Chapter 6

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Zinc

(endorsed 1996)

GUIDELINE

Based on aesthetic considerations (taste), the concentration of zinc in drinking water should be less than 3 mg/L.

No health-based guideline value is proposed for zinc.

GENERAL DESCRIPTION

Zinc is widely distributed and occurs in small amounts in almost all rocks, commonly as the sulfide.

It is used as a coating to prevent corrosion of iron and steel products, and in the manufacture of brass. Zinc oxide is an important component in the manufacture of paint and rubber products, including tyres.

In surface and ground waters, the concentration of zinc from natural leaching is usually less than 0.01 mg/L. Tap water can contain much higher concentrations as a result of corrosion of zinc-coated pipes and fittings. Zinc concentrations in galvanised iron rainwater tanks are typically 2 mg/L to 4 mg/L but have been reported as high as 11 mg/L.

Taste problems can occur if the zinc concentration in drinking water exceeds 3 mg/L. Water with a zinc concentration above 5 mg/L tends to be opalescent, develops a greasy film when boiled, and has an undesirable dry 'metallic' taste.

Zinc is present in plant and animal tissues, and food is the major source of zinc intake. Drinking water usually makes a negligible contribution to total intake.

TYPICAL VALUES IN AUSTRALIAN DRINKING WATER

In major Australian reticulated supplies, the concentration of zinc ranges up to 0.26 mg/L, with a typical concentration of 0.05 mg/L.

TREATMENT OF DRINKING WATER

Zinc concentrations in drinking water can be reduced by alum coagulation at pH 6.5–7 (30% removal) or by lime softening at pH 9.5 to pH 10 (60% removal).

MEASUREMENT

The concentration of zinc in drinking water can be determined by flame atomic absorption spectroscopy or inductively coupled plasma emission spectroscopy (APHA Method 3500-Zn Parts B or C 1992). The limits of determination are approximately 0.02 mg/L.

HEALTH CONSIDERATIONS

Zinc is an essential element for humans. The recommended intake for adults is 12 mg per day. Nutritional zinc deficiency results in retarded growth, anorexia, mental lethargy, skin changes and night blindness.

Approximately 20–30% of dietary zinc is absorbed by the gastrointestinal tract. Highest concentrations are found in the liver, kidney, bone, retina, prostate and muscle.

In humans, consumption of very high amounts of zinc can result in nausea, vomiting, diarrhoea and abdominal cramps. The major effects of long-term exposure to zinc are copper deficiency, anaemia and gastric erosion.

In animal studies, zinc has been reported to reduce the toxic effects of nickel and cadmium. High doses over long periods may, however, be toxic to nerve cells of mammals.

There is no evidence that occupational exposure to zinc increases the risk of cancer.

Zinc has been shown to induce chromosomal aberrations in mammalian cells, but is inactive in bacterial mutation tests.

DERIVATION OF GUIDELINE

The guideline value for zinc in drinking water has been based on the taste threshold of 3 mg/L. Higher zinc concentrations can impart an undesirable taste and a cloudy appearance. Zinc concentrations over 0.5 mg/L may indicate corrosion problems.

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NOTE: Important general information is contained in PART II, Chapter 6