GUIDELINES FOR

CANADIAN DRINKING WATER QUALITY

DIMETHOATE and OMETHOATE

Guideline Technical Document

Health Canada Santé Canada

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Guidelines for Canadian Drinking Water Quality - Guideline Technical Document - Dimethoate and Omethoate

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GUIDELINE VALUE: **The maximum acceptable concentration (MAC) for dimethoate and omethoate in drinking water is 0.02 mg/L (20 µg/L).**

The toxicological effects of dimethoate are the result of omethoate, its oxygen analogue metabolite (oxon). Since omethoate can be formed through the environmental degradation of dimethoate or during treatment of water containing dimethoate, an additive approach should be taken in which the sum of the detected concentrations of dimethoate and omethoate (expressed as a dimethoate equivalent value) does not exceed the MAC for dimethoate.

EXECUTIVE SUMMARY

This guideline technical document was prepared in collaboration with the Federal-Provincial-Territorial Committee on Drinking Water and is based on assessments of dimethoate (which included an assessment of omethoate) completed by Health Canada's Pest Management Regulatory Agency and its supporting documents.

Exposure

Canadians can be exposed to dimethoate through the diet, through occupational exposure and, to a lesser extent, through drinking water. Dimethoate is a broad spectrum organophosphate pesticide used to control a wide range of insects and mites on both agricultural and non-agricultural sites. In 2018 (the most recent year for which data are available), more than 25 000 kg of dimethoate as active ingredient were sold in Canada. Dimethoate can be released into the environment as spray drift during application. Although water-soluble, it rapidly breaks down, is non-persistent in the environment and therefore is unlikely to contaminate groundwater.

Dimethoate is not usually found in drinking water sources in Canada, although low levels of dimethoate have been found in a few Canadian provinces. The maximum reported concentration was well below the MAC.

Omethoate is a breakdown product of dimethoate in the environment. It is also produced during treatment of source water containing dimethoate. However, limited Canadian water monitoring data did not report any samples with omethoate above the detection limit.

Health effects

Dimethoate primarily targets the nervous system through its metabolite omethoate, which is more toxic than dimethoate. Dimethoate has also been found to cause increased offspring deaths in animals.

Analytical and treatment considerations

The development of drinking water guidelines takes into consideration the ability to both measure the contaminant and remove it from drinking water supplies. Several analytical methods are available for measuring dimethoate and omethoate in drinking water at concentrations well below the MAC.

At the municipal level, treatment technologies that are available to effectively decrease dimethoate from drinking water include activated carbon adsorption, oxidation, membrane filtration and biological processes. These treatment technologies are capable of achieving treated water concentrations well below the MAC. Although dimethoate may be removed using common oxidants used for disinfection (e.g., chlorine), utilities should ensure that they minimize the formation of by-products, such as omethoate, without compromising the effectiveness of disinfection.

In cases where dimethoate removal is desired at a small or household level, for example when the drinking water supply is from a private well, a residential drinking water treatment unit may be an option. Although there are no treatment units currently certified for the removal of dimethoate from drinking water, activated carbon adsorption and reverse osmosis technologies are expected to be effective. Since these technologies do not result in the formation of omethoate, only removal of dimethoate is needed at the residential-scale. When using a residential drinking water treatment unit, it is important to take samples of water entering and leaving the treatment unit and to send them to an accredited laboratory for analysis to ensure that adequate dimethoate removal is occurring.

Application of the guidelines

Note: *Specific guidance related to the implementation of drinking water guidelines should be obtained from the appropriate drinking water authority.*

The guideline value for dimethoate and the additive approach for omethoate are protective against health effects from exposure to dimethoate and omethoate in drinking water over a lifetime. Any exceedance of the MAC should be investigated and followed by the appropriate corrective actions, if required. For exceedances in source water where there is no treatment in place, additional monitoring to confirm the exceedance should be conducted. If it is confirmed that source water dimethoate concentrations are above the MAC, an investigation to determine the most appropriate way to reduce exposure to dimethoate should be conducted. This may include use of an alternate water supply or installation of treatment units. Where treatment is already in place and an exceedance occurs, an investigation should be conducted to verify treatment and to determine whether adjustments are needed to lower the treated water concentration below the MAC. When oxidation processes are used to degrade dimethoate, omethoate monitoring should also be conducted to ensure that the sum of their concentrations, calculated using the additive approach, is below the MAC.

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1.0 EXPOSURE CONSIDERATIONS

1.1 Sources and uses

Dimethoate is a broad spectrum organophosphate insecticide and acaricide used to control a wide range of insects and mites on both agricultural and non-agricultural sites (Health Canada, 2011, 2015). It acts by interrupting the transmission of nerve impulses, thereby inhibiting cholinesterase (ChE) (Health Canada, 2011). There are no domestic products or residential uses of dimethoate in Canada (Health Canada, 2011). More than 25 000 kg of dimethoate as active ingredient were sold in Canada in 2018 (the most recent year for which data are available) (Health Canada, 2020a).

Dimethoate can be released into the environment as spray drift and runoff during field application (Health Canada, 2015). It is very soluble in water and is not likely to volatilize from moist soils or surface waters (Health Canada, 2011). It does not adsorb onto soil and is therefore highly mobile in soil (WHO, 2004; Health Canada, 2011, 2015). Despite this, dimethoate is unlikely to contaminate groundwater as it quickly breaks down into omethoate in soil via microbiological and hydrolytic degradation (the main inactivating pathway of dimethoate in the environment) (WHO, 2004; Health Canada, 2011, 2015). Phototransformation is not an important transformation route for dimethoate in soil and water (Health Canada, 2011). Dimethoate has a half-life of 2 to 122 days in soil and 18 hours to 8 weeks in water, although it is relatively stable at pH 2–7 (HSDB, 2010; WHO, 2017). Overall, dimethoate is non-persistent in the environment (WHO, 2004; Health Canada, 2011, 2015).

Omethoate is the major toxic degradation product of dimethoate in the environment (US EPA, 2006a). It is also an organophosphate pesticide that acts by inhibiting ChE. However, it is not registered for use as a pesticide in Canada or the United States (US EPA, 2004; APVMA, 2011). Omethoate has high to very high mobility in soil (EFSA, 2006). With laboratory half-life values of 0.9 to 2.8 days being reported in soil, it is unlikely to be persistent (EFSA, 2006).

In addition to being an environmental degradate, omethoate is produced during chlorination of drinking water, with 11% to 23% of dimethoate being converted to omethoate (Marin, 2010). Omethoate is also a toxicologically important metabolite of dimethoate in mammals and is more toxic than its parent chemical (Health Canada, 2011). For that reason, this assessment of dimethoate also includes information on omethoate.

1.2 Substance identity

Dimethoate ($C_5H_{12}NO_3PS_2$), or O,O-dimethyl S-methylcarbamoylmethyl phosphorodithioate, is a white crystalline solid belonging to the dithiophosphates chemical group (Health Canada, 2011). Dimethoate can contain low levels of impurities, such as omethoate and isodimethoate, which have a higher ChE inhibition potential than dimethoate (EFSA, 2018).

Omethoate ($C_5H_{12}NO_4PS$), or O,O-dimethyl S-(N-methylcarbomoylmethyl) phosphorothioate, is a synthetic, colourless liquid (Lewis et al., 2016). It is an oxygen analogue metabolite (oxon) of dimethoate and plays an important role in the toxic effects of dimethoate in insects and mammals (APVMA, 2010). Some of the physical and chemical properties of dimethoate and omethoate are summarized in Table 1.

TABLE 1: Properties of dimethoate and omethoate relevant to their presence in drinking water.

Property	Dimethoate[a]	Interpretation	Omethoate[b]	Interpretation
CAS RN	60-50-1	Not applicable	1113-02-6	Not applicable
Molecular weight (g/mol)	229.4	Not applicable	213.2	Not applicable
Water solubility (g/L)	23.3 at pH 5	High solubility in water	500 at 20 °C	High solubility in water
Vapour pressure (mPa)	0.25 at 25 °C	Very low volatility; not likely to volatilize from moist soils or water surfaces	19.0 at 20 °C	Moderately volatile
Henry's law constant (Pa m^3mol^{-1})	1.42×10^{-6}	Not likely to volatilize from moist soils or water surfaces	4.62×10^{-9} at 25 °C	Not likely to volatilize from moist soils or water surfaces
n-octanol:water partition coefficient (log K_{ow})	0.704	Unlikely to bioaccumulate	-0.9	Unlikely to bioaccumulate
Dissociation constant (pKa)	2.0 at 20 °C	Hydrolyzes moderately under acidic and neutral conditions and hydrolyzes easily under basic conditions	Not available	Not applicable

CAS RN: Chemical Abstracts Service registry number

[a] Dimethoate data from Health Canada, 2011

[b] Omethoate data from Lewis et al., 2016

1.3 Exposure

Potential exposure to dimethoate is primarily through the diet and from occupational exposure during handling and application of products containing dimethoate (Health Canada, 2011, 2015). Drinking water is a minor source of dimethoate exposure (Health Canada, 2011, 2015). Omethoate exposure is possible through the diet from residues in foods and through drinking water as a result of the oxidation of dimethoate during water treatment and environmental degradation of dimethoate (Health Canada, 2011).

Based on aggregate dietary and drinking water risks assessed by Health Canada (2015), exposure to dimethoate from foods and drinking water is not of concern (Table 2). The World Health Organization (WHO) has estimated a total daily intake of 0.001 µg/kg body weight (bw) (0.000001 mg/kg bw) of dimethoate from food, considerably lower than the 0.00011 mg/kg bw/d estimated by Health Canada's Pest Management Regulatory Agency (PMRA) for the Canadian general population (Health Canada, 2015; WHO, 2017).

TABLE 2: Chronic dietary and aggregate dietary and drinking water exposure of Canadians to dimethoate and omethoate (Health Canada, 2015)

Population Group (in years)	Exposure from Food[a]		Exposure from Food and Water[a]	
	mg/kg bw/d	% ADI[b]	mg/kg bw/d	% ADI[b]
General Population	0.00011	6	0.000147	7
All Infants (< 1)	0.000107	5	0.000230	12
Children 1–2	0.000262	13	0.000318	16
Children 3–5	0.000244	12	0.000296	15
Children 6–12	0.000166	8	0.000202	10
Male 13–19	0.000105	5	0.000132	7
Male 20–49	0.000091	5	0.000126	6
Adults 50+	0.000078	4	0.000115	6
Female 13–49	0.000088	4	0.000122	6

ADI: acceptable daily intake

[a] Exposure accounts for both dimethoate and omethoate residues. 3x chronic toxicological adjustment factor (or TAF, discussed in Section 3.0) was applied to omethoate residue estimates (Health Canada, 2020b).

[b] ADI = 0.002 mg/kg bw per day

Water monitoring data from the provinces and territories (municipal and non-municipal supplies), the PMRA and Environment Canada and Climate Change (Environment Canada, 2011) (Appendix B) were available for dimethoate.

Data provided by the provinces and territories, as well as by the First Nations and Inuit Health Branch (FNIHB) of Indigenous Services Canada, indicate that dimethoate levels are below the method reporting limit (MRL) or method detection limit (MDL) in most samples collected from a variety of water supplies in Canada, including surface water and groundwater as well as treated and distributed water where monitoring occurred (British Columbia Ministry of Health, 2019; Indigenous Services Canada, 2019; Manitoba Sustainable Development, 2019; Ministère de l'Environnement et de la Lutte contre les changements climatiques du Québec, 2019; Nova Scotia Environment, 2019; Prince Edward Island Department of Communities, Land and Environment, 2019; Saskatchewan Water Security Agency, 2019; Ontario Ministry of the Environment, Conservation and Parks, 2020). The data provided in Tables 3 and 4 are for dimethoate only. The exposure data provided reflect the different MDLs of accredited laboratories used within and amongst the jurisdictions, as well as their respective monitoring programs. The data provided by the provinces and territories do not indicate the timing of monitoring in relation to the pesticide's application and runoff events. As a result, the exposure data and their statistical analysis provide only a limited picture. Table 3 summarizes the monitoring data for jurisdictions in which all samples were reported below the MDL. Table 4 summarizes the data for jurisdictions in which dimethoate detections were reported. The maximum dimethoate concentration reported was 2.5 µg/L in samples from both Saskatchewan and Ontario. There were no monitoring data available in New Brunswick, Newfoundland and Labrador, or Yukon (New Brunswick Department of Environment and Local Government, 2019; Newfoundland and Labrador Department of Municipal Affairs and Environment, 2019; Government of Yukon Environmental Health Services, 2019).

TABLE 3: Summary of monitoring data in which dimethoatea was not detected.

Jurisdiction (MDL µg/L)	Monitoring Period	Municipal/ Non-municipal	Water Type (Municipal: ground/surface – raw, treated, distributed)	# Detects/ Samples
British Columbia (2)	2013–2018	Municipal	Surface – raw	0/18
FNIHB Ontario Region (0.1–2.5)	2014–2018	Public water systems	Ground – raw	0/13
			Ground – treated	0/190
			Ground – distribution	0/16
			Surface – raw	0/33
			Surface – treated	0/308
			Surface – distribution	0/23
		Semi-public water systems	Ground – raw	0/3
			Ground – treated	0/16
			Ground – distribution	0/68
			Surface – raw	0/1
			Surface – treated	0/9
			Surface – distribution	0/2
		Public water systems	Ground – treated	0/3
			Ground – distribution	0/50
			Surface – treated	0/5
FNIHB Atlantic Region (2.5–10)	2014–2018	Public water systems	Ground – treated	0/4
			Ground – distribution	0/4
			Surface – treated	0/1
FNIHB Quebec (0.01–0.03)	2014–2018	—	Drinking water system	0/4
Manitoba[b] (0.1)	2015–2020	Ambient	Lake	0/14
			River/stream	0/187
Nova Scotia (1.5–5)	2007–2018	Municipal	Ground – raw	0/71
			Ground – treated	0/35
			Surface – raw	0/35
			Surface – treated	0/40
			Distributed	0/1

FNIHB: First Nations and Inuit Health Branch

[a] Results are for dimethoate only as no omethoate data are available

[b] The samples for Manitoba are from 3 lake locations and 11 river/stream locations from a total of 10 waterbodies.

TABLE 4: Summary of dimethoate detections in select provinces in Canada[a]

Jurisdiction (MDL µg/L)	Monitoring Period	Water Type (Municipal: ground/surface – raw, treated, distributed and Non-Municipal: ground)	# Detects/ samples	Maximum Conc. (µg/L)
Ontario (0.0002–5)	2010–2020	Ground – raw (municipal)	0/194	–
		Ground – treated (municipal)	2/4259	0.1
		Surface – raw (municipal)	0/154	–
		Surface – treated (municipal)	2/4192	2.5
		Distribution (municipal)	1/60	2.5
Prince Edward Island (0.04)	2004–2017	Ground – raw (municipal)	0/665	–
		Ground – raw (non-municipal)	1/614	0.1
Quebec (0.01–0.9)	2012–2018	Ground – distribution (municipal)	0/291	–
		Surface – distribution (municipal)	4/1040	0.4
		Ground – raw[b] (municipal)	0/46	–
		Ground – treated[b] (municipal)	0/17	–
		Ground – distribution[b] (municipal)	0/5	–
		Ground – raw[c] (municipal)	0/82	–
		Ground – raw[c] (non-municipal)	0/132	–
Saskatchewan (0.0001–10)	2014–2019	Ground and surface – distribution (municipal)	2/32	2.5
		Ground and surface – treated (municipal)	0/4	–
		Ground – raw (municipal)	0/16	–

MDL: method detection limit

[a] Results are for dimethoate only as no omethoate data are available

[b] Potato Project 2017–2018: During the period covered, analysis results of dimethoate pesticide found in raw, treated or distributed groundwater were obtained by the Ministry from 9 drinking water supplies.

[c] Small Systems Project 2012–2018: During the period covered, analysis results of dimethoate found in raw groundwater were obtained by the Ministry from 25 drinking water supplies.

On the basis of an extensive review of available water monitoring data, the PMRA estimated environmental exposure concentrations of 0.03 µg/L and 0.08 µg/L (95th percentile of the mean concentration for each study site, including half level of detection for non-detects) of dimethoate in groundwater and surface water, respectively (Health Canada, 2011). Dimethoate was detected in only 1 of 163 samples taken from a total of 15 reservoirs in Manitoba, Saskatchewan and Alberta (May 2003 to April 2004). The detection limit was 25.10 ng/L. Reservoirs received primarily snowmelt and rainfall runoff from agricultural crop lands. Dimethoate was not detected in treated drinking water samples (n = 28; collection July 2004 and 2005) collected in the same study (Donald et al., 2007).

Canadian omethoate water monitoring data were limited to Nova Scotia Groundwater Observation Network reports (2007–2012, 2015) and consistently showed omethoate below the detection limit of 1 µg/L in up to 40 observation wells monitored annually or biennially (Government of Nova Scotia, 2007–2012, 2015).

In foods, residues of dimethoate and omethoate can potentially occur in plant and animal commodities (Health Canada, 2015). In plants, dimethoate-related residues were found at higher concentrations in the foliage or outer portions of plant samples as compared to the grain and root samples (Health Canada, 2015). In the Canadian Food Inspection Agency's 2015/16 Annual Report (2019), residues of dimethoate and dimethoate plus omethoate were detected in 60 of 1801 samples of fruits and vegetables (fresh, frozen and processed). Of these 60 detects, the highest values were seen in leafy vegetables (e.g., leaf lettuce, kale, fine herbs). The single sample exceeding its maximum residue limit (0.1 ppm) was reported for fine herbs (5.77600 ppm) (CFIA, 2019). In animal commodities (goats and hens), the highest dimethoate-related residue concentrations (primarily omethoate and dimethoate carboxylic acid) were in the liver and kidneys, followed by eggs and milk. The lowest concentrations were in muscle and fat (Health Canada, 2015).

2.0 HEALTH CONSIDERATIONS

All pesticides, including dimethoate, are regulated by the PMRA. The PMRA conducts extensive evaluations and cyclical reviews of pesticides, taking into account unpublished and proprietary information as well as foreign reviews by other regulatory agencies, such as the United States Environmental Protection Agency (US EPA). This health assessment of dimethoate, including discussion of omethoate, is based primarily on the PMRA evaluations (Health Canada, 2011, 2015) and supporting documents. Additionally, any reviews and relevant literature available since the PMRA evaluations were completed were also considered.

2.1 Kinetics

Absorption, distribution and elimination of dimethoate were unaffected by sex, dose or route of exposure (Health Canada, 2011). The major metabolites of dimethoate were thiophosphate and phosphate esters (NHMRC, NRMMC, 2011). Although omethoate is a minor metabolite (1%–6%), it is responsible for the ChE inhibition seen following dimethoate exposure (Health Canada, 2011; NHMRC, NRMMC, 2011).

Absorption: Both dimethoate and omethoate were rapidly and almost completely absorbed from the gastrointestinal tract of rats following oral administration (APVMA, 2010; Health Canada, 2011). Dermal absorption of dimethoate ranged from 7% to 11% in rats (APVMA, 2010). In an in vitro study, rat skin absorbed more dimethoate than human skin (Davies, 1999).

Distribution: Dimethoate is rapidly distributed to tissues, especially the liver, bile, kidneys and erythrocytes, but it is unlikely to accumulate (APVMA, 2010; Health Canada, 2011). In rats, tissue retention from single radiolabelled oral doses of either 10 or 100 mg/kg bw of dimethoate was 0.3 and 7 ppm, respectively (Health Canada, 2011).

Omethoate is also widely distributed in tissues (highest levels in thyroid) and showed minimal tissue retention with less than 0.05% of administered doses remaining in tissues 48 hours after oral dosing in rats (Health Canada, 2011; NHMRC, NRMMC, 2011).

Metabolism: Dimethoate is extensively metabolized based on oral exposure studies in rats (Health Canada, 2011). The hydrolytic pathway is the major metabolic pathway and yields dimethoate carboxylic acid (major metabolite: 29%–46%), which is subsequently metabolized to dimethyldithiophosphate, dimethylthiophosphoric acid and dimethyl phosphoric acid (Kirkpatrick, 1995; Health Canada, 2011). The oxidative pathway, a minor pathway, involves the oxidation of dimethoate to its oxon, omethoate (minor metabolite: 1%–6%), which then undergoes limited metabolism (Kirkpatrick, 1995; Health Canada, 2011; NHMRC, NRMMC, 2011). Loss of carbon dioxide by dimethoate is also a minor metabolic pathway (Health Canada, 2011). An in vitro interspecies comparative metabolism study, assessed in conjunction with human in vivo data, did not identify any dimethoate metabolites unique to humans (EFSA, 2018).

Although omethoate is not extensively metabolized (88% is eliminated unchanged within 8 hours), its identified metabolites include N-methyl-methyl-sylphinyl-acetamide (major metabolite: 13%–22%), O-desmethylated omethoate (9%), O,O-dimethyl phosphoric acid and O,O-dimethyl phosphorothioic acid (Health Canada, 2011; NHMRC, NRMMC, 2011).

Elimination: Elimination of dimethoate and its metabolites is rapid in rats, with 91% –97% of a given dose excreted within 5 days mostly in the urine (85%–91%), with lesser amounts in feces (1%–2%), expired air (2%–3%) and the carcass (1%–2%) (Kirkpatrick, 1995; APVMA, 2010; Health Canada, 2011). The major urinary metabolites (53%–87%) are dimethoate carboxylic acid, thiophosphate and phosphate esters; 1%–2% of dimethoate is excreted unchanged in the urine, while omethoate accounts for 1%–6% of the urinary metabolites (Kirkpatrick, 1995; NHMRC, NRMMC, 2011; Health Canada, 2011).

Omethoate is quickly eliminated unchanged (95%–98% as omethoate), primarily in the urine, with another 2%–5% excreted in the feces (Health Canada, 2011). Excretion profiles for omethoate were independent of dose or sex in animal studies, although one study showed male rats excreted more radiolabeled omethoate in the feces at the high dose (10 mg/kg bw) compared to the low (0.5 mg/kg bw) dose (Health Canada, 2011).

2.2 Health effects

The toxicity databases for both dimethoate and omethoate are well characterized in animals, covering several endpoints and various types of exposure, although information regarding toxicity in humans is limited (see US EPA, 2007; APVMA, 2010, 2011; Health Canada, 2011, 2015 for more thorough reviews). Dimethoate primarily targets the nervous system by inhibiting acetylcholinesterase (AChE), an enzyme that breaks down neurotransmitters and that is necessary for normal functioning of the nervous system (Health Canada, 2011). AChE is the primary ChE in the body and can be measured in brain tissue, erythrocytes and plasma (WHO, 2004; Health Canada, 2011; EFSA, 2018).

In animal studies, dimethoate caused increased pup mortality and effects on reproduction (Brooker *et al.*, 1992; Mellert et al., 2003; Myers, 2001b; *US EPA, 2004;* APVMA, 2010; Health Canada, 2011).

2.3 Effects in humans

The PMRA's assessments and supporting documents (US EPA, 2007; Health Canada, 2011, 2015) did not discuss the effects of dimethoate or omethoate in humans. Data available from the literature related to cancer included a pooled case-control study and a prospective study (Latifovic et al., 2020; Pardo et al., 2020). Studies on non-cancer endpoints were limited to volunteer studies, a few case studies and a prospective study and indicated that acute exposure to dimethoate and omethoate produce typical signs of organophosphate poisoning.

Cancer

Latifovic et al. (2020) assessed the risk of Hodgkin lymphoma (HL) using self-reported pesticide use data from the North American Pooled Project (NAPP), a pooled case-control study of data from four population-based studies conducted in the US and Canada (controls, n = 3889). The odds ratio (OR) for HL was elevated for those aged ≤ 40 years exposed to dimethoate (OR: 3.43, 95% Confidence Interval or CI: 1.04–11.34); however, the estimate was based on small numbers (8 exposed cases, 5 exposed controls) and was not statistically significant. No statistically significant associations were found among cases older than 40 years or for overall cases. The study showed a statistically significant

elevated risk of HL for those under 40 years exposed to two or more organophosphate insecticides (OR: 2.96, 95% CI: 1.33–6.61, p-trend < 0.01). HL cases were on average younger than controls, more likely to have a family history of lymphatic or hematopoietic cancer and more likely to have a history of doctor-diagnosed mononucleosis (Epstein-Barr virus which causes mononucleosis has been linked to increased risk of developing HL).

Strengths of the study include the large sample size of the NAPP, the availability of medical history and the use of both trade and generic chemical names in questionnaires sent to participants. Limitations of the study include exposure measurement error, recall bias, use of proxy respondents, non-differential and differential exposure misclassification, and potentially uncontrolled confounding. Although the sample size for the NAPP was large, the numbers of exposed participants for many pesticides were low. Such small numbers may result in chance findings (Latifovic et al., 2020).

Using data from the Agricultural Health Study (AHS) collected from a large prospective cohort of licensed pesticide applicators and their spouses (over 89,000 participants) since 1993 from Iowa and North Carolina, Pardo et al. (2020) found a statistically significant association between dimethoate ever use and increased aggressive prostate cancer risk (n = 54 exposed cases, hazard ratio or HR: 1.37, 95% CI: 1.04, 1.80) compared to never users. This association was found in Phase 1 (1993–1997) take-home questionnaires only (n = 20 923). The association was no longer statistically significant when Phase 2 (1999–2003) and Phase 3 (2005–2010) data were included (n = 55 exposed cases, HR: 1.29, 95% CI: 0.98, 1.70). The authors suggest that the lack of statistical significance may have been due to a decrease in sample size relating to non-response in the follow-up questionnaires.

Overall, strengths of the AHS include its large size; the collection of baseline, health and lifestyle information, and genetic factors; the use of cancer registries, the detailed information on pesticide use; and the many different pesticides and diseases assessed. Its limitations include: the indirect assessment of exposure (questionnaire-based), the lack of exposure refinement measurements (no induction time or latency discussion), and selection bias when controlling for multiple confounders due to the exclusion of many subjects with missing data, especially in later Phases (Sathiakumar et al., 2011). The authors were unable to conduct exposure-response analyses because lifetime duration of use information was only collected during the Phase 3 questionnaire (Pardo et al., 2020).

Non-cancer

The no-observed-adverse-effect-level (NOAEL) for ChE inhibition was 0.2 mg/kg bw per day in 9 male and female volunteers given dimethoate for 39 days (Edson et al., 1967). This NOAEL was supported in seven other studies, each involving 6 to 20 volunteers who received doses ranging from 0.04 to 1.0 mg/kg bw per day for up to 57 days (WHO, 2004).

Case studies and reports of accidental and deliberate ingestion of dimethoate were available from the literature. In a prospective study reviewing 264 cases of intentional ingestion of dimethoate (plasma concentrations of 160.0 to 674.0 µmol/L), acute dimethoate poisoning resulted in hypotensive shock, impaired respiratory function, AChE inhibition (including coma) and, in 61 cases, death (Eddleston et al., 2005). Similar symptoms were seen in individual case studies of dimethoate poisoning and included bradycardia (slowed heart rate), respiratory depression/insufficiency (breathing difficulties), marked gait ataxia (uncoordinated movement), seizures and coma (LeBlanc et al., 1986; De Bleeker et al., 1992; Fonseka et al., 2003; Hoffmann and Papendorf, 2006).

Effects were similar in case studies involving omethoate ingestion (Lotti et al., 1981; Tsatsakis et al., 1998; Pavlic et al., 2002). Omethoate is unlikely to cause delayed neuropathy in humans based on enzyme studies using autopsy material (Lotti et al., 1981).

2.4 Effects in animals

ChE inhibition and pup mortality were the main effects of dimethoate exposure in animal studies and occurred concurrently in key reproductive and developmental studies (Table 5). Dimethoate was not genotoxic, carcinogenic, or teratogenic. In acute studies, dimethoate was moderately toxic via the oral route of exposure and slightly toxic via the dermal and inhalation routes (Table 6) (Health Canada, 2011).

ChE inhibition was the most sensitive indicator of toxicity with brain and erythrocyte ChE being the earliest affected endpoints in sub-chronic and chronic dietary studies (Health Canada, 2011). In laboratory animals, oral range-finding, chronic/carcinogenicity, 2-generation reproductive, 1-generation reproductive toxicity, developmental neurotoxicity (DNT), and comparative ChE studies using dimethoate showed effects on the nervous system, particularly the inhibition of ChE in the brain, plasma and erythrocytes of treated animals, both adults and offspring (Hellwig et al., 1986a; Burford et al., 1990a, 1990b; Brooker and Stubbs, 1991; Brooker et al., 1992; Myers, 2001a, 2001b; Mellert et al., 2003; US EPA, 2004, 2006a; Farag et al., 2006, 2007; APVMA, 2010; Health Canada, 2011). Brain ChE levels were generally the most sensitive indicator of ChE toxicity, occurring at doses similar to or lower than those causing ChE inhibition in erythrocytes (FIFRA, 2005; US EPA, 2006b; Health Canada, 2011). Erythrocyte ChE inhibition was indicative of adverse changes in peripheral nervous tissue in acute and short-term studies only. In studies of longer duration, erythrocyte ChE inhibition alone was not considered to be a toxicologically adverse effect due to the limitations related to the low rate of re-synthesis of erythrocyte ChE over extended periods of time (US EPA, 2006b; Health Canada, 2011). Plasma ChE was the least affected and was considered a marker of exposure rather than a toxicologically adverse effect (APVMA, 2011; Health Canada, 2011).

In chronic studies using dimethoate, rats were slightly more sensitive than other species to ChE inhibition based on NOAEL values of 0.05 to 1.3 mg/kg bw per day and lowest-observed-adverse-effect-level (LOAEL) values of 0.25 to 3 mg/kg bw per day compared to LOAELs of 3.75 mg/kg bw per day in mice and 0.73 mg/kg bw per day in dogs (Hellwig et al., 1986a; Burford et al., 1990a, 1990b; Farag et al., 2006; US EPA, 2006a; Farag et al., 2007; APVMA, 2010; Health Canada, 2011). Both young (including fetuses) and adult animals had similar sensitivity to the ChE-inhibiting effects of dimethoate as seen in the range-finding study for the DNT study and the comparative ChE study. In the comparative ChE study, adults and offspring had the same NOAEL values (0.5 mg/kg bw per day for acute exposure and 0.1 mg/kg repeat exposure) (Myers, 2001c; US EPA, 2004; Health Canada, 2011). Overall, no pronounced sex differences were apparent in the available database for dimethoate. A comparison of data from rat studies of different durations showed toxicity increased with repeat-dose exposure compared to a single exposure. However, the differences in the methods of exposure (gavage versus dietary) are a confounding factor (Health Canada, 2011).

Several oral toxicity studies were available that assessed effects in the young following in utero exposure. These studies included prenatal developmental toxicity studies in rats and rabbits, two 2-generation reproductive toxicity studies in rats, and a cross-fostering study in rats designed to further investigate pup mortality seen in the previously mentioned studies (Health Canada, 2011). Two studies in mice were also available (Farag et al., 2006, 2007). Additionally, studies assessing neurotoxicity in the developing rat were available including a comparative ChE study, a range-finding DNT study (which included ChE assessment), and the main DNT study in which ChE activity was not assessed.

In addition to ChE inhibition, increased pup mortality was seen in two 2-generation reproductive studies and in a 1-generation range-finding reproductive toxicity study, as well as in the range-finding study for the DNT study. In the main DNT study, increased pup mortality was also seen; however, brain ChE was not measured so no conclusions can be made regarding ChE inhibition in the study. The DNT study did, however, assess behavioural and neuropathological effects in dams and offspring, with offspring (but not dams) showing effects at ≥ 0.5 mg/kg bw per day. A dose-related increase in pup deaths was observed in the DNT study in the absence of overt signs of maternal toxicity during early lactation in mid- and high-dose pups (including total litter loss in one female in the 0.5 mg/kg bw per day dose group and in three females in the 3.0 mg/kg bw per day dose group). Affected pups were small in size, cold to the touch and had little food in their stomachs. No adverse maternal or reproductive effects were seen. The offspring NOAEL was 0.1 mg/kg bw per day based on increased pup mortality and on changes in motor activity (Myers, 2001b; US EPA, 2004). Increased pup deaths and total litter loss were also seen in the range-finding study for the main DNT study but occurred at a maternally toxic dose level of 6.0 mg/kg bw per day (Myers, 2001a; APVMA, 2010; Health Canada, 2011).

The comparative ChE study found no significant treatment-related effects on any reproductive or developmental parameters, including number of live births, corpora lutea, implantations, or total resorptions, or on pre- and post-implantation loss, fetal body weights or sex ratio. No clinical signs or increased mortality were observed in adult male or female rats, fetuses or offspring at any dose (Myers, 2001c; US EPA, 2004; Health Canada, 2011). At the lowest dose showing pup mortality in the DNT study, the comparative study did find equivalent levels of brain ChE inhibition (10%–13%) between subpopulations (pregnant dams, fetuses, 4-day old pups, 21-day old pups and adult rats exposed for 11 days) (Health Canada, 2011).

Given the increased incidence of pup mortality in the DNT study and the potential disruption in dam behaviour related to ChE inhibition, a limited cross-fostering study was conducted to determine the influence of pre- and post-natal maternal exposure on pup mortality. Pregnant dams were dosed with 0, 3 or 6 mg/kg bw per day of dimethoate from gestation day (GD) 6 to postnatal day (PND) 11. On PND 1, some litters were reallocated from control dams to treated dams and vice versa, as described in Table 5. Pups were not directly treated with dimethoate. Treated dams (both doses) had forelimb hair loss and were more restless, scattering their litters; however, neurobehavioural testing did not show any treatment-related effects. The number of pups with no milk in their stomachs was increased in litters cared for by treated dams (both doses). Pup mortality was increased and was positively correlated with the dam's dose level and duration of treatment, but was also somewhat related to maternal restlessness and litter scattering. The cross-fostering study therefore did not resolve whether the pup mortality was due to maternal neglect or dimethoate exposure. The study identified a LOAEL of 3 mg/kg bw per day for both maternal and pup toxicity (Myers, 2004; Health Canada, 2011).

TABLE 5: NOAEL and benchmark dose lower limit ($BMDL_{10}$) values for brain ChE inhibition caused by dimethoate in selected studies (adapted from Health Canada, 2011)

Study (References)	Method	NOAEL (mg/kg bw per day)	$BMDL_{10}$ for brain ChE inhibition (mg/kg bw per day)	Effects (mg/kg bw per day)
DNT main study (Myers, 2001b; US EPA, 2004)	23–24 pregnant CD rats/dose gavaged with 0, 0.1, 0.5 or 3.0 mg/kg bw per day in water from GD 6 to PND 10; Pups exposed in utero and via lactation until PND 10 then gavaged at maternal doses from PND 11 to 21	0.1 (offspring) 3.0 (maternal, developmental)	Not calculated	**Dams:** no adverse effects **Developmental/ reproductive:** no treatment-related effects **Pups:** ≥ 0.5: increased deaths including total litter loss with pups small, cold to the touch and little/no food in stomachs (dams of affected litters were underactive/inattentive), increased horizontal activity (PND 17 in males) 3.0: decreased motor activity, righting reflexes, and rearing ***Note:*** *ChE not measured in this study; see ChE data in the comparative ChE companion study*
Comparative ChE companion study to DNT stud (Myers, 2001c; US EPA, 2004)	Same gavage dosing as main DNT; **Acute exposure:** 8 PND 11 pups or 8 adult CD rats/sex/dose **Repeat exposure:** pregnant CD rats 9/dose/day from GD 6–20 and terminated or 10/dose/day GD 6 to PND 10 followed by 1/sex/litter offspring treated from PNDs 11–21, or 8 adults/dose for 11days	0.5 (acute: pups and adults) 0.1 (repeat: fetuses, pups, maternal, and adults)	1.3–2 (acute: pups and adults) 0.2–0.7 (repeat: fetuses, pups, maternal, and adults)	**Acute exposure:** 3.0: decreased brain and plasma ChE (PND 11pups and adults), decreased erythrocyte ChE (adult females), **Repeat exposure:** Maternal/ adult ≥ 0.5: decreased brain ChE (GD 20) 3.0: decreased erythrocyte and plasma ChE (GD 20) **Fetal/Offspring** ≥ 0.5: decreased brain ChE (fetuses, PND 21 pups), decreased erythrocyte ChE (PND 21 female pups) 3.0: decreased brain ChE (PND 4 male pups), decreased erythrocyte ChE (fetuses, PNDs 4 and 21 male pups)

Study (References)	Method	NOAEL (mg/kg bw per day)	$BMDL_{10}$ for brain ChE inhibition (mg/kg bw per day)	Effects (mg/kg bw per day)
Range-finding for DNT study (Myers, 2001a; APVMA, 2010	10 pregnant CD rats/dose gavaged with 0, 0.2, 3.0 or 6.0 mg/kg bw/day from GD 6 to PND 10; plus 5 dams/dose gavaged from GD 6–20 for ChE determination Pups exposed in utero and via lactation until PND 10 then gavaged from PND 11–21 at maternal doses (2 pups/sex/litter).	0.2 (maternal, offspring) 3.0 (developmental)	0.2–0.4 (dams, fetuses, pups)	**Maternal:** ≥ 3.0: decreased maternal weight gain during gestation, decreased brain, erythrocyte and plasma ChE (GD 20) **Developmental/ reproductive:** 6.0: decreased pup weight at birth (PND 1) **Offspring**: ≥ 3: decreased brain, erythrocyte and plasma ChE at GD 20 and PND 21 6.0: increased deaths and total litter loss in PND 1–4, decreased viability index at PND 4 (precull), decreased pup weight gain (PND 1–11) ***Note:*** *Due to small sample size, parameters were not analysed statistically except body weight*
Cross-fostering (Myers, 2004)	Pregnant CD rats gavaged with 0 (100 dams), 3 (25 dams) or 6 (50 dams) mg/kg bw/day from GD 6 to PND 10, litters cross-fostered on PND 1 as follows: control litters (¼ reared by their own control dam, ¼ to each of 3 and 6 mg/kg groups and ¼ discarded), 3 mg/kg litters (all to control), 6 mg/kg litters (½ each to control and 6 mg/kg groups)	LOAEL of 3 (maternal and offspring)	Not calculated	**Maternal:** 3: forelimb hair loss, marginal decreased weight gain, increased restlessness and scattering of pups **Offspring:** 3: decreased milk consumption, increased blood urea, slight increased mortality 6: increased mortality, hematological and blood chemistry changes, decreased surface righting reflex on PND 10, increased weight gain PND1–11 (post-natal treatment only

Study (References)	Method	NOAEL (mg/kg bw per day)	$BMDL_{10}$ for brain ChE inhibition (mg/kg bw per day)	Effects (mg/kg bw per day)
Chronic/ Carcinogenicity (Hellwig et al., 1986b; US EPA, 2002, 2006a)	65 Wistar rats/sex/dose fed diets containing 0, 5, 25 or 100 ppm (equal to 0, 0.25, 1.25, or 5 mg/kg bw per day) for 2 years; additional 20 animals/sex given 1 ppm equal to 0.05 mg/kg bw per day to assess ChE inhibition)	0.05 mg/kg bw/day based on ChE inhibition	0.22–0.31	≥ 0.25: decreased brain ChE and erythrocyte ChE, increased incidence of vascular tumors (combined hemangioma and hemangiosarcoma in the spleen, lymph node and skin) ≥ 1.25: decreased plasma ChE 5: transiently decreased body weight gain in males; increased mortality (females only near end of the study), increased anemia in males, increased leukocytes
2-generation reproduction - Sprague Dawley (Brooker et al., 1992; US EPA, 2004; APVMA, 2010)	28 Sprague Dawley rats/sex/dose fed 0, 1, 15 or 65 ppm (equal to 0.08, 1.2 or 5.46 mg/kg bw per day in males and 0, 0.09, 1.3 or 6.04 mg/kg bw per day for females) in diet for 2 generations; 2 litters per generation	0.08/0.09 males/females (parental) 1.2/1.3 males/females (reproductive, offspring)	0.3–0.7	**Parental:** ≥ 1.2/1.3: decreased brain and erythrocyte ChE 5.46/6.04: decreased plasma ChE **Reproductive:** 5.46/6.04: decreased fertility (both generations), decreased litter size (day 1 after birth). **Offspring:** 5.46/6.04: decreased brain ChE, decreased weight gains and increased mortality

Study (References)	Method	NOAEL (mg/kg bw per day)	$BMDL_{10}$ for brain ChE inhibition (mg/kg bw per day)	Effects (mg/kg bw per day)
2-generation reproduction – Wistar (Brooker et al., 1992; US EPA, 2004; APVMA, 2010)	25 Wistar rats/sex/dose fed 0, 0.2, 1.0 or 6.5 mg/kg bw per day in diet for 2 generations Brain ChE measured in pups of the controls and 6.5 mg/kg/day groups only	0.2 (parental) 6.5 (reproductive) 1.0 (offspring)	0.2–0.5	**Parental:** ≥ 1.0: decreased brain and erythrocyte ChE in males 6.5: decreased lactational weight gains in F1 females; focal vacuolization of epididymides in P and F1 males, decreased prostate weights, decreased secretion of prostate, increased vacuolization of cauda epididymides and diffuse epithelial atrophy of prostate gland in F1 males **Reproductive:** Reproductive performance unaffected. **Offspring:** 6.5: decreased weight gain in F1b; decreased brain ChE in F1b females PND 4 pups (10% decrease) (no effect seen in F1b PND 4 male pups, or in F2b PND 4 pups of both sexes)
Male-mediated reproduction (Farag et al., 2007)	20 male CD-1 mice/dose gavaged with 0, 7, 17 or 28 mg/kg bw per day 5 d/week; mated with untreated females	7 (parental and reproductive)	Not calculated	**Paternal:** ≥ 15: cholinergic signs; decreased brain and muscle ChE 28: decreased body weight and body weight gain **Reproductive:** ≥ 15: decreased absolute and relative testes weight; decreased fertility index; decreased sperm counts; increased degenerative changes in seminiferous tubules 28: decreased live fetuses per litter; increased dead fetuses per litter; increased early resorptions per litter

Study (References)	Method	NOAEL (mg/kg bw per day)	$BMDL_{10}$ for brain ChE inhibition (mg/kg bw per day)	Effects (mg/kg bw per day)
Prenatal Developmental Toxicity (Farag et al., 2006)	24–28 pregnant F344 rats gavaged with 0, 7, 15 or 28 mg/kg bw per day from GD 6–15	7 (maternal and fetal)	Not calculated	**Maternal:** ≥ 15: cholinergic toxicity; decreased brain ChE 28: decreased food consumption; decreased body weight gain, decreased percent weight gain; decreased absolute kidney weight **Fetal/Reproductive:** ≥ 15: decreased brain ChE; increased embryo lethality (post-implantation loss, total resoprtions); decrease in number of live fetuses; decreased mean fetal weight

BMDL: benchmark dose limit; ChE: cholinesterase; DNT: developmental neurotoxicity; GD: gestation day; NOAEL: no-observed-adverse-effect-level; PND: post-natal day

In addition to pup mortality and changes in motor activity, dimethoate also caused reproductive effects (decreased pregnancy rates, decreased litter size, decreased pup weight gain, prostate effects) in two 2-generation reproduction rat studies (Brooker *et al.*, 1992; Mellert et al., 2003; *US EPA, 2004;* APVMA, 2010; Health Canada, 2011). Dimethoate affected reproduction in both male and female mice. The reported effects were observed at oral dose levels (LOAEL of 15 mg/kg bw per day for both male and female mice) that were well above those at which brain ChE inhibition was observed in the database (Farag et al., 2006, 2007).

The available toxicology profile of omethoate is similar to that of dimethoate, but omethoate was a more potent ChE inhibitor in subchronic and chronic studies, with NOAEL values of 0.04 mg/kg bw per day for Wistar rats and 0.1 mg/kg bw per day for mice and a LOAEL of ≥ 0.125 mg/kg bw per day for Beagle dogs being reported (Hoffmann and Schilde, 1984; Schladt, 1995, 2001; Health Canada, 2011). Omethoate is also much more acutely toxic than dimethoate based on the median lethal dose 50% (LD_{50}) and median lethal concentration 50% (LC_{50}) values obtained in oral, dermal and inhalation studies (Table 6) (Health Canada, 2011). For both dimethoate and omethoate, clinical signs of acute toxicity were consistent with those of acute organophosphate poisoning (e.g., muscular fibrillation, salivation, lacrimation, urinary incontinence, diarrhea, respiratory distress, prostration, gasping, coma and death) (Health Canada, 2011).

TABLE 6: Acute toxicity values for dimethoate and omethoate

Acute Value (unit)	Species	Dimethoate	Omethoate	Reference
LD_{50} oral (mg/kg bw)	Rat	310–600	22–65	WHO, 2004; EFSA. 2006; Health Canada, 2011
LD_{50} oral (mg/kg bw)	Mouse	150–160	27–36	EFSA. 2006; APVMA, 2010; Health Canada, 2011
LD_{50} oral (mg/kg bw)	Rabbit	300	50	Health Canada, 2011
LD_{50} dermal (mg/kg bw)	Rabbit	>2000	No data	Health Canada, 2011
LD_{50} dermal (mg/kg bw)	Rat	>2000	145–232	APVMA, 2010; Health Canada, 2011
LC_{50} (mg/L)	Rat	>2	0.282	Health Canada, 2011

Omethoate was not teratogenic in two separate studies using pregnant Long Evans FB rats (20 to 24 per dose) and pregnant Wistar rats (25 per dose) gavaged with 0, 0.3, 1.0 or 3.0 mg/kg bw per day of omethoate on GD 6 through 15. However, in Long Evans rats, decreased fetal weight and increased resorptions were observed in the high-dose group in the presence of maternal toxicity. The NOAEL for maternal and developmental effects was 1.0 mg/kg bw per day (Bayer, 1975; Holzum, 1990a; Health Canada, 2011).

Developmental effects (decreased pup weight and increased postnatal loss) and reproductive effects (increased implantation loss, increased pre-coital interval, decreased litter size and increased epithelial vacuolation in epididymides of males) were seen in Wistar rats in the presence of parental toxicity in a 2-generation reproduction study using omethoate. The NOAEL was 0.5 ppm for developmental effects and 3 ppm for reproductive effects, while the LOAEL for parental effects was 0.5 ppm (Dotti et al., 1992; Health Canada, 2011). Developmental studies using rabbits showed increased incidence of contracted joints in pups of Himalayan rabbits but not of New Zealand White rabbits. In the absence of historical control data on Himalayan rabbits and a lack of a dose-response relationship, it is not certain whether the increase was due to omethoate. Other developmental effects included decreased fetal weight (Long Evans rats) and increased resorptions (Long Evans rats and Himalayan rabbits). However, developmental effects were reported in the presence of maternal toxicity (decreased maternal weight gain or decreased ChE activity) (Tesh et al., 1982; Holzum, 1990b; Health Canada, 2011).

2.5 Genotoxicity and carcinogenicity

The available genotoxicity studies with dimethoate yielded negative results, with the exception of a positive result reported in one in vitro Unscheduled DNA Synthesis (UDS) assay at cytotoxic levels (Health Canada, 2011).

Briefly, dimethoate was not genotoxic in several in vitro (Ames tests, Chinese hamster ovary/ hypoxanthine-guanine phosphoribosyltransferase (HGPRT)) gene mutation assay, UDS assay and in vivo (mouse dominant lethal assay, bone marrow cytogenic assay in rats, UDS assay) assays (Health Canada, 2011). Positive results were reported in one in vitro UDS assay but at cytotoxic levels; both a second in vitro UDS assay and an in vivo UDS assay using male Wistar rats were negative (Health Canada, 2011).

Overall, the weight-of-evidence indicates that dimethoate does not have genotoxic potential (Health Canada, 2011).

Although a 2-year study in which Wistar rats were given dimethoate at 0.5, 4 or 32 ppm (equivalent to 0.04/0.05, 0.30/0.44, 2.92/3.93 mg/kg bw per day in males/females) in drinking water showed an increased incidence of vascular tumours in males only (Health Canada, 2011, 2015). The results are considered equivocal based on the lack of a dose-response relationship, on the presence of tumours in one sex only, on marginal statistical significances, and on lower than expected incidences in control animals (4%) when compared to historical control data (16% and 22%).

The PMRA has concluded that dimethoate is unlikely to pose a carcinogenic risk to humans based on the weight of scientific evidence (Health Canada, 2015). No treatment-related tumorigenicity was evident in mice following chronic dietary exposure to dimethoate. Although there was an increased incidence of vascular tumours (combined hemangiomas and hemangiosarcoma in the spleen, lymph nodes and skin) in male rats in the dietary carcinogenicity study, these tumours achieved only marginal statistical significance, did not show a clear dose-response relationship, did not affect mortality, and were observed in one sex and species only. Furthermore, as previously noted, dimethoate is not considered to have genotoxic potential and the organophosphate class of chemicals do not show evidence of tumorigenicity of the vascular system.

The Australian Pesticides and Veterinary Medicines Authority (APVMA), analogous to the PMRA, did not consider dimethoate to be genotoxic or carcinogenic (APVMA, 2010).

The US EPA has classified dimethoate as "Group C - possible human carcinogen". This is based on equivocal hemolymphoreticular tumours in male B6C3F1 mice, the weak (no dose response) effect of combined spleen, skin and lymph tumours in male Wistar rats, and positive mutagenic activity (positive gene mutation and structural chromosome aberrations, bacterial mutation and clastogenic effects in vitro and in vivo) associated with dimethoate (US EPA, 1995, 2007). The International Agency for Research on Cancer (IARC) has not reviewed the carcinogenicity of dimethoate.

For omethoate, genotoxicity assays were mostly negative, except for positive results observed in an in vivo mouse spot test, a gene mutation assay at very high dose levels and in in vitro assays for DNA repair and sister chromatid exchange. No effects were observed in in vivo assays of DNA repair and sister chromatid exchange (Health Canada, 2011; NHMRC, NRMMC, 2011).

No carcinogenicity was evident in rats and mice following chronic dosing with omethoate (Health Canada, 2011). The APVMA did not consider omethoate to be genotoxic or carcinogenic (APVMA, 2011). Neither the US EPA nor the IARC have reviewed the carcinogenicity of omethoate.

2.6 Mode of action

Dimethoate causes neurotoxicity when it is activated in vivo to its oxon metabolite, omethoate (US EPA, 2004). Like other organophosphate pesticides, the oxon inhibits ChE through phosphorylation of the enzyme active site. This inhibition leads to an accumulation of acetylcholine and to the continuous stimulation of cholinergic receptors throughout the central and peripheral nervous systems resulting in cholinergic toxicity (US EPA, 2004).

The mode of action of dimethoate in causing pup mortality is not well understood (US EPA, 2006a).

2.7 Selected key endpoint

The toxicological database for dimethoate is extensive and includes prenatal developmental toxicity studies in rats and rabbits, two multi-generation reproduction studies, a DNT study, a comparative ChE study (examining fetuses, pups, pregnant animals and adult animals) and a special cross-fostering study (Health Canada, 2011). From these studies, two potential points of departure (POD) for dimethoate were identified: inhibition of brain ChE and pup mortality (Table 5).

ChE inhibition has been consistently seen in a wide variety of studies (sub-chronic and chronic dietary, developmental and reproductive, comparative ChE). Rats appeared to be slightly more sensitive than other species (i.e., mouse and dog) to ChE inhibition based on NOAEL/LOAEL values. Overall, no pronounced sex differences were apparent in the available database, despite a few studies in rats that showed females were slightly more sensitive than males to the inhibitory effects of dimethoate. Although no adverse maternal toxicity was seen in the DNT study, a dose-related increase in pup deaths was observed at ≥ 0.5 mg/kg bw per day (LOAEL) and was lower than the pup mortality observed in the DNT range-finding study (LOAEL = 6 mg/kg bw per day) and other reproductive studies.

The NOAEL for offspring in the main DNT study was determined by the US EPA and PMRA to be 0.1 mg/kg/day, based on increased pup death and increases in motor activity. In the companion ChE study, the NOAEL for ChE inhibition was 0.1 mg/kg/day following repeated administration; similar inhibition levels were seen in adults and young animals and there were no differences in the NOAELs among age groups. Overall, there was no indication of sensitivity of the fetus or young animals compared to parental animals across the database. At the lowest dose showing an effect on pup mortality, a comparable level of brain ChE inhibition (10% to 13%) was observed between subpopulations (pregnant dams, fetuses, 4-day old pups, 21-day old pups and adult rats exposed for 11 days). A cross-fostering gavage study of dimethoate in rats showed that pup mortality ensued from either prenatal exposure, post-natal exposure or combined pre- and post-natal exposure. The cross-fostering study therefore did not resolve whether pup mortality was due to maternal neglect or exposure to dimethoate (Myers, 2004; US EPA, 2004; Health Canada, 2011).

Benchmark dose (BMD) modelling was undertaken to better reflect the POD for the brain ChE inhibition responses as well as that of pup mortality. The BMD approach is a scientifically more advanced method compared to the NOAEL approach for deriving a POD, since it makes use of all of the available dose-response data from a given study (or studies if using data from multiple studies) and it provides a quantification of the uncertainties in the dose-response data. Detailed BMD calculations are available in Dimethoate: Issues Related to the Hazard and Dose Response Assessment jointly prepared by the US EPA and PMRA (US EPA, 2004). The dataset for BMD analyses was considered robust in that the similarity of protocols of several studies yielded replicate information. Further, rocbust dose-response curves were attainable from studies of varying modes of administration and durations. BMD analysis was undertaken using an exponential dose-response model and a lower confidence limit of 95% (BMDL). An increase of 5% above background (BMD_5) was considered the smallest detectable change for pup mortality. For brain ChE inhibition, a BMD_{10} was the limit of sensitivity for detecting a statistically significant decrease in ChE activity (Health Canada, 2011).

BMD_{10} (0.20 to 1.0 mg/kg bw per day) and $BMDL_{10}$ (0.2 to 0.7 mg/kg bw per day) values for brain ChE inhibition following repeated dosing did not show any age-related differences. $BMDL_{10}$ (1.3 to 2.0 mg/kg bw) estimates for brain ChE inhibition following single doses of dimethoate were also comparable for pups and adults (Table 5) (US EPA, 2004). PMRA selected a $BMDL_{10}$ for brain ChE inhibition of 0.2 mg/kg bw per day based on similar values obtained from several repeat-dose oral studies (i.e., 8-day exposures to adult male rats in the comparative cholinesterase gavage study, ~15-day exposures to pregnant dams in the range-finding gavage study, 2-year exposures in the chronic dietary study and > 3-month exposures in the multi-generation reproduction dietary study). The BMD analyses for brain ChE inhibition showed similar dose-response curves and BMD_{10} values for all ages following similar exposure durations (Health Canada, 2011).

With respect to potential pre- and post-natal toxicity, prenatal developmental toxicity studies in rats and rabbits provided no indication of increased susceptibility of rat or rabbit fetuses to in utero exposure to dimethoate or omethoate. Similarly, there was no indication of increased susceptibility in the offspring compared to parental animals in the reproduction studies. An increase in pup mortality in repeat-dose studies was observed, with the most sensitive study being the dimethoate DNT study, although no clear association could be made with a specific level of brain ChE inhibition. BMD modelling was undertaken to better reflect the point of departure for pup mortality. An increase of 5% above background (BMD_5) was considered the smallest detectable change for pup mortality. A meta-analysis of pup mortality in the dimethoate database yielded a BMD_5 of 1.1 mg/kg bw per day and a $BMDL_5$ of 0.64 mg/kg bw per day. The BMD analyses also indicated that use of the lower 95% confidence limit ($BMDL_{10}$ = 0.2 mg/kg/bw) for brain ChE inhibition would be protective to the $BMDL_5$ for pup mortality (Health Canada, 2011).

The PMRA and the US EPA jointly consulted the US Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA) Scientific Advisory Panel (SAP) regarding its dimethoate hazard and dose-response assessment and its BMD modelling (US EPA and Health Canada, 2004b; Health Canada, 2011). SAP agreed that while the underlying cause of pup mortality could not be determined from the data, the selection of brain ChE inhibition as a critical effect would be protective against pup mortality (FIFRA, 2005; US EPA, 2004; US EPA, 2006b; Health Canada, 2011).

In the prenatal developmental and reproductive toxicity studies, there was no indication of sensitivity of the fetus or young animal compared to parental animals. Similarly, based on BMD analyses for brain ChE inhibition data from the comparative ChE and DNT studies, juvenile animals exhibited similar sensitivity to brain ChE inhibition as adult animals following exposure to dimethoate. The BMD analyses also indicated that protection against brain ChE inhibition will also result in protection against pup mortality. This position was supported by a US EPA FIFRA Scientific Advisory Panel (2004). Therefore, although increased pup mortality was noted in the absence of maternal toxicity in the main DNT study (which did not assess ChE inhibition), brain ChE inhibition is considered to be the most sensitive endpoint for dimethoate toxicity, and is considered to be protective for the increased pup mortality noted in the main DNT study.

The PMRA has therefore identified the inhibition of brain ChE as the most sensitive indicator of dimethoate toxicity and the $BMDL_{10}$ of 0.2 mg/kg bw per day as the POD. This value is consistent with NOAELs of 0.2 mg/kg bw per day of dimethoate observed in human volunteer studies previously discussed in Section 2.3.

3.0 DERIVATION OF THE HEALTH-BASED VALUE

A BMD approach was used for the determination of the acceptable daily intake (ADI) rather than the NOAEL/LOAEL approach since it offers better dose-response characterization by including all experimental data to determine POD independently of pre-established dose level. The $BMDL_{10}$ of 0.2 mg/kg bw per day for ChE inhibition was selected as the basis for the current risk assessment as it was protective of both ChE inhibition and pup mortality. An uncertainty factor of 100 was applied to account for interspecies extrapolation (10-fold) and intraspecies variability (10-fold) (Health Canada, 2011).

Using this $BMDL_{10}$, the ADI for dimethoate (Health Canada, 2011) was calculated as follows:

$$\text{ADI} = \frac{0.2 \text{ mg/kg bw per day}}{100}$$

$$= 0.002 \text{ mg/kg bw per day}$$

where:

- 0.2 mg/kg bw per day is the $BMDL_{10}$, based on ChE inhibition; and
- 100 is the uncertainty factor, selected to account for interspecies variation (×10), intraspecies variation (×10).

Based on the ADI of 0.002 mg/kg bw per day, a health-based value (HBV) for dimethoate in drinking water was derived as follows:

$$\text{HBV} = \frac{0.002 \text{ mg/kg bw per day} \times 74 \text{ kg} \times 0.20}{1.53 \text{ L/day}}$$

$$= 0.02 \text{ mg/L (20 µg/L)}$$

where:

- 0.002 mg/kg bw per day is the ADI calculated using a $BMDL_{10}$ of 0.2 mg/kg bw per day (Health Canada, 2011);
- 74 kg is the adult body weight (Health Canada, 2021);
- 1.53 L per day is the daily volume of tap water consumed by an adult (Health Canada, 2021);
- 0.20 is the default allocation factor for drinking water (Krishnan and Carrier, 2013).

This document applies an additive approach for addressing omethoate in drinking water. Generally, when chemical residues (omethoate) are combined and expressed in parent equivalents (dimethoate), the residues are converted to stoichiometric equivalents by multiplying the chemical residue level by the molecular weight (MW) ratio (parent/residue). The MWs of dimethoate and omethoate are 229 g/mol and 213 g/mol, respectively. This yields a MW ratio of 229/213=1.075. Additionally, the available data showed that omethoate is a more potent ChE inhibitor than dimethoate. To account for this increased toxicity, omethoate (expressed as a stoichiometric equivalent) detected in source or drinking water should be multiplied by a toxicity adjustment factor (TAF). PMRA has calculated a TAF of 3 for omethoate based on ratios of dimethoate and omethoate benchmark doses derived from female rat brain ChE BMD_{10} responses (Health Canada, 2011). The resulting value for the concentration of omethoate (expressed as a dimethoate equivalent value) is added to the measured concentration of dimethoate. The sum of the detected concentrations of dimethoate and omethoate (with omethoate expressed as a dimethoate equivalent) should not exceed the MAC for dimethoate.

Below is a sample calculation showing the use of the TAF to convert omethoate into a dimethoate equivalent value and the summation of the omethoate (as dimethoate equivalent value) and dimethoate in order to compare the value to the MAC. The calculation assumes a measured concentration of 0.5 µg/L for omethoate and of 0.3 µg/L for dimethoate in drinking water.

Dimethoate equivalent value = omethoate measured value x MW ratio x TAF
= 0.5 µg/L x 1.075 x 3
= 1.6125 µg/L

Sum of dimethoate in example = Dimethoate value + Dimethoate equivalent value
= 0.3 µg/L + 1.6125 µg/L
= 1.9125 µg/L (rounded to 1.9 µg/L)

This sum (1.9 µg/L) is then compared to the MAC (20 µg/L).

4.0 ANALYTICAL AND TREATMENT CONSIDERATIONS

Information on analytical and treatment considerations is readily available for dimethoate, but is limited for omethoate. Standardized analytical methods are available for the analysis of dimethoate. However, none are available for omethoate and, therefore, a research method for analysis is presented. In terms of treatment, there are several studies on various technologies for dimethoate removal and only a few studies for the removal of omethoate by adsorption. As omethoate is formed through oxidation of dimethoate, the overall treatment approach should be to remove dimethoate while minimizing the formation of omethoate.

4.1 Analytical methods to detect dimethoate and omethoate

Standardized methods available for the analysis of dimethoate in source and drinking water and their respective MDLs are summarized in Table 7. MDLs are dependent on the sample matrix, instrumentation, and selected operating conditions and will vary between individual laboratories. These methods are subject to a variety of interferences, which are outlined in the respective references.

A number of accredited laboratories in Canada were contacted to determine the MDLs and MRLs for dimethoate analysis. The MDLs were in the lower range of those reported in Table 7. The MRLs were between 0.03 and 0.2 µg/L using modified EPA 8270; and 0.5 µg/L using modified EPA 8141 (ALS Environmental, 2019; CARO Analytical Services – Richmond Laboratory, 2019; Element Materials Technology Canada Inc., 2019; SGS Environmental Services, 2019).

The MDLs or MRLs from provincial and territorial data are in the range of 0.0001 to 10 µg/L (see Section 1.3).

Additional analytical methods that are not currently standardized are available for the measurement of dimethoate in water. These methods are based on high performance liquid chromatography (HPLC) with tandem mass spectrometry (Charalampous et al., 2015). MDLs similar to those of the standard methods listed below have been reported and these methods are suitable for use in commercial laboratories (Haiste-Gulde and Sacher, 2019).

There is no standardized method available for the detection of omethoate. A method developed by Cheminova A/S for the determination of dimethoate and omethoate in tap and surface water (US EPA, 2000a) was evaluated by the US EPA. The method is based on gas chromatography and mass spectroscopy and has a level of quantification of 0.05 µg/L. Although the US EPA recognizes that the method may be useful for analysis of omethoate (and dimethoate), they do not consider it an independently validated method (US EPA, 2000b). A few studies present methods for omethoate detection in water using HPLC that use various detection systems (Hayama et al., 2008; Ling et al., 2011; Zheng et al., 2016). A method using HPLC with tandem mass spectrometry was successfully demonstrated to detect a concentration of 0.05 µg/L with appropriate quality control (Hayama et al., 2008).

Drinking water utilities should discuss sampling requirements with the accredited laboratory conducting the analysis to ensure that quality control procedures are met and that MRLs are low enough to ensure accurate monitoring at concentrations below the MAC. Sample processing considerations for the analysis of dimethoate in drinking water (e.g., sample preservation, storage) can be found in the references listed in Table 7. It is important to note that quenching is critical if an oxidant is present in samples in order to prevent additional degradation of dimethoate or omethoate prior to analysis.

TABLE 7: Standardized analytical methods developed by the US EPA for the analysis of dimethoate in drinking water

Method[a] (Reference)	Methodology	MDL (µg/L)
Method 527 (US EPA, 2005)	Capillary Column Gas Chromatography/Mass Spectrometry (GC/MS)	0.025
Method 8141B (US EPA, 2000c)	Gas Chromatography	0.26
Method 8270D (US EPA, 1998)	Gas Chromatography/ Mass Spectrometry (GC/MS)	20 (estimated quantitation limit)

MDL: method detection limit

[a] All methods are subject to matrix interferences caused by contaminants that are co-extracted from the sample and present in solvents, reagents, and glassware. Interfering contamination may also occur when a sample containing low concentrations of analytes is analyzed immediately following a sample containing relatively high concentrations of analytes.

4.2 Treatment considerations

Treatment technologies that are available to effectively decrease dimethoate concentrations in drinking water include activated carbon adsorption, membrane filtration (nanofiltration [NF] and reverse osmosis [RO]) and biological filtration. Although chlorination can achieve 100% removal (Ormad et al., 2008; WHO, 2017), omethoate and other by-products are formed in the degradation process (Caregnato et al., 2013; Tian et al., 2014). At the residential scale, certified treatment devices relying on RO or activated carbon adsorption are expected to be effective for removal of dimethoate.

4.2.1 Municipal-scale treatment

The selection of an appropriate treatment process for a specific water supply will depend on many factors, including the raw water source and its characteristics, the operational conditions of the selected treatment method, and the water utility's treatment goals. Bench or pilot testing is recommended to ensure the source water can be successfully treated and optimal process design is established.

When using oxidation or advanced oxidation processes or biological processes for pesticide removal in drinking water, it is important to be aware of the potential for formation of by-products due to degradation of the target compound (Ikehata and Gamal El-Din, 2006; Beduk et al., 2012; Li et al., 2019a). Omethoate is an oxidation degradation by-product of dimethoate that is formed through treatment (oxidation), but there is minimal research on the removal of omethoate itself from water. Accordingly, the objective should be both to remove dimethoate and to select a treatment technology that will minimize the formation of omethoate and other by-products. With such an approach, subsequent removal of omethoate and other by-products should not be required. In addition, water utilities should consider the potential for the formation of disinfection by-products depending on the oxidant selected and the source water quality.

4.2.1.1 Conventional treatment

Conventional filtration (chemical coagulation, clarification, and rapid sand filtration) and chlorine disinfection will reduce dimethoate concentrations through oxidation during the disinfection step (Ormad et al., 2008). However, formation of by-products through oxidation may occur.

Coagulation and flocculation alone have limited effectiveness for removing dimethoate. A bench-scale study by Ormad et al. (2008) using river water with an initial dimethoate concentration of 1.108 µg/L and pH of 8.0 was conducted, comparing the removal efficiency with three different coagulant doses of aluminum sulphate (10 mg Al/L, 20 mg Al/L and 40 mg Al/L). Even with a high coagulant dose, a low removal efficiency of only 35% was achieved for all doses.

4.2.1.2 Activated carbon adsorption

Activated carbon adsorption is a widely used technology to reduce the concentration of micropollutants, including pesticides, in drinking water (Haist-Gulde and Happel, 2012; van der Aa et al., 2012). Activated carbon can be applied in two ways: in slurry applications using powdered activated carbon (PAC) or in fixed bed reactors with granular activated carbon (GAC) (Chowdhury et al., 2013).

Data generated through bench-scale testing to determine adsorption coefficients for pesticides are useful in predicting whether activated carbon adsorbs a particular pesticide (US EPA, 2011). In general, pesticides with an adsorption capacity constant (e.g., Freundlich coefficient) greater than 200 µg/g $(L/µg)^{1/n}$ are considered to be amenable to removal by carbon adsorption (Speth and Adams, 1993; Speth and Miltner, 1998; US EPA, 2011). However, it is important to note that the presence of natural organic matter (NOM) adds complexity to activated carbon treatment because NOM competes directly for adsorption sites or fouls the carbon by blocking pores (Chowdhury et al., 2013). Since the capacity of activated carbon can be affected by many factors, including the compound's ionic character and the solution pH, appropriate testing (e.g., jar tests, rapid small scale column tests) should be conducted to confirm removal.

A study by Brauch and Kühn (1988) states that the Freundlich isotherms for atrazine and dimethoate are similar and that the high value of Freundlich isotherm indicates that dimethoate is expected to be removed by activated carbon.

POWDERED ACTIVATED CARBON

Many pesticides have been found to strongly adsorb to PAC (Chowdhury et al., 2013), and its use offers the advantage of providing virgin carbon when required (e.g., during the pesticide application season) (Miltner et al., 1989). The capacity of PAC to remove pesticides by adsorption depends on its dose, its characteristics (type, particle size), the contact time, the adsorbability of the contaminant and the competition for adsorption sites from NOM (Haist-Gulde and Happel, 2012; Chowdhury et al., 2013).

Two bench-scale studies were conducted to evaluate the application of PAC in the removal of dimethoate; they are presented in Table 8. The study by Ormad et al. (2008) investigated several treatment options and found that removal by PAC was better than that observed for coagulation/flocculation. The study by Miguel et al. (2008) evaluated two different PACs with two types of water and found that one PAC performed better with distilled water, while the other performed better with natural water. This finding highlights the need to conduct jar tests to assess performance.

The removal of dimethoate from water depends on the water matrix, the PAC type and the contact time; the observed reduction rates ranged from 30% to 60% (Miguel et al., 2008; Ormad et al., 2008).

TABLE 8: Dimethoate removal via powdered activated carbon

Influent (µg/L)	PAC Dose (mg/L)	Removal	Process Description	Reference
1.108	10	60%	Bench-scale: Untreated river water: pH 8.0 Reaction time not provided	Ormad et al. (2008)
0.5	10 (wood-based)	40%	Bench-scale: Distilled water: pH 5.5; DOC = 0 Residence time = 10 min	Miguel et al. (2008)
0.5	10 (bituminous-based)	30%		
0.5	10 (wood-based)	35%	Bench-scale: Natural water: pH 8.0; DOC = 3 mg C/L Residence time = 10 min	
0.5	10 (bituminous-based)	45%		

DOC: dissolved organic carbon; PAC: powdered activated carbon

GRANULAR ACTIVATED CARBON

The use of GAC is an effective approach for treating organic contaminants that are regularly found in source water at concentrations of concern (Chowdhury et al., 2013). The capacity of GAC to remove pesticides by adsorption depends on its characteristics (type, particle size, reactivation method), the filter velocity, empty bed contact time (EBCT), the adsorbability of the contaminant, and the filter run time (Haist-Gulde and Happel, 2012). In addition, because GAC fixed bed adsorbers are typically operated on a continuous basis, the GAC can become fouled (or preloaded) with NOM and may be completely or partially ineffective for pesticide removal (Knappe et al., 1999; Summers et al., 2010; Haist-Gulde and Happel, 2012; Chowdhury et al., 2013).

A pilot-scale study was conducted evaluating removal of 33 organic pollutants (including dimethoate) using GAC (Summers et al., 2014). Four different waters with different pH and dissolved organic carbon (DOC) levels were evaluated and the results are presented in Table 9. The authors stated that dimethoate was moderately adsorbed by GAC.

TABLE 9: Dimethoate removal via granular activated carbon at pilot-scale (Summers et al., 2014)

Influent (ng/L)	Bed Volumes to 10% Breakthrough	Water	GAC	EBCT (min)	Bed Length (cm)	Operating Conditions
115 ± 27	70 000	Water type 1: DOC = 3.9 mg/L pH 7.0	Bituminous Mean particle diameter = 0.92 mm	7	58	Bed diameter = 25.4 mm Hydraulic loading = 5 m/h
	> 46 000			15	125	
	52 000	Water type 2: DOC = 2.8 mg/L pH 7.7	Bituminous Mean particle diameter = 1.29 mm	7.5	63	
	120 000	Water type 3: DOC = 2.1 mg/L pH 6.0	Bituminous Mean particle diameter = 0.92 mm	7	58	
	75 000	Water type 4: DOC = 1.7 mg/L pH 6.2				

DOC: dissolved organic carbon; EBCT: empty bed contact time; GAC: granular activated carbon

4.2.1.3 Membrane filtration

In general, NF and RO are effective pressure-driven membrane processes for the removal of pesticides from drinking water. Their effectiveness in removing pesticide is dependent on the membrane characteristics, pesticide properties, feed water composition, operating conditions and membrane fouling (Van der Bruggen and Vandecasteele, 2003; Plakas and Karabelas, 2012).

Since the main mechanism for pesticide removal using NF and RO membranes is size exclusion, the molecular weight cut-off (MWCO) of the membrane is an important characteristic. The molecular weight of dimethoate is 229 Da; membrane technology could be effective if the MWCO of the chosen membrane is appropriate. Retention of small pesticide molecules by larger pore-size membranes can also be influenced by the physicochemical interactions between the pesticide and the membrane surface (Plakas and Karabelas, 2012).

Three bench-scale studies investigated four different polyamide NF membranes (NF90, NF200, NF270 and DK) to assess removal of high concentrations of dimethoate from aqueous solutions (Ahmad et al., 2008a, 2008b; Tan et al., 2019). The membrane separation process can be affected by the surface morphology of the membrane (related to

roughness) and the pore-size distribution (related to the pore size and porosity) (Hilal et al., 2015). The membrane characteristics, along with the MWCO, are presented in Table 10. The first bench-scale study illustrated higher rejection with higher operating pressure and lower initial concentration of dimethoate (Ahmad et al., 2008a) (Table 11). The second study showed that for three of the membranes (NF200, NF270 and DK), an increase in pH resulted in increased rejection and decreased permeate flux (Ahmad et al., 2008a), while the fourth membrane (NF90) was relatively unaffected by changes in pH.

The bench-scale study by Tan et al. (2019) investigated removal of atrazine and dimethoate through four different feed waters (deionized, distilled, tap and river; Table 12). The dimethoate rejection results from the deionized and distilled waters were similar when compared to those of the previous studies conducted using deionized water. Increased dimethoate rejection was observed for tap and river waters, and the authors noted that this may be due to binding of other ions and NOM with dimethoate to form larger particles. Atrazine was found to have better rejection in all cases when compared to dimethoate, even though dimethoate has a larger molecular weight. This may be a result of dimethoate being more polar and less hydrophobic than atrazine, thereby decreasing the potential for rejection.

Bellona et al. (2004) present a flow-chart using the characteristics of the pesticide in water (e.g., molecular weight, log K_{ow}, molecular diameter) and those of the membrane properties (e.g., MWCO, pore size) to determine the potential for removal of dimethoate by membrane filtration. It is important to perform appropriate testing prior to full-scale implementation with membrane and source water under the proposed operating conditions to ensure that adequate dimethoate removal is occurring.

TABLE 10: Membrane characteristics used in studies to assess removal of high concentrations of dimethoate from aqueous solutions.

Membrane[a]	MWCO (Da)	Average Roughness (nm)	Average Porosity (%)	Average Pore Size (nm)
NF90	90[b,c]	22.7632[d]	17.1[d]	0.55[d]
NF200	—	2.7098[d]	15.5[d]	0.31[d]
NF270	150[c]	3.36[d]	11.7[d]	0.71[d]
DK	150–300[b]	—	—	0.55[e]

[a] Polyamide membranes

MWCO : molecular weight cut-off

[b] Li et al. (2019b)

[c] Zhu et al. (2007)

[d] Hilal et al. (2005)

[e] Kovács and Samhaber (2008)

TABLE 11: Dimethoate removal via nanofiltration

Influent (mg/L)	Rejection (%)[a,b]				Conditions	Process Description[c]	Reference
	NF90	NF200	NF270	DK			
2	85	55	25	75	P = 6 x 10^5 Pa	Bench-scale: Deionized water; 25 ± 2 °C Membranes surface charge at pH 7 is negative	Ahmad et al. (2008a)
	84	40	22	65	P =12 x 10^5 Pa		
20	85	60	35	80	P = 6 x 10^5 Pa		
	84	55	34	70	P =12 x 10^5 Pa		
10	80	42	22	41	P = 6 x 10^5 Pa pH 4		Ahmad et al. (2008b)
	82	55	38	40	pH 7		
	80	68	45	50	pH 9		
10 (10 mg/dm^3)	80	54	40	52	Deionized	Bench-scale: Investigation of dimethoate removal with four different waters (Table 12) P = 6 x 10^5 Pa	Tan et al. (2019)
	80	55	41	51	Distilled		
	85	70	48	58	Tap		
	87	70	50	58	River		

P: pressure

[a] Rejection estimated from graph

[b] Recovery not specified

[c] Effective membrane area = 1.46 x 10^{-3} m^2

TABLE 12: Composition of feed water used by Tan et al. (2019)

Parameter	Distilled Water (mg/L)	Tap Water (mg/L)	River Water (mg/L)
COD	Not detected	Not detected	20.3
Aluminum	0.013	0.075	0.011
Barium	12	15	21
Calcium	0.11	2.94	1.22
Chloride Ion	0.4	7.6	4.5
Chromium	0.006	0.015	0.020
Copper	0	4	3
Magnesium	0.01	2.24	3.20
Nitrate	0.1	0.2	0.3
Sulphate	1	18	12
Zinc	0.04	0.05	0.10
Lead	0.001	0.005	0.009

COD: chemical oxygen demand

4.2.1.4 Oxidation

Chemical oxidation using chlorine and ozone (O_3) can be effective in removing dimethoate from water depending on a variety of factors, including oxidant dose, contact time, disinfectant demand, temperature, and pH.

By-products that may be formed from the degradation of dimethoate through the use of chlorine are phosphorothioic acid, N-methyl-2-(methylthio) acetamide and omethoate (Tian et al., 2014). Omethoate was found to comprise 11% to 23% of the degraded dimethoate (see Section 1.1). Omethoate is of concern due to its health impacts as described in Section 2.0.

Several bench-scale studies evaluating various oxidants are presented in Table 13. Chlorine was found to have high removal (100%) in the study by Ormad et al. (2008). Ozone was evaluated through two bench-scale studies by the same authors, in which different removal efficiencies were observed (75% and 25%). The varying performance illustrates the need for pilot-scale testing.

A bench-scale study examining O_3 degradation of 23 pesticides found that dimethoate was easily degraded (Meijers et al., 1995). Under all conditions, the degradation of dimethoate achieved a minimum of 83% and a maximum of 97%.

Another bench-scale study was conducted to evaluate dimethoate degradation by chlorine and by-product formation under typical water treatment conditions (Tian et al., 2014). The authors found that bromide and humic acid accelerated the degradation of dimethoate by chlorine. Conversely, the presence of ammonia inhibited degradation due to the formation of monochloramine, which has lower reactivity with dimethoate than chlorine.

TABLE 13: Removal of dimethoate via oxidation

Oxidant	Influent (µg/L)	Initial Oxidant Dose (mg/L) or (g O_3/g DOC)	Removal	Process Description		Reference
Chlorine	1.108	18 mg/L (using NaClO)	100%	Bench-scale: Untreated river water; pH 8.0; Investigated removal of 44 pesticides including dimethoate Reaction time not provided		Ormad et al. (2008)
Ozone	1.108	4.3 mg/L	75%			
	0.5	3.0 mg/L	25%	Bench-scale: River water; pH 8.0; Conductivity 750 µS/cm; DOC = 3 mg/L; Alkalinity = 200 mg $CaCO_3$/L Investigated removal of 44 pesticides including dimethoate Reaction time not provided		Ormad et al. (2010)
	0.9-6.4[a]	0.53 g/g	83%	pH = 7.2; 5 °C; C^*t_{10} = 2.0	Bench-scale: River water; DOC = 2.2 mg C/L; Br^- = 100 µg/L, HCO_3^- = 1.6 mM; 23 pesticides	Meijers et al. (1995)
		0.55 g/g	85%	pH = 7.2; 20 °C; C^*t_{10} = 1.0		
		0.95 g/g	96%	pH = 8.3; 20 °C; C^*t_{10} = 1.0		
		1.0 g/g	97%	pH = 7.2; 5 °C; C^*t_{10} = 7.3		
		1.0 g/g	97%	pH = 7.2; 20 °C; C^*t_{10} = 3.3		
		1.0 g/g	97%	pH = 8.3; 20 °C; C^*t_{10} = 1.1		

C^*t_{10} – Disinfection criterion (mg*min/L); DOC: Dissolved organic carbon

[a] A range of initial concentrations for all 23 pesticides was provided rather than an exact concentration.

REMOVAL OF OMETHOATE

Ling et al. (2011) performed batch experiments on a 1.0 mg/L omethoate solution to determine the degradation by O_3 alone as well as with a catalyst. The catalysts that were used in the study were activated carbon (AC) and Fe(III) deposited on activated carbon (Fe-AC). The removal percentages of omethoate under various conditions are presented in Table 14. It was found that the best removal efficiency was for ozone with 5% Fe-AC combined and that removal was much higher than that for ozone alone. The authors examined each catalyst individually without O_3 to determine whether omethoate was being removed by adsorption, and both exhibited poor removal efficiencies. Therefore, the authors concluded that O_3 in the presence of Fe-AC resulted in the formation of hydroxyl radicals, and it was these radicals that degraded the omethoate.

A later study investigated reaction rates for omethoate degradation using O_3 and hydroxyl radicals (Qiang et al., 2013). Omethoate degraded more slowly with the use of ozone (0.04 $M^{-1}s^{-1}$) than with the use of hydroxyl radicals ($5.3x10^8$ $M^{-1}s^{-1}$) at a pH of 7.5 and temperature of 20 °C. The authors stated that the presence of the catalyst, Fe-AC, generated hydroxyl radicals from O_3, resulting in the improved degradation of omethoate than achieved by ozone alone.

TABLE 14: Removal percentage of omethoate under various conditions

Oxidant	Influent Omethoate (mg/L)	Initial Oxidant Dose (mg/L)	Catalyst (or Oxidant) Added	Removal	Process Description	Reference
Ozone	1.0	1.0	None	37.6%	Bench-scale study; Reaction time = 30 min; pH 7.5; 20 ± 2 °C	Ling et al., 2011
			20 mg/L AC	58.0%		
			20 mg/L 5% Fe-AC	82.4%		
None		—	20 mg/L AC	6.5%		
			20 mg/L 5% Fe-AC	5.7%		

AC: activated carbon; Fe-AC: Fe(III) deposited on activated carbon

4.2.1.5 Biological treatment

Biological treatment involves targeting the removal of the biodegradable organic material fraction. The effectiveness of biological treatment depends, therefore, on the initial concentration, source water properties, the microbial community, the contact time, the soil properties and the temperature (Drewes et al., 2009; Diem et al., 2013). The main biological treatment processes for drinking water include riverbank filtration (RBF), rapid granular media filtration without the maintenance of a disinfectant residual across the bed, and slow sand filtration.

RIVERBANK FILTRATION

Riverbank filtration (RBF) involves locating vertical or horizontal water supply wells near a river in order to use the riverbank and adjacent aquifer as a natural filter to remove contaminants. As water proceeds to the groundwater table, contaminant concentrations are lowered through adsorption, biodegradation and dilution with groundwater (Piet and Zoeteman, 1980; Bize et al., 1981; Kuehn and Mueller, 2000; Ray et al., 2002). Natural attenuation through RBF is one of the most basic and inexpensive methods of water treatment (Verstraeten and Heberer, 2002; Sørensen et al., 2006).

Several studies were conducted to evaluate organic micropollutant (OMP) removal through RBF (Bertelkamp et al., 2015; Bertelkamp et al., 2016a, 2006b). Two different oxic soils and one suboxic/anoxic soil were used in these studies and the properties are presented in Table 15.

TABLE 15: Soil properties used in riverbank filtration (RBF) studies

Parameter	Oasen (oxic)	Vitens (oxic)	Vitens (suboxic/deep anoxic)
Porosity	0.35	0.33	—
Cation exchange capacity (meq/kg dry wt)	9.19	42.13	14.07
Clay (v/v%)	0.50	3.72	1.71
Silt (v/v%)	0.52	3.58	2.50
Sand (v/v%)	98.98	92.69	95.79
d_{medium} (µm)	330.62	380.38	394.84

The first pilot-scale study was conducted to determine the effects of soil type (Bertelkamp et al., 2015) (Table 16). River water spiked with a mixture of 20 OMPs (including dimethoate), each at a concentration of 0.5 µg/L, was used in two pilot tests with different soils, namely Oasen and Vitens. The authors concluded that the microbial community composition seems to be mainly determined by aqueous phase rather than soil type, which is evidenced by the fairly similar biodegradation rates for dimethoate between the two soils (0.42 and 0.37 day^{-1}). From the biodegradation rates, the authors also estimated a 99% dimethoate removal. The required residence time in the oxic zone would be approximately 11.6 days and 13.1 days for the Oasen and Vitens soils, respectively. Prior to moving into the anoxic zones, the water only remains within the oxic zone of an RBF system for the first couple of hours to days (site-dependent) so that less removal of dimethoate would be expected.

A column study was conducted to determine impact on degradation rate under different conditions (Bertelkamp et al., 2016a). Four river feed waters with different organic fractions (hydrophilic, hydrophobic, transphilic and river water organic matter [RWOM]) were used in the evaluation. Three different phases were studied to simulate stable, OMP shock-load and DOC shock-load operations. The first phase represented the RBF under stable operation and had a similar biodegradation rate to that of the previous study. The second phase, with higher initial concentrations of OMPs, resulted in a higher degradation rate for dimethoate. The third phase had differing results depending on the water used.

A pilot-scale study using river water was carried out using three different pilot set-ups to investigate degradation in different redox zones (Bertelkamp et al., 2016b). The first pilot was to evaluate degradation in the oxic zone, the second in the suboxic zone and the third in the anoxic zone. For dimethoate, the highest degradation rate occurred in the oxic zone.

TABLE 16: Removal of dimethoate via riverbank filtration (RBF)

Influent (µg/L)	Biodegradation rate (day^{-1})	Column[a] Set-up/Soil	Process Description		Reference
0.5	0.42	Pilot A: 2 columns in series/Oasen	Pilot-scale study; River water: mixture of 20 OMPs – 0.5µg/L each; Hydraulic loading rate = 0.5 L/d		Bertelkamp et al. (2015)
	0.37	Pilot B: 2 columns in series/Vitens			
0.5	0.55 Hydrophilic 0.22 RWOM 0.39 Transphilic	Phase 1 (Stable operation): 1 column/Oasen	0.5 µg/L each OMP DOC = 4 mg/L	Column study: River water; mixture of 20 OMPs Loading rate = 0.2 L/d	Bertelkamp et al. (2016a)
2	0.60 Hydrophilic 0.42 RWOM 0.43 Transphilic 0.36 Hydrophobic	Phase 2 (OMP shock-load): 1 column/Oasen	2 µg/L each OMP DOC = 4 mg/L		
2	0.45 Hydrophilic 1.01 Transphilic	Phase 3 (DOC shock-load): 1 column/Oasen	2 µg/L each OMP DOC = 8 mg/L		
0.5	0.39	Pilot A (Oxic): 2 columns in series/ Vitens	Pilot-scale study: River water: pH 8.01 ± 0.28; DOC = 3.81 ± 0.74 mg/L; NO_3^- = 8.60 ± 3.05 mg/L; PO_4^{3-} = 0.07 ± 0.07 mg/L; Cl^- = 56.32 ± 18.74 mg/L; SO_4^{2-} = 46.95 ± 9.63 mg/L; NH_4^+ = 0.08 mg/L; K^+ = 3.71 ± 0.80 mg/L; Mg^{2+} = 10.79 ± 1.79 mg/L; Ca^{2+} = 52.63± 14.69 mg/L; Mixture of 15 OMPs Hydraulic loading rate = 0.5 L/day		Bertelkamp et al. (2016b)
	0.06	Pilot B (Suboxic): 10 columns in series (Vitens: first 4 oxic/ last 6 suboxic/ anoxic)			
	0.11	Pilot C (Anoxic): 22 columns in series (Vitens: first 4 oxic/ last 18 suboxic/ anoxic)			

DOC: dissolved organic carbon; OMP: organic micropollutant; RWOM: river water organic matter

[a] Column: L = 1 m; D = 36 mm; transparent PVC.

ENGINEERED BIOLOGICAL FILTRATION

Engineered biological filtration involves the use of granular media filters (i.e., anthracite/ sand or GAC) without the maintenance of a disinfectant residual across the bed. Biological activity within the filters can be influenced by a number of factors, including water quality, temperature, oxidant dose and type, and backwashing procedures (Huck et al., 2001).

A full-scale study investigating two different treatment trains was conducted to determine the impact on dimethoate removal (Yang et al., 2019). The treatment trains varied in the location of the sand filter in relation to the biologically active carbon (BAC) (Table 17). The influent concentrations were very low, but in both treatment trains, dimethoate was removed by the BAC. A bench-scale study was conducted to evaluate the overall performance of biological filters in removing 34 OMPs (Zearley and Summers, 2012) including dimethoate. The influent concentration used in this study was quite low; however, good removal of dimethoate occurred, with increasing removal at the higher EBCT.

TABLE 17: Removal of dimethoate via biological filtration

Influent (µg/L)	Removal or Effluent Concentration	EBCT (min)	Overall Process Description	Reference
8.65 ng/L	6.43 ng/L	16	Full-scale: in operation for 47 months; 4 x 10^5 m^3/day capacity; 4-month study Raw water: turbidity 18.8–46.0 NTU; COD 4.50 – 6.84 mg/L Flow rate through BAC = 8.3 m/hr Treatment train: preO_3-coagulation-sedimentation-sand filtration-postO_3-BAC	Yang et al. (2019)
12.59 ng/L	5.13 ng/L		Full-scale: in operation for 33 months; 3 x 10^5 m^3/day capacity; 4-month study Raw water: turbidity 18.8–46.0 NTU; COD 4.50 – 6.84 mg/L Flow rate through BAC = 8.3 m/hr Treatment train: preO_3-coagulation-sedimentation-postO_3-BAC-sand filtration	
0.038	75%	7.9	Bench-scale study: dechlorinated tap water; spiked to TOC 3 mg/L; pH 7.7; alkalinity 40 mg/L as $CaCO_3$ 2 columns in series: each column: 11 mm inner diameter; 32 cm high Sand media: biologically active from full-scale plant; 0.45 mm effective size Hydraulic loading rate of 2.4 m/hr; temperature = 20 ± 2 °C	Zearley and Summers (2012)
	81%	15.8		

BAC: biologically active carbon; COD: chemical oxygen demand; EBCT: empty bed contact time; NTU: nephelometric turbidity unit; TOC: total organic carbon.

4.2.1.6 Combined technologies

A full-scale study examining two different treatment trains showed removal of dimethoate for the different processes (Yang et al., 2019). One treatment train had the sand filter prior to ozonation and BAC, whereas the other had the sand filter after the BAC (Table 18).

TABLE 18: Full-scale study showing two different treatment trains for dimethoate removal (Yang et al., 2019)

Influent (ng/L)	Effluent (ng/L)	Treatment Stage	Other Parameter Information	Overall Process Description
35.17	30.19	Sedimentation	Turbidity[a]: Raw water = 31 NTU Effluent water = 0.12 NTU COD: Raw water = 3.96 mg/L Effluent water = 1.56 mg/L	Full-scale: In operation for 47 months; 4 x 10^5 m^3/day capacity; 4-month study Treatment train: preO_3-coagulation-sedimentation-sand filtration-postO_3-BAC PreO_3 dose 0.5 mg/L; aluminum sulphate dose = 40 mg/L; sedimentation time = 105 min; sand filtration velocity = 7.9 m/h; post O_3 dose = 1 mg/L; BAC EBCT = 16 min and flow rate = 8.3 m/hr
	9.40	Sand filtration		
	8.65	Post-ozonation		
	6.43	BAC		
17.08	18.17	Sedimentation	Turbidity[a]: Raw water = 31 NTU Effluent water = 0.04 NTU COD: Raw water = 3.92 mg/L Effluent water = 1.72 mg/L	Full-scale: In operation for 33 months; 3 x 10^5 m^3/day capacity; 4-month study Treatment train: preO_3-coagulation-sedimentation-postO_3-BAC-sand filtration PreO_3 dose 0.5 mg/L; aluminum sulphate dose = 40 mg/L; sedimentation time = 105 min; sand filtration velocity = 7.9 m/h; post O_3 dose = 1 mg/L; BAC EBCT = 16 min and flow rate = 8.3 m/hr
	12.59	Post-ozonation		
	5.13	BAC		
	3.47	Sand filtration		

COD: chemical oxygen demand; BAC: biologically active carbon; EBCT: empty bed contact time; NTU: nephelometric turbidity unit.

[a] Estimated from graph

The bench-scale study by Ormad et al. (2008) evaluated pre-oxidation by O_3 and chlorine, coagulation and adsorption using PAC as discussed in the previous sections. As part of this study, they also investigated combinations of these technologies (Table 19). Wherever chlorine was one of the applied processes, 100% removal of dimethoate always occurred; however, formation of by-products should be considered. The technology providing the worst removal of dimethoate was that of coagulation.

TABLE 19: Bench-scale study by Ormad et al. (2008) showing oxidation, coagulation, adsorption and combination of technologies

Influent (µg/L)	Removal (%)	Treatment Type	Overall Process Description
1.108	100	Chlorine	Bench-scale study River water: Chlorine demand of 18 mg Cl_2/L; pH of 8.0 Description of treatment processes: 1. Ozone dose = 4.3 mg O_3/L 2. Chlorine dose = 18 mg Cl_2/L (NaClO) 3. PAC dose = 10 mg/L 4.Coagulation doses = 10, 20 and 40 mg Al/L Reaction times not provided
	100	Chlorine + coagulation (10 mg Al/L)	
	100	Chlorine + coagulation (20 mg Al/L)	
	75	Ozone	
	75	Ozone + coagulation (20 mg Al/L)	
	85	Ozone + coagulation (40 mg Al/L)	
	60	PAC	
	75	Ozone + PAC	
	35	Coagulation (10 mg Al/L)	
	35	Coagulation (20 mg Al/L)	
	35	Coagulation (40 mg Al/L)	
	100	Chlorine + PAC + coagulation (20mg Al/L)	
	95	Ozone + PAC + coagulation (20 mg Al/L)	

PAC: powdered activated carbon

4.2.2 Residential-scale treatment

In cases where dimethoate removal is desired at the household level (e.g., when a household obtains its drinking water from a private well), a residential drinking water treatment unit may be an option for decreasing dimethoate concentrations in drinking water. Before a treatment unit is installed, the water should be tested to determine the general water chemistry and the dimethoate concentration in the source water.

To verify that a treatment unit is effective, water entering and leaving the treatment unit should be sampled periodically and submitted to an accredited laboratory for analysis. Units can lose removal capacity through use and time and need to be maintained and/or replaced. Consumers should verify the expected longevity of the components in the treatment unit according to the manufacturer's recommendations and service it when required. Systems classified as residential scale may have a rated capacity to treat volumes greater than that needed for a single residence, and thus may also be used in small systems.

Health Canada does not recommend specific brands of drinking water treatment units, but it strongly recommends that consumers use units that have been certified by an accredited certification body as meeting the appropriate NSF International Standard/ American National Standard (NSF/ANSI) for drinking water treatment units. The purpose of

these standards is to establish minimum requirements for the materials, design and construction of drinking water treatment units that can be tested by a third party. This ensures that materials in the unit do not leach contaminants into the drinking water (i.e., material safety). In addition, the standards include performance requirements that specify the removal that must be achieved for specific contaminants (e.g., reduction claim) that may be present in water supplies. Certification organizations (i.e., third party) provide assurance that a product conforms to applicable standards and must be accredited by the Standards Council of Canada (SCC). Accredited organizations in Canada include the following:

- CSA Group
- NSF International
- Water Quality Association
- UL LLC
- Bureau de normalisation du Québec (available in French only)
- International Association of Plumbing and Mechanical Officials
- Truesdail Laboratories Inc.

An up-to-date list of accredited certification organizations can be obtained from the SCC.

The drinking water treatment technologies that are expected to be effective for dimethoate removal at the residential-scale include adsorption and RO. Currently, dimethoate is not included in the performance requirements (e.g., reduction claims) of NSF/ANSI standards. However, consumers can use a treatment unit that is certified to the standards for adsorption or reverse osmosis to ensure that the material safety has been tested.

Water that has been treated using RO may be corrosive to internal plumbing components. Therefore, these units should be installed only at the point-of-use. Also, as large quantities of influent water are needed to obtain the required volume of treated water, these units are generally not practical for point-of-entry installation.

5.0 MANAGEMENT STRATEGIES

All water utilities should implement a risk management approach, such as the source-to-tap or water safety plan approach, to ensure water safety (CCME, 2004; WHO, 2012, 2017). These approaches require a system assessment to characterize the source water, describe the treatment barriers that prevent or reduce contamination, identify the conditions that can result in contamination, and implement control measures. Operational monitoring is then established, and operational/management protocols are instituted (e.g., standard operating procedures, corrective actions and incident responses). Compliance monitoring is determined and other protocols to validate the water safety plan are implemented (e.g., record keeping, consumer satisfaction). Operator training is also required to ensure the effectiveness of the water safety plan at all times (Smeets et al., 2009).

5.1 Monitoring

Dimethoate can be present in groundwater and surface water in areas where it is being used depending on the type and extent of its application, environmental factors (e.g., amount of precipitation, soil type, hydrogeological setting) and environmental fate (e.g., mobility, leaching potential, degradation) in the surrounding area. Water utilities should consider the potential for dimethoate to enter source water (e.g., raw water supply to the drinking water system) based on site-specific considerations.

When it is determined that dimethoate may be present and monitoring is necessary, surface and groundwater sources should be characterized to determine the concentration of dimethoate. This should include monitoring of surface water sources during periods of peak use and rainfall events and/or annual monitoring of groundwater. Where baseline data indicate that dimethoate is not present in source water, monitoring may be reduced.

Where treatment is required to remove dimethoate, operational monitoring should be implemented to confirm whether the treatment process is functioning as required. The frequency of operational monitoring will depend on the water quality, fluctuations of the raw water concentrations and the treatment process. Responsible authorities should be aware of the impact of NOM on activated carbon systems, as it may impact water quality objectives for dimethoate removal.

Where treatment is in place for dimethoate removal, compliance monitoring (i.e., paired samples of source and treated water to confirm the efficacy of treatment) should be conducted, at a minimum, on an annual basis. When a treatment process is utilized in the

presence of dimethoate (i.e. oxidation or chlorination), monitoring of omethoate should be conducted as it is a by-product of dimethoate that is of health concern and is used to calculate the equivalent dimethoate concentration (see Section 3.0). The sum of these should not exceed the MAC for dimethoate. Monitoring of other degradation by-products should also be considered.

6.0 INTERNATIONAL CONSIDERATIONS

Other national and international organizations have drinking water guidelines, standards and/or guidance values for dimethoate and omethoate in drinking water. Variations in these values can be attributed to the age of the assessments or to differing policies and approaches (e.g., BMDL vs NOEL/NOAEL), including the choice of key study and the use of different consumption rates, body weights and source allocation factors (Table 20).

Australia's National Health and Medical Research Council has set a guideline value of 0.007 mg/L for dimethoate in drinking water based on ChE inhibition observed in humans and a value of 0.001 mg/L for omethoate based on inhibition of AChE in a 2-year rat study. For dimethoate, the WHO has a guideline value of 0.006 mg/L (6 µg/L) based on potential effects on reproductive performance in rats (WHO, 2017). The US EPA states that it has made a determination not to regulate dimethoate in drinking water because it thought it did not occur at levels and frequencies of public health concern (US EPA, 2016). Neither the US EPA nor the WHO has a guideline value for omethoate (US EPA, 2006b).

TABLE 20: Comparison of international drinking water values for dimethoate and omethoate

Agency (Year)	Value (mg/L)	Key Endpoint	$BMDL_{10}$/ NO(A)EL (mg/kg bw/d)	UF	ADI (mg/ kg bw/d)	BW (kg)	DW Intake (L/d)	AF (%)	Comments
Health Canada - MAC (2020)	0.02	ChE inhibition	0.2 ($BMDL_{10}$)[a]	100	0.002	74	1.53	20	Omethoate levels in drinking water are addressed using an additive approach and not a separate MAC
WHO (2003)	0.006	Reproductive performance in rats	1.2 (NOAEL)	500	0.002	60	2	10	UF based on 10 for intra species, 10 for interspecies and 5 for concern regarding whether NOAEL could be a LOAEL. (WHO, 2017)
Australia (2010)	0.007	ChE inhibition in 57-day human volunteer study	0.2 (NOEL)	100	0.02	70	2	10	ADI was established in 1988. No reference given for key study.
Australia (2011) Omethoate	0.001	ChE inhibition in 2-year rat study	0.04 (NOEL)	100	0.0004	70	2	10	ADI was established in 2005. No reference given for key study.
EU (2019)	0.1 µg/L	Omethoate and dimethoate are not approved for use by the European Union (EC, 2019).							

ADI: acceptable daily intake; AF: allocation factor; BMDL: benchmark dose limit; BW: body weight; ChE: cholinesterase; DW: drinking water; LOAEL: lowest-observed-adverse-effect-level; NOAEL: no-observed-adverse-effect-level; NOEL: No-observed-effect-level; UF: uncertainty factor

[a] Benchmark dose (BMD) modelling offers a better dose-response characterization than NOEL/NOAEL approaches since all experimental data are used to determine the PODs rather than pre-established dose levels as is the case with NOEL/NOAEL approaches.

7.0 RATIONALE

Dimethoate is a broad spectrum organophosphate pesticide registered in Canada to control a wide range of insects and mites on both agricultural and non-agricultural sites. Despite its widespread use in Canada, data provided by provinces and territories that monitor for dimethoate in source and drinking water indicate that when detected, levels of dimethoate are well below the MAC. The main target of dimethoate is the inhibition of ChE, although increased pup mortality is also a concern. The anticholinesterase activity of dimethoate is due to its metabolite omethoate. Omethoate is also a major environmental degradate of dimethoate and can be produced during drinking water treatment.

Health Canada, in collaboration with the Federal-Provincial-Territorial Committee on Drinking Water, developed a MAC of 0.02 mg/L (20 µg/L) for dimethoate based on the following considerations:

- An HBV of 0.02 mg/L (20 µg/L) based on ChE inhibition in several repeat-dose animal studies;
- The MAC would be protective of both ChE inhibition and pup mortality observed in several repeat-dose animal studies;
- The additive approach for omethoate is protective of health in cases where omethoate is detected in source or treated water;
- Dimethoate and omethoate can be accurately measured at concentrations well below the MAC;
- Drinking water treatment technologies are available to remove dimethoate to below the MAC; and
- Omethoate can be reduced by controlling or minimizing its formation.

The MAC for dimethoate and cumulative approach for omethoate are protective of potential health effects from dimethoate and omethoate exposure. As part of its ongoing guideline review process, Health Canada will continue to monitor new research in this area, including the outcomes of the PMRA's evaluations, and recommend any change to this guideline technical document that it deems necessary.

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APPENDIX A: LIST OF ABBREVIATIONS

AC	Activated carbon
AChE	Acetylcholinesterase
ADI	Acceptable daily intake
AHS	Agricultural Health Study
ANSI	American National Standards Institute
APVMA	Australian Pesticides and Veterinary Medicines Authority
BAC	Biologically active carbon
BMD	Benchmark dose
BMDL	Benchmark dose lower limit
BW	Body weight
CDW	Federal-Provincial-Territorial Committee on Canadian Drinking Water
ChE	Cholinesterase
CI	Confidence interval
COD	Chemical oxygen demand
DNT	Developmental neurotoxicity
DOC	Dissolved organic carbon
DW	Drinking water
EBCT	Empty bed contact time
Fe-AC	Fe(III) deposited on activated carbon
FIFRA	Federal Insecticide, Fungicide, and Rodenticide Act
FNIHB	First Nations and Inuit Health Branch
GAC	Granular activated carbon
GD	Gestation day
HBV	Health-based value
HL	Hodgkin lymphoma
HPLC	High performance liquid chromatography
HR	Hazard ratio
IARC	International Agency for Research on Cancer

LC_{50}	Median lethal concentration
LD_{50}	Median lethal dose
LOAEL	Lowest-observed-adverse-effect-level
MAC	Maximum acceptable concentration
MDL	Method detection limit
MRL	Method reporting limit
MWCO	Molecular weight cut-off
NAPP	North American Pooled Project
NF	Nanofiltration
NOAEL	No-observed-adverse-effect-level
NOEL	No-observed-effect-level
NOM	Natural organic matter
NSF	NSF International
OMP	Organic micropollutant
OR	Odds ratio
PAC	Powdered activated carbon
PMRA	Pest Management Regulatory Agency
PND	Postnatal day
POD	Point of departure
RBF	Riverbank filtration
RO	Reverse osmosis
RWOM	River water organic material
SAP	Scientific Advisory Panel
SCC TAF:	Standards Council of Canada Toxicity adjustment factor
UDS	unscheduled DNA synthesis
UF	Uncertainty factor
US EPA	United States Environmental Protection Agency
WHO	World Health Organization

APPENDIX B: CANADIAN WATER QUALITY DATA

TABLE B: Levels of dimethoate and transformation products in Canadian sources from the Environment Canada National Water Quality Surveillance Program (2003–2005)

Jurisdiction (year sampled)	No. Detects/ Samples	MDL (ng/L)	Range (ng/L)	
			Min	Max
Surface Water				
BC – Lower Fraser Valley and Okanagan Basin (2003–2005)	15/85	0.075	<0.075	604
BC – Lower Fraser Valley (2003–2005)	—	—	1.4	604
BC – Lower Fraser Valley (2003–2005)[a]	—	—	0.02	233
ON (2004)	10/228	25.1	28.9	175
ON (2005)	2/160	25.1	24.7	33
ON – 10 isolated lakes (2003–2005)	31/163	0.023	<0.023	5.87
QC (2003)	1/50	40	<40	280
QC (2004)	6/69	5–40	<5	90
QC (2005)	0/62	40	—	—
NB (2003–2005)	4/57	40–450	—	—
PEI (2003–2005)	0/82	50	—	—
NS (2003–2005)	0/19	40	—	—
Rivers				
AB, SK, MB – 8 sites (2003)	0/13	25.1	—	—
Reservoir Water				
AB, SK, MB – 15 sites (2003–2004)	1/30	25.10	5.98	25.1
Runoff				
BC – Lower Fraser Valley (2003–2005)	—	—	200	3000
BC – Okanagan Basin (2003–2005)	—	—	1.2	17.5
Air				
ON – 4 sites (2004–2005)	0/12	0.007	<0.007	—

MDL : method detection limit

[a] Represents transformation product diazinon-oxon

Note: *Adapted from Environment Canada, 2011*