GUIDELINES FOR

CANADIAN DRINKING WATER QUALITY

BROMOXYNIL

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GUIDELINE VALUE: **The maximum acceptable concentration (MAC) for bromoxynil in drinking water is 0.03 mg/L (30 µg/L).**

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 bromoxynil completed by Health Canada's Pest Management Regulatory Agency and supporting documents.

Exposure

Bromoxynil is a registered herbicide used to control broadleaf weeds in food and feed crops. In 2018 (the most recent year for which data are available), more than 1 million kilograms of bromoxynil were sold in Canada. Bromoxynil may be released into the environment as surface run-off, through spray drift or while adsorbed to dust particles.

Canadian data indicate that bromoxynil is not commonly found in source or drinking water but may be found at low levels in source and drinking water in agricultural areas where it is applied. Bromoxynil is rarely detected in foods.

Health effects

Animal studies indicate that bromoxynil primarily targets the liver. At higher doses, bromoxynil has been found to cause developmental effects (skeletal effects, decreased pup weight) but no reproductive effects. There are no human studies on the effects of bromoxynil on the liver. The MAC of 0.03 mg/L (30 µg/L) is based on an increase in clinical signs (i.e., effects founded on actual observation as distinguished from theoretical or experimental effects; panting, salivation, liquid feces, pale gums) and liver weight, as well as decreases in body weight and body weight gain observed in a one-year dog study.

Analytical and treatment considerations

The establishment 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 bromoxynil in water at concentrations well below the MAC.

At the municipal level, there is limited information on the efficiency of treatment technologies to remove bromoxynil from drinking water. Oxidation, advanced oxidation processes and biofiltration achieved a wide range of removals. Activated carbon adsorption and membrane processes are expected to be effective. Although bromoxynil may be removed using oxidation, utilities should be aware of the potential formation of degradation by-products. Pilot- and/or bench-scale testing are recommended prior to full-scale implementation.

For bromoxynil removal at a small system 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 bromoxynil from drinking water, technologies that are expected to be effective include adsorption (activated carbon) and reverse osmosis. When using such a treatment unit, it is important to send samples of water entering and leaving the treatment unit to an accredited laboratory for analysis to ensure that adequate bromoxynil 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 guidelines for bromoxynil is protective against health effects from exposure to bromoxynil 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 bromoxynil concentrations are above the MAC then an investigation to determine the most appropriate way to reduce exposure to bromoxynil should be conducted. This may include use of an alternate water supply or installation of treatment. Where treatment is already in place and an exceedance occurs, an investigation should be conducted to verify treatment and determine if adjustments are needed to lower the treated water concentration below the MAC.

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1.0 EXPOSURE CONSIDERATIONS

1.1 Sources and uses

Bromoxynil phenol (3,5-dibromo-4-hydroxybenzonitrile, parent compound) and its ester derivatives are commonly grouped together under the name "bromoxynil". However, it is the phenolic form of bromoxynil that is known as "bromoxynil" (US EPA, 1998; CCME, 1999a). Henceforth, "bromoxynil" will be used to denote bromoxynil phenol.

Bromoxynil is a contact, post-emergent and selective benzonitrile herbicide used to control a wide spectrum of annual broadleaf weeds in food and feed crops (Health Canada, 2019a). It acts by inhibiting photosynthesis, which stops energy production and negatively affects plant respiration (US EPA, 1998). Bromoxynil and its octanoate and heptanoate esters are currently registered in Canada for use in commercial class products. There are no registered domestic class products in Canada containing bromoxynil or its ester derivatives (Health Canada, 2019a). Bromoxynil was on Health Canada's Pest Management Regulatory Agency (PMRA) yearly list of "Top 10 Herbicide Active Ingredients Sold in Canada" in 2018 (the most recent year for which data are available) with more than 1,000,000 kg of active ingredient (bromoxynil) being sold for use on terrestrial feed and food crops (Health Canada, 2020a).

Bromoxynil and its octanoate and heptanoate esters are released into the environment as spray drift that results from agricultural applications and as surface runoff from treated areas (Anderson et al., 1998; CCME, 1999a, Waite et al., 2005; Health Canada, 2019a). In addition, dust particles with adsorbed bromoxynil, bromoxynil octanoate and/or bromoxynil heptanoate can also contaminate surface water (CCME, 1999a).

Bromoxynil is moderately soluble in water (see Table 1). Based on the rapid aerobic and anaerobic conversion of bromoxynil to carbon dioxide, it has a low potential to contaminate groundwater (US EPA, 1998; Health Canada, 2008). Its half-life in prairie wetland ponds is reported as 9–17 days, though residues (> 2 ng/L) may remain up to 120 days after application (Muir et al., 1991). In soil, bromoxynil's half-life is reported to be 4.12 days and its dissipation rate is reported to be 91.25% over 21 days (Chen et al., 2011).

Both bromoxynil octanoate and bromoxynil heptanoate are chemically and physically similar to each other so that information relating to the environmental fate of the octanoate ester is relevant to the heptanoate ester (US EPA, 1998; Health Canada, 2008). Both esters are almost insoluble in water and readily hydrolyze to bromoxynil at alkaline pH, with half-lives of 1.7 to 34.1 days, depending on pH (CCME, 1998a; US EPA, 1998; Health Canada, 2008). Bromoxynil octanoate is rapidly degraded in both water and soil with photolysis half-lives of 2–4.6 days and microbial degradation half-lives of 12 hours to 3.7 days. Bromoxynil octanoate is mobile in sand, sandy loam and loam soils. Since bromoxynil octanoate readily degrades to bromoxynil via hydrolysis, the potential for ground water contamination (and exposure) from bromoxynil octanoate is low. Bromoxynil octanoate is also not expected to persist in surface waters (US EPA, 1998).

The reported vapour pressure and Henry's law constant (see Table 1) indicate that bromoxynil and its octanoate and heptanoate esters should not readily volatilize from surface water environments and undergo long-range airborne transport (US EPA, 1998; Health Canada, 2008).

1.2 Substance identity

Bromoxynil (CAS RN 1689–84–5, $C_7H_3Br_2NO$) is a colourless and odourless solid (CCME, 1999b). Bromoxynil octanoate (CAS RN 1689–99–2, $C_{15}H_{17}Br_2NO_2$) and bromoxynil heptanoate (CAS RN 56634–95–8, $C_{14}H_{15}Br_2NO_2$) are brown crystalline solids (US EPA, 1998). In their evaluations, the United States Environmental Protection Agency (US EPA) (1998) and PMRA (Health Canada, 2019a) focused on data for bromoxynil octanoate as it was found to be chemically and physically similar to bromoxynil heptanoate. Therefore, some of the physico-chemical properties of bromoxynil and bromoxynil octanoate are summarized in Table 1.

Table 1. Properties of bromoxynil and its octanoate ester relevant to their presence in drinking water

Property	Bromoxynil	Interpretation	Bromoxynil octanoate	Interpretation
CAS RN	1689–84–5	Not applicable	1689–99–2	Not applicable
Molecular formula	$C_7H_3Br_2NO$	Not applicable	$C_{15}H_{17}Br_2NO_2$	Not applicable
Molecular weight (g/mol)	276.9	Not applicable	403.1	Not applicable
Water solubility (mg/L)	130 at 20°C	Moderate solubility in water	3 at 25°C	Low solubility in water
Vapour pressure (volatility) (mPa)	6.3×10^{-3} at 20°C	Low volatility, unlikely to be present in air	1.9×10^{-1} at 25°C	Low volatility, unlikely to be present in air
Henry's law constant	5.3×10^{-4} Pam^3/mol [a]	Low potential to volatilize from water surfaces or moist soils	9.76×10^{-8} $atmm^3/mol$ [b]	Low potential to volatilize from water surfaces or moist soils
Dissociation constant	p*K*a = 3.86	Bromoxynil dissociates rapidly to anion at environmental pHs	No dissociation	Not applicable
n-Octanol: water partition coefficient ($logK_{ow}$)	2.8	Unlikely to bioaccumulate	5.4	Unlikely to bioaccumulate

Information is adapted from Health Canada (2008) unless mentioned otherwise.

[a] Cicotti, 1994.

[b] US EPA, 1998.

1.3 Exposure

The general Canadian population can potentially be exposed to bromoxynil through food and drinking water (Health Canada, 2019a).

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

The exposure data provided reflect different method detection limits (MDL) of accredited laboratories used within and amongst the jurisdictions, as well as their respective monitoring programs. As a result, the statistical analysis of exposure data provides only a limited picture. Data provided by the provinces and territories indicate that bromoxynil

levels are below the method reporting limit (MRL) or MDL in most samples collected. These samples were 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; Saskatchewan Water Security Agency, 2019; Ontario Ministry of the Environment, Conservation and Parks, 2020). Table 2 summarizes the monitoring data for jurisdictions in which all reported samples were below the MDL. Table 3 summarizes the data for jurisdictions in which bromoxynil detections were reported. The maximum concentration of 6.69 µg/L was reported in the distribution system from surface water in Quebec.

There were no monitoring data available in New Brunswick, Newfoundland and Labrador, Prince Edward Island and Yukon (New Brunswick Department of Environment and Local Government, 2019; Newfoundland and Labrador Municipal Affairs and Environment, 2019; Prince Edward Island Department of Communities, Land and Environment, 2019; Yukon Environmental Health Services, 2019).

Table 2. Summary of non-detect monitoring data for bromoxynil

Jurisdiction (MDL µg/L)	Monitoring Period	Type of Water System	Water Type (Municipal: ground/surface—raw, treated, distributed)	# Detects/ samples
British Columbia (0.02–0.5)	2013–2018	Municipal	Surface—raw	0/18
FNIHB Ontario Region (0.2–0.5)	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
		Private Water Systems	Ground—treated	0/3
			Ground—distribution	0/50
			Surface—treated	0/5
FNIHB Atlantic Region (0.5)	2014–2018	Public Water Systems	Ground—treated	0/4
			Ground—distribution	0/4
			Surface—treated	0/1
FNIHB Quebec Region (0.02)	2014–2018		Drinking water system	0/4
Nova Scotia (0.3–1)	2007–2018	Municipal	Ground—raw	0/72
			Ground—treated	0/35
			Surface—raw	0/35
			Surface—treated	0/39
			Distributed	0/1
Saskatchewan (0.05)	2014–2019	Municipal	Ground & surface—distribution	0/35
			Ground & Surface—treated	0/4
			Ground—raw	0/17

FNIHB—First Nations and Inuit Health Branch; MDL—method detection limit.

Table 3. Summary of bromoxynil detections in select provinces in Canada

Jurisdiction (MDL µg/L)	Water Type (Municipal: ground/surface—raw, treated, distributed and Non-Municipal: ground)	# Detects/ samples	Max. Value (µg/L)
Manitoba [2012–2018] (0.02–0.17)	Surface—ambient	17/393	0.188
Ontario [2011–2020] (0.02–3)	Ground—treated	4/3889	2
	Surface—treated	3/3750	0.5
	Unknown—distributed	0/60	-
Quebec [2012–2018] (0.02–3)	**Municipal [2013–2018]:**		
	Ground—distribution	0/389	-
	Surface—distribution	6/1312	6.69
	Municipal (Special projects) :		
	Potato project [2017–2018][a]:		
	Ground—raw	0/46	-
	Ground—treated	0/17	-
	Ground—distribution	0/5	-
	Small systems [2012–2018][b]:		
	Ground—raw	0/83	-
	Non-municipal:		
	Ground—raw	0/19	-

MDL—method detection limit.

[a] Potato Project 2017–2018: During the period covered, analysis results of bromoxynil pesticide found in raw, treated or distributed ground water were obtained by the Ministère de l'Environnement et de la Lutte contre les changements climatiques du Québec (2019) from 9 drinking water supplies.

[b] Small Systems Project 2012–2018: During the period covered, analysis results of bromoxynil found in raw ground water were obtained by the Ministère de l'Environnement et de la Lutte contre les changements climatiques du Québec (2019) from 25 drinking water supplies.

As part of its assessment, PMRA (Health Canada, 2019a) noted that there were no quantifiable detections of bromoxynil in Canadian groundwater sources. Bromoxynil was detected in surface water in the provinces of Alberta, Manitoba, Saskatchewan, Ontario and Quebec. The Canadian data show that the overall detection frequency is less than 50% in most studies, with maximum single concentrations in potential surface water sources of drinking water being less than or equal to 0.96 µg/L.

A study of 15 drinking water reservoirs (fed primarily from crop land snowmelt and occasional rainfall runoffs) in Alberta, Manitoba and Saskatchewan detected bromoxynil in 54% of 206 reservoir samples taken between 2003 and 2004, with mean and maximum concentrations of 2.4 ng/L and 384 ng/L, respectively (detection limit = 0.99 ng/L) (Donald et al., 2007). The authors stated that significantly higher mean concentrations were found in July after herbicide application (May to early July, 29.6 ± 12.5 ng/L) as compared to April/May (1.5 ± 0.3 ng/L) after the snowmelt runoff.

Rivers from areas in Quebec where corn and soy are intensely cultivated were also sampled for bromoxynil from 2015 to 2017. For these years, the average detection frequency was 6.4% and the maximum concentration was 0.51 µg/L in the Chibouet, des Hurons, Saint-Régis and Saint-Zéphirin Rivers. In 2015, the bromoxynil detection frequency was 18.2%, 18.2% and 27.3% in the Chaudière, Beaurivage and Le Bras Rivers, respectively, with detected bromoxynil concentrations < 5 µg/L. In 2016, the bromoxynil detection frequency was 10% in the Yamaska River, with detected bromoxynil concentrations < 5 µg/L (Giroux, 2019).

In 2001 and 2002, bromoxynil was detected at one municipal wastewater treatment plant out of seven plants surveyed in Quebec; the detection frequency was 3% and the maximum concentration was 0.26 µg/L (MDL = 0.02 µg/L) (Giroux and Therrien, 2005).

Health Canada (2020b) has set maximum residue limits for a variety of food products (including fruits, vegetables and animal tissue/organs) of 0.02–0.9 ppm of bromoxynil. Domestic and imported food products (i.e., fresh fruits, fresh vegetables, seeds, tree nuts, peanuts and processed fruit and vegetable products) were sampled and tested by the Canadian Food Inspection Agency between April 1, 2015 and March 31, 2016. No samples (n = 798) tested positive for bromoxynil contamination (CFIA, 2019).

The potential bystander inhalation exposure via spray drift that results from agricultural applications of bromoxynil is expected to be negligible and is not considered to significantly contribute to the overall exposure to bromoxynil (Heath Canada, 2019a). Results from a 3-year (2003–2006) national air surveillance program by the Canadian Atmospheric Network for Currently Used Pesticides showed atmospheric concentrations of bromoxynil varied within years and time periods with averages ranging from 4.7 to 1,840 pg/m^3 (n = 8 locations, MDL = 1.2 pg/m^3) (Yao et al., 2008).

Bromoxynil was detected in soil at one sampling site in the Canadian Atmospheric Network for Currently Used Pesticides surveillance study in 2005; the average concentration was 6.23 ng/g (MDL = 0.2 ng/g) (Yao et al. 2008).

2.0 HEALTH CONSIDERATIONS

All pesticides, including bromoxynil, are regulated by PMRA. PMRA conducts extensive evaluations and cyclical reviews of pesticides, including unpublished and proprietary information, as well as foreign reviews by other regulatory agencies such as the US EPA. As such, this health assessment is primarily based on PMRA's evaluations (Health Canada, 2008, 2019a) and supporting documentation. Additionally, any reviews and relevant literature available since PMRA's evaluations were completed were also considered.

2.1 Kinetics

Bromoxynil, bromoxynil octanoate and bromoxynil heptanoate pharmacokinetics are considered to be identical in animals (US EPA, 1998; EFSA 2017). Therefore, pharmacokinetic studies using the octanoate or heptanoate ester are indicative of the pharmacokinetic behaviour of bromoxynil (US EPA, 1998).

Absorption: Bromoxynil is readily absorbed (> 80%) following oral exposure in animals (Salama et al., 2016; EFSA, 2017). In rats, the dermal absorption of bromoxynil increases with duration of exposure. Amounts of 0.10, 1.0 and 10.0 mg/rat resulted in percent dermal absorption at 10 hours of 1.92%, 1.74% and 1.24%, respectively, and at 24 hours of 3.12%, 3.24% and 3.02%, respectively (US EPA, 1998).

Distribution: Bromoxynil was observed in the liver, kidneys and brain (only tissues analyzed) within 0.5 hours following oral administration (12.9 mg/kg of body weight [bw]) in male rats. Peak concentrations of bromoxynil were reached at 48 hours in serum, liver and brain and at 24 hours in kidneys following administration (Salama et al., 2016). Similarly, in rats administered radiolabelled (^{14}C) bromoxynil octanoate by gavage, radioactivity was distributed in most tissues with the highest concentrations observed in blood, plasma (peak concentrations reached at 7–10 hours), liver, kidneys and thyroid (especially in females). Generally, females presented higher levels of radioactivity in tissues than males (US EPA, 1998). Bromoxynil is not expected to accumulate in animal tissue (Salama et al., 2016; EFSA, 2017).

Metabolism: Bromoxynil is metabolised via hydrolysis and conjugation. Although bromoxynil metabolites have not been identified in the database, no unique human metabolite is expected (EFSA, 2017). In rats, bromoxynil octanoate was rapidly and nearly completely converted to the parent compound (bromoxynil) via ester hydrolysis and bromoxynil was the only chemical species identified in rat tissues (US EPA, 1998).

Elimination: In male rats, bromoxynil was mainly excreted in urine following oral administration. Within 24 hours, 2.80% and 0.01% of bromoxynil were eliminated in urine and feces, respectively. By 168 hours, the urinary and fecal cumulative excretions of bromoxynil were 21.90% and 14.11%, respectively. The elimination half-lives (measured in the serum, liver, brain and kidneys) ranged from 34.8 (kidneys) to 62.0 hours (liver) (Salama, et al., 2016). At seven days following administration of radiolabelled (^{14}C) bromoxynil octanoate in rats, 84%–89% and 76%–80% of radioactivity was excreted in the urine of males and females, respectively, and 6%–10% in the feces of both males and females. Free and conjugated bromoxynil were the only chemical species present in urine. Bromoxynil octanoate was identified only in feces (US EPA, 1998).

2.2 Health effects

The database for the toxicity of bromoxynil is adequate as it covers several endpoints and various types of exposure (see US EPA, 1998 for a more thorough review). As bromoxynil and bromoxynil octanoate have been determined to be toxicologically equivalent, studies on both forms were considered in this section (Health Canada, 2019a). In general, bromoxynil and its octanoate ester have a low to high acute oral toxicity in experimental animals depending on the species tested (i.e., guinea pigs being the most sensitive species). As well, bromoxynil and its octanoate ester have low dermal acute toxicity and were well-tolerated in repeated-dose dermal toxicity studies in rabbits. Repeated-dose oral toxicity studies in animals show that the liver is the most sensitive endpoint.

2.3 Effects in humans

In terms of acute exposures to bromoxynil or bromoxynil octanoate, no relevant human data were available.

Agricultural Health Study: Regarding longer term exposures, epidemiological studies have investigated various outcomes following bromoxynil exposure. The Agricultural Health Study (AHS) is a large, ongoing questionnaire-based prospective cohort study of licensed pesticide applicators and their spouses (over 89,000 participants) who live in Iowa and North Carolina that investigates cancer and non-cancer endpoints. It began in 1993 with the collection of baseline information on farming practices (including pesticide use), lifestyle and health. Follow-up interviews/questionnaires (including dietary information) and DNA collection were done periodically. Cancer registries were used to assess cancer incidence. Overall, strengths of the AHS include its large size; the inclusion of a large number of women; the collection of baseline, health and lifestyle information and genetic factors; the use of cancer registries 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 (Sathiakumar et al., 2011).

Cancer: Koutros et al. (2016), examining AHS data from 1993 to 1997, found an association between exposure to bromoxynil and the incidence of bladder cancer. However, the use of bentazon and bromoxynil were moderately correlated in the data and the authors suggest that bentazon might be more important in driving the observed bladder cancer risk than bromoxynil.

Non-cancer: Examining non-cancer endpoints, Hoppin et al. (2017) did not find an association between bromoxynil use and wheeze among pesticide applicators based on AHS data collected from 2005 to 2010. Baumert et al. (2018) did not find an association between bromoxynil use and sleep apnea based on an asthma case-control study nested within the prospective AHS (2005–2010).

Semchuk et al. (2007) investigated the association between the detection of antinuclear antibodies (an autoimmunity indicator) and exposure to bromoxynil in a cross-sectional study of 208 residents (94 women, 114 men) of a cereal-producing region in Saskatchewan. In male participants, the presence of antinuclear antibodies was inversely associated with detectable concentrations of bromoxynil in blood samples. Weaknesses of the study included, but were not limited to, low sample size and lack of exploration of additional factors such as chronic illnesses. In addition, the authors suggested that the results cannot be generalized beyond the study population or study area as the study was conducted during the spring herbicide application season in a farming area of Saskatchewan with specific characteristics (e.g., use of herbicides, climate, farm size).

Yang et al. (2014) examined potential associations between early gestational exposures (based on residential proximity) to agricultural pesticides applied in the San Joaquin Valley of California in any year during 1997–2006 and incidence of selected birth defects. Exposure to bromoxynil octanoate was associated with spina bifida (a neural tube defect); however, the authors determined that the associations they observed might have emerged by chance alone considering the limitations of the study (e.g., modest sample sizes, multiple comparisons, other sources of pesticides such as occupation or home use were not considered).

Overall, the epidemiological database provides only uncertain indications of associations between bromoxynil or bromoxynil octanoate exposure and various health outcomes. These limitations prevent using their results in a quantitative risk assessment.

2.4 Effects in animals

Toxicity studies were available for both bromoxynil and bromoxynil octanoate. Bromoxynil has been shown to be toxic to experimental animals with oral median lethal dose (LD_{50}) values reported for some species as follows: 63 mg/kg of bw in guinea pigs, 81–440 mg/kg bw in rats, 100–245 mg/kg bw in mice and 260–2,000 mg/kg bw in rabbits (US EPA, 1998; CCME, 1999b). Dermal LD_{50} values of > 2,000 mg/kg (abraded skin, male and female) in rabbits and inhalation median lethal concentration (LC_{50}) values of 0.150 mg/L (female) and 0.269 mg/L (male) in rats have been reported. For bromoxynil octanoate, the reported oral LD_{50} values were 238 mg/kg bw (female) and 400 mg/kg bw (male) in rats; the dermal LD_{50} values were 1,310 mg/kg (intact skin, female) and > 2,000 mg/kg (abraded skin, male) in rabbits and the inhalation LC_{50} were 0.72 mg/L (female) and 0.81 mg/L (male) in rats (US EPA, 1998).

Liver effects: Repeated-dose toxicity studies in rats, mice and dogs showed that bromoxynil affects the liver (Johnson et al., 1980; Hamada, 1988; Harling et al., 1988; Higgins, 1989; Williams, 1994). Dogs were the most sensitive species. Effects consisted of changes in liver enzymes, histopathological changes and increased absolute and relative liver weights (US EPA, 1998; Health Canada, 2019b).

In a one-year study, beagles (6/sex/dose) were administered 0, 0.1, 0.3, 1.5 or 7.5 mg/kg bw per day of technical grade bromoxynil in gelatin capsules. Increased absolute liver weights and liver/body weight ratios, changes in biochemical parameters including greater alanine aminotransferase (ALT) and urea values and lower alkaline phosphatase (ALP) and protein values were observed in both female and male dogs at the highest dose. Greater liver weights were observed in both female and male dogs receiving 1.5 mg/kg bw per day (Harling et al., 1988; Health Canada, 2019b).

Similar effects were seen in both rats and mice. In a two-year combined chronic feeding/carcinogenicity study by Hamada (1988), Sprague Dawley rats (70/sex/dose) were fed 60–600 ppm (equivalent to 2.6–28 mg/kg bw per day in males and 3.3–41 mg/kg bw per day in females) of technical grade bromoxynil. In male rats, increased incidence of histopathological changes was observed in the liver at 190 ppm (spongiosis hepatis) and at 600 ppm (spongiosis hepatis and foci of eosinophilic cellular alteration). In a study by Johnson et al. (1980), Swiss albino mice were fed 10–100 ppm (equivalent to 1.3–13 mg/kg bw per day) of technical grade bromoxynil for 18 months. Increased incidence of hyperplastic nodules in the liver (non-neoplastic lesions) was observed in the male mice at the mid- (30 ppm) and high-dose (100 ppm). CD-1 mice (60/sex/dose) were fed 20–300 ppm (equivalent to 3.1–46 mg/kg bw per day in males and 3.7–53 mg/kg bw per day in females) of technical grade bromoxynil for 18 months. Increased liver weights, increased incidence of diffusely dark livers and increased incidence of non-neoplastic microscopic lesions in the liver of both male and female mice were observed

in the high-dose group. Histopathologic lesions in the liver included hepatocellular centrilobular hypertrophy, hepatocellular degeneration/necrosis and pigment in hepatocytes and Kupffer cells. Similar non-neoplastic lesions were also observed in the liver of some male and female mice of the 75 ppm group (Williams, 1994).

Two oral subchronic studies showed similar hepatic effects in Sprague Dawley rats (15/sex/dose) and CD-1 mice (10/sex/dose) given dietary doses of 400–1,456 ppm (equivalent to 28–168 mg/kg per day in males and 35–250 mg/kg per day in females) of technical grade bromoxynil for 13 weeks and 10–3,000 ppm (equivalent to 1.3–390 mg/kg per day) of technical grade bromoxynil for 12 weeks, respectively; the highest dose used in each study was highly toxic (Wolfe, 1990; Williams, 1992). Increased aspartate aminotransferase, increased ALT and increased ALP were observed in male rats at 755 ppm. In female rats, increased ALP was observed at 755 and 1,456 ppm (Wolfe, 1990). Increased liver weights and hepatocellular hypertrophy were observed in male mice at 100 ppm and higher; degeneration and vacuolization were also observed in the hepatocytes of male mice at 300 ppm and higher. For female mice, increased liver weights, hepatocellular hypertrophy, degeneration and vacuolization were observed at 300 ppm and higher. At 1,000 ppm and higher, additional pathological effects in the liver (not specified) were observed in female and male mice (Williams, 1992).

In a 13-week study, Sprague Dawley rats (20–30/sex/dose) were given dietary doses of 150–1,100 ppm (equivalent to 11–91 mg/kg per day in males and 13–111 mg/kg per day in females) of technical grade bromoxynil octanoate. Increased liver weights were observed in female rats at 600 ppm (Henwood, 1992).

Reproductive and developmental toxicity: In a two-generation reproduction study, Sprague Dawley rats (24/sex/dose) were fed 10–250 ppm (equivalent to 0.8–21 mg/kg per day) of technical grade bromoxynil in their diet during 14 weeks prior to mating; no effect was observed on the reproductive function at any level (Higgins, 1989).

Developmental toxicity studies were conducted using bromoxynil (in rats, rabbits and mice) and bromoxynil octanoate (in rats and rabbits). An increased incidence of supernumerary ribs (most commonly the 14th rib) was the developmental effect that was most observed in both oral and dermal studies and was considered by PMRA to be the most sensitive endpoint of developmental toxicity (Health Canada, 2019a).

In the Higgins (1989) study, developmental toxicity in offspring included decreased body weight during lactation and delayed eye opening at 250 ppm. In three oral developmental toxicity studies where technical grade bromoxynil (1.7–40 mg/kg per day) was administered by gavage to groups of pregnant Sprague Dawley rats on gestation days (GD) 6–15 or 5–17 inclusive, increased incidence of supernumerary ribs was observed at a dose level

as low as 5 mg/kg per day. Additional effects included increased post-implantation loss (12.5 mg/kg per day) and decreased fetal body weights (35 and 40 mg/kg per day). Increased incidence of late intrauterine deaths and an increase in the total incidence of minor anomalies were also observed at the dose level of 35 mg/kg per day. Finally, increased number of small fetuses, increased incidence of soft tissue and skeletal abnormalities (including anophthalmia [missing eyes], microphthalmia [smaller than normal eyes or tiny eyes], short renal papilla and spinal and thoracic bone abnormalities) were observed at the dose level of 40 mg/kg per day (Copping, 1981; Rubin and Nyska, 1987; US EPA, 1998). Similar effects were observed in two oral developmental toxicity studies where technical grade bromoxynil was administered by gavage to groups of pregnant New Zealand white rabbits (15–60 mg/kg per day, GD: 5–20 and 6–18); increased incidence of all forms of supernumerary ribs was observed at the lowest dose (Copping and Brown, 1983; Holson, 1984). In pregnant CD-1 mice that were given technical grade bromoxynil by oral gavage (11–96 mg/kg per day, GD: 6–15 inclusive), statistically significant increased litter incidence of 14th rib, decreased fetal weights and decreased numbers of fetuses with ossified caudal vertebrae were observed at the highest dose.

When bromoxynil octanoate was administered by gavage to pregnant Sprague Dawley rats (2.4–21.8 mg/kg, GD 6–15 inclusive), statistically significant increased litter incidence of 14th rib and reduced fetal weights were observed at the highest dose (US EPA, 1998).

In dermal developmental toxicity studies, supernumerary ribs were noted at 50 mg/kg bw per day (bromoxynil) and 15 mg/kg bw per day (bromoxynil octanoate) in rats. No developmental toxicity was observed at up to 80 mg/kg bw per day in a dermal study conducted with a formulation containing bromoxynil octanoate on groups of pregnant New Zealand white rabbits (US EPA, 1998; Health Canada, 2019a).

Fetal effects in rodents always occurred in the presence of maternal toxicity, which included decreases in body weight, food consumption and body weight gain and increases in mortality and liver weights. In rabbits, fetal effects occurred at dose levels lower than those causing toxicity in maternal animals but higher than those causing hepatotoxicity in dogs (Health Canada, 2019a).

Other effects: Effects on the cardiovascular system were observed in both rats and beagle dogs but occurred only at the highest doses tested (rats: 1,100 ppm of technical grade bromoxynil octanoate [equivalent to 91 mg/kg per day in males and 111 mg/kg per day in females], beagle dogs: 7.5 mg/kg bw per day of technical grade bromoxynil). As well, clinical signs (panting, salivation, liquid feces, pale gums) and increased prostate weights were observed in beagle dogs at 7.5 mg/kg bw per day of technical grade bromoxynil (see section 2.7) (Henwood, 1992; Harling et al., 1988).

Decreases in body weight gain were also observed in subchronic and chronic oral toxicity studies in rats and dogs dosed with bromoxynil or bromoxynil octanoate (Noel et al., 1965; Hamada, 1988; Harling et al., 1988; Higgins, 1989; Wolfe, 1990; Henwood, 1992; Makin, 1993).

2.5 Genotoxicity and carcinogenicity

Based on the collective data from several in vitro and in vivo tests, bromoxynil is not mutagenic or genotoxic (EFSA, 2017; Health Canada, 2019a).

Bromoxynil was negative in two in vivo studies (mouse micronucleus assays) (Holmstrom and McGregor, 1982; Holmstrom et al., 1991). Negative in vitro studies included unscheduled DNA synthesis assay; transformation assay using cultures of mouse C3H/10T1/2C18 cells; sister chromatid exchange assay using cultures of Chinese hamster ovary (CHO) cells (both with and without activation); mouse lymphoma forward mutation assay (without activation); chromosome aberration assay (CHO, without activation); CHO/Hypoxanthine-guanine phosphoribosyltransferase (HGPRT) mutation assay (both with and without activation) and Ames study using *Salmonella typhimurium* (both with and without activation) (Cifone and Balinas, 1982; Galloway and Lebowitz, 1982; Myhr and McKeon, 1982; Rundell and Matthews, 1982; Cifone, 1991; Lawlor, 1991). However, positive results were obtained in three in vitro studies: mouse lymphoma forward mutation assay (with activation); bacterial DNA repair test using *Escherichia coli* indicator strain (with and without activation) and chromosome aberration assay (CHO, with activation) (Cifone and Balinas, 1982; Galloway and Lebowitz, 1982; Jagannath et al., 1982). Although bromoxynil was positive in three in vitro studies, negative results were obtained in the majority of in vitro studies as well as in in vivo tests.

Bromoxynil octanoate was negative in vitro (Ames study using *Salmonella typhimurium* [both with and without activation] and in unscheduled DNA synthesis assay) and in vivo (mouse micronucleus assay) (Dillon, 1993; US EPA, 1998).

Carcinogenicity studies using bromoxynil were conducted in rats and mice. Swiss albino mice (60/sex/dose) were administered 10–100 ppm (equivalent to 1.3–13 mg/kg bw per day) of technical grade bromoxynil in their diet. The combined incidence of hepatic adenomas and carcinomas in males increased in a dose-related manner, the increase being statistically significant at the highest dose. No treatment-related increased incidence of tumours was seen in female Swiss mice (Williams, 1994). CD-1 mice (60/sex/dose) were administered 20–300 ppm (equivalent to 3.1–46 mg/kg bw per day in males and 3.7–53 mg/kg bw per day in females) of technical grade bromoxynil in their diet. The combined incidence of hepatic adenomas and carcinomas in males was increased relative

to control animals at every dose level tested but the dose response was not linear. An increased incidence of hepatic adenomas and carcinomas (combined) was noted in female CD-1 mice at the highest dose (US EPA, 1998; Health Canada, 2019a).

No neoplastic lesions were associated with treatment in a two-year combined chronic feeding/carcinogenicity study where Sprague Dawley rats (70/sex/dose) were administered 60–600 ppm (equivalent to 2.6–28 mg/kg bw per day in males and 3.3–41 mg/kg bw per day in females) of technical grade bromoxynil in their diet (Hamada, 1988).

Bromoxynil was found to be carcinogenic in mice but not in rats. The US EPA (1998) has classified bromoxynil as a Group C, possible human carcinogen based primarily on observed liver tumours in mice and used a linear no-threshold model to estimate the carcinogenic risk from bromoxynil for the general population. The International Agency for Research on Cancer has not reviewed the carcinogenicity of bromoxynil. In its special review for bromoxynil and its associated end-use products, PMRA (Health Canada, 2019a) concluded that the reference values selected for characterization of non-cancer risks resulting from repeated exposure to bromoxynil are protective of any residual concerns regarding the oncogenic potential of bromoxynil (see section 2.7).

2.6 Mode of action

Bromoxynil is an uncoupling agent that disrupts oxidative phosphorylation, which may be responsible for the hepatotoxicity observed in toxicological studies (EFSA, 2017).

Bromoxynil has also been shown to increase the incidence of hepatic adenomas and carcinomas in mice. It was proposed that the generation of hepatocellular tumours could be the result of a mode of action (MOA) involving activation of the peroxisome proliferator-activated receptor (PPARα) or the constitutive androstane receptor (CAR). As such, the PPARα activation leads to alterations in cell growth pathways, subsequent perturbation of cell growth and survival, then selective clonal expansion of pre-neoplastic cells and, ultimately, the production of hepatic tumours (Health Canada, 2019a). The CAR activation can cause an increase in hepatocyte replicative DNA synthesis, an induction of detoxification enzymes and transporters and an increase in altered hepatic foci and hepatocellular adenomas/carcinomas (Lake, 2018). The role of PPARα activity could not be clearly differentiated from that of CAR (Health Canada, 2019a).

2.7 Selected key study

In its special review for bromoxynil and its associated end-use products (PSRD2019-01), PMRA (Health Canada, 2019a) identified the liver as the most sensitive target organ in the database. As such, an unpublished one-year oral toxicity study in the dog in which the endpoint includes liver effects has been considered the key study for the human health risk assessment of bromoxynil in drinking water (Health Canada, 2019a, 2019b). For the derivation of the acceptable daily intake (ADI), PMRA often selects critical toxicity studies that are less than chronic in duration, including developmental neurotoxicity, reproductive toxicity, developmental toxicity and 1-year dog toxicity studies. When a toxicity study with a less than chronic duration is selected for derivation of the ADI, it is selected because the critical endpoint is protective of chronic effects and addresses all endpoints of concern in the toxicology database (Health Canada, 2021a).

In this study, technical grade bromoxynil was administered in gelatin capsules to groups of beagle dogs (6/sex/dose) at dose levels of 0 (control), 0.1, 0.3, 1.5 or 7.5 mg/kg bw per day. The administration of bromoxynil resulted in clinical signs such as panting for animals receiving 1.5 or 7.5 mg/kg bw per day and salivation, liquid feces and pale gums principally for animals receiving 7.5 mg/kg bw per day. Reductions in body weight and body weight gain were recorded for male animals receiving 1.5 mg/kg bw per day or higher and in female animals receiving 7.5 mg/kg bw per day. Statistically significant reductions in red blood cell parameters (packed cell volume, hemoglobin and red blood cells) were recorded in high dose animals of both sexes. Reductions in these parameters were recorded in males at 1.5 mg/kg bw per day as well; however, they did not attain statistical significance. Changes in biochemical parameters included greater urea and ALT values and lower ALP and protein values for male and female animals receiving 7.5 mg/kg bw per day. Organ weight analysis indicated greater liver weights for animals that received 1.5 or 7.5 mg/kg per day, lower spleen weights for males that received 7.5 mg/kg bw per day and greater prostate weights for males that received 7.5 mg/kg bw per day (Health Canada, 2019b). An oral no-observed-adverse-effect level (NOAEL) of 0.3 mg/kg bw per day was identified in this study based on increases in clinical signs and liver weight and decreases in body weight and body weight gain observed at the lowest-observed-adverse-effect level of 1.5 mg/kg bw per day (Health Canada, 2019a, 2019b).

Although bromoxynil was found to be carcinogenic in mice, PMRA's review of the available toxicology database determined that bromoxynil is not genotoxic based on the collective results from several in vitro and in vivo studies. In long-term dietary studies, bromoxynil phenol was carcinogenic in mice, but not rats. There was evidence of a dose-related increase in the combined incidence of hepatocellular adenomas and carcinomas in mice treated with bromoxynil, compared to controls. The MOA for hepatocellular adenomas

and carcinomas focused on the generation of hepatocellular tumours through the activation of PPARα, leading to alterations in cell growth pathways, subsequent perturbation of cell growth and survival, then selective clonal expansion of pre-neoplastic cells and, ultimately, the production of hepatic tumours. Overall, the key events for the liver tumour MOA were clear and demonstrable to support a receptor-mediated cell proliferative MOA. The strongest evidence was for a PPARα-mediated process, but PMRA found that the influence of CAR activity could not be excluded. The dose and temporal concordance were generally acceptable for the parameters that were observed; however, there was a lack of information available to describe the onset of PPARα activation and the subsequent alteration of cell growth pathways at non-tumorigenic dose levels. Despite this shortcoming, the key events were consistently observed throughout the database and were in accordance with liver effects anticipated in a receptor-mediated cell proliferative pathway. The MOA was considered by PMRA to be biologically plausible and coherent. However, as the role of PPARα activity could not be clearly differentiated from that of CAR, it was determined that human relevance could not be discounted on the basis of the available data. It was concluded that the hepatic cancer risk in humans (regardless of whether PPARα or CAR-mediated) could be addressed through a threshold approach and that the use of a q1* for cancer risk assessment was overly conservative. The ADI of 0.003 mg/kg bw per day, based on a NOAEL of 0.3 mg/kg bw per day in the dog 1-year study and a composite assessment factor of 100, provides a margin of 1,000 to the lowest tumorigenic dose of 3 mg/kg bw per day in mice (Health Canada, 2021a). Therefore, the ADI is considered protective of potential carcinogenicity in humans and the application of an additional factor to the ADI to protect for potential carcinogenicity is not required.

The ADI of 0.003 mg/kg bw per day is also protective of any concerns regarding the potential developmental toxicity of bromoxynil in humans. The full complement of studies required to assess potential toxicity of the young was available for bromoxynil. No sensitivity of the young animal was noted in the rat reproductive toxicity study; effects in offspring were observed at the same dose level that produced toxicity in adult animals. With respect to potential pre-natal toxicity, developmental effects occurred in the presence of maternal toxicity in rats and mice. Developmental effects at the lowest dose levels were limited to variations (increased incidence of supernumerary ribs) or decreased fetal body weight, neither of which is considered a serious endpoint. More serious endpoints, malformations, occurred at higher dose levels. In rabbits, developmental effects occurred below dose levels resulting in maternal toxicity; these effects included variations, malformations and reduced fetal weight/size. Overall, an increased incidence of supernumerary ribs in rats (observed at the lowest-observed-adverse-effect level (LOAEL) of 12 mg/kg bw per day) was the most sensitive developmental endpoint in the toxicology database. Concern for this finding was tempered by the fact that it was not a serious endpoint and it was observed in the

presence of maternal toxicity. In consideration of this, the Pest Control Products Act (PCPA) factor (which takes into account the completeness of the data with respect to the exposure of and toxicity to infants and children, as well as the potential pre- and post-natal toxicity) was reduced to one-fold when this endpoint was selected for risk assessment. Selection of this endpoint and the accompanying PCPA factor provides adequate margins to the observed malformations; it is also protective of the identified sensitivity of the rabbit fetus. The ADI of 0.003 mg/kg bw per day was established based on a lower point of departure from the 1-year dog dietary toxicity study (0.3 mg/kg bw per day) and provided an adequate margin of 4,000 to the lowest dose level (12 mg/kg bw per day) at which developmental effects were observed (Health Canada, 2021a). Therefore, the ADI is protective of potential developmental effects and the application of an additional factor to the ADI to protect for potential developmental effects is not required.

The NOAEL from the dog study is considered to be most appropriate for the derivation of the ADI and the assessment of repeated dietary exposures to bromoxynil owing to the relevant route of exposure and the sensitive endpoints at the LOAEL, which are protective of other repeat-dose non-cancer effects, including those in the long-term mouse and rat studies, as well as residual concerns regarding the carcinogenic potential of bromoxynil (Health Canada, 2021a).

3.0 DERIVATION OF THE HEALTH-BASED VALUE

As noted above, the NOAEL of 0.3 mg/kg bw per day for increases in clinical signs and liver weight and decreases in body weight and body weight gain in dogs was selected as the basis for the current risk assessment. Using the NOAEL of 0.3 mg bromoxynil/kg bw per day, an uncertainty factor of 100 (10 for intraspecies and 10 for interspecies) and a PCPA of 1, an ADI for bromoxynil (Health Canada, 2008, 2019a, 2019b) is calculated as follows:

$$\text{ADI} = \frac{\text{0.3 mg/kg bw per day}}{100}$$

$$= \text{0.003 mg/kg bw per day}$$

Where:

- 0.3 mg/kg bw per day is the NOAEL, based on increases in clinical signs and liver weight and decreases in body weight and body weight gain in beagle dogs; and
- 100 is the uncertainty factor, selected to account for interspecies variation (×10) and intraspecies variation (×10).

Based on the ADI of 0.003 mg/kg bw per day, a health-based value (HBV) for bromoxynil in drinking water was derived as follows:

$$\text{HBV} = \frac{\text{0.003 mg/kg bw per day} \times \text{74 kg} \times 0.20}{\text{1.53 L/day}}$$

$$\approx \text{0.03 mg/L (30 µg/L)}$$

Where:

- 0.003 mg/kg bw per day is the ADI calculated using a NOAEL of 0.3 mg/kg bw per day (Health Canada, 2019);
- 74 kg is the adult body weight (Health Canada, 2021b);
- 1.53 L per day is the daily volume of tap water consumed by an adult (Health Canada, 2021b);
- 0.20 is the allocation factor for drinking water. Since drinking water is not a major source of exposure to bromoxynil and there is evidence of bromoxynil in other exposure sources (i.e., food), a floor value of 0.20 (20%) was applied, implying that drinking water might contribute anywhere from 0% to 20% of the daily dose (Krishnan and Carrier, 2013).

4.0 ANALYTICAL AND TREATMENT CONSIDERATIONS

4.1 Analytical methods to detect bromoxynil

Standardized methods available for the analysis of bromoxynil in source and drinking water and their respective MDLs are summarized in Table 4. 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 MDLs and MRLs for bromoxynil analysis. The MDLs were in the same order of magnitude as those reported in Table 4 and the MRLs ranged between 0.1 and 0.5 µg/L (AGAT Laboratories Ltd., 2019; ALS Environmental [Waterloo], 2019; Bureau Veritas Laboratories, 2019; CARO Analytical Services [Richmond Laboratory], 2019; Element Materials Technology Canada Inc., 2019; SGS Environmental Services, 2019).

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 and method interferences for the analysis of bromoxynil in drinking water (e.g., sample preservation, storage) can be found in the references listed in Table 4. It is important to note that quenching is critical if an oxidant is present in samples in order to prevent additional degradation of bromoxynil prior to analysis.

Table 4. Standardized methods for the analysis of bromoxynil in water

Method (Reference)	Methodology	Interferences/Comments	MDL (µg/L)
EPA 8270D Rev. 5 (US EPA, 2014)	Gas Chromatography with Mass Spectrometry Detection (GC/MS)	None listed in method	10[a]
USGS-NWQL: O–1131–95 (Werner et al., 1996)	High Performance Liquid Chromatography with Ultraviolet Detection (HPLC-UV)	None listed in method	0.035
USGS-NWQL: O–2060–01 (Furlong et al., 2001)	High Performance Liquid Chromatography with Mass Spectrometry Detection (HPLC-MS)	None listed in method	0.0155

MDL—method detection limit.

[a] Estimated Quantitation Limit.

4.2 Treatment considerations

Treatment technologies are available to decrease bromoxynil concentrations with varying effectiveness in drinking water. These include activated carbon, membrane filtration, oxidation, advanced oxidation processes (AOPs) and biofiltration. Studies have concluded that granulated activated carbon (GAC) can remove bromoxynil from water (Baup et al., 2000, 2002; Yang et al., 2004). Published performance data for bromoxynil removal are available for oxidation, AOPs technologies and biofiltration and indicate wide range of removal efficiencies (39% to 99%) (Preuss et al. 1996; Bourgine et al., 1997; Chelme-Ayala et al., 2010a, 2010b, 2011). Pilot-scale testing is an important step for water utilities considering these processes for pesticide removal in drinking water. At the residential scale, certified treatment devices relying on reverse osmosis (RO) or activated carbon adsorption are expected to be effective for removal of bromoxynil.

4.2.1 Municipal-scale

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

The surface water study by Donald et al. (2007) discussed in Section 1.3 also presented bromoxynil concentrations in treated water from 15 drinking water reservoirs. Each drinking water supply had various treatment processes, but all included chlorination

and most included flocculation (alum) settling, activated carbon and/or sand filtration. The raw data were not provided thus only overall statistics could be determined, not the performance of individual treatment processes. The mean bromoxynil concentrations in reservoir and treated water were 2.4 ng/L and 1 ng/L, respectively (n = 163), with a maximum bromoxynil concentration in the treated water of 227 ng/L. From 12 paired samples, a mean bromoxynil reduction of 46% was determined (range between 0% and 98%).

When using oxidation or AOPs 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., 2019). The primary objective should be removal of the pesticide with the secondary objective being the minimization of by-product formation if they are of health concern. 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) alone is not effective but the addition of chlorine during the disinfection step will reduce bromoxynil concentrations through oxidation. However, degradation processes like oxidation result in the formation of by-products (see Section 4.2.1.5). No studies on the removal of bromoxynil through conventional filtration were found in the literature.

4.2.1.2 Activated carbon adsorption

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

There is very limited published literature on the removal of bromoxynil using activated carbon and no data on performance. As such, prior to full-scale implementation it is essential to conduct appropriate pilot- or bench-scale testing. Bromoxynil removal from natural water using activated carbon can be negatively affected by competition from other contaminants or natural organic matter (NOM), biofilm development, temperature, influent concentration, activated carbon characteristics and hydraulic loading rate (Speth and Miltner, 1998; Haist-Gulde and Happel, 2012).

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 [K]) greater than 200 $\mu g/g \cdot (L/\mu g)^{1/n}$ are considered to be amenable to removal by carbon adsorption (Speth and Adams, 1993; Speth and Miltner, 1998, US EPA, 2011). The authors noted, however, that the capacity of activated carbon is affected by many factors, including the compound's ionic character and the solution pH.

Two bench-scale studies present Freundlich coefficients for the adsorption of bromoxynil, diuron and atrazine to different activated carbons (Baup et al., 2000, 2002). The authors reported in both batch studies that bromoxynil exhibited an adsorption in between diuron and atrazine, indicating that activated carbon is a good option for bromoxynil removal. Long-term studies, over a 90-day period, were conducted using both granular and powdered forms of activated carbon (Baup et al., 2002). The authors observed that short-term adsorption was better with PAC than GAC and stated that this may be due to better accessibility to pores and adsorption sites. A bench-scale study evaluating adsorption showed that adsorption capacity declined with increasing pH (see Table 5) (Yang et al., 2004).

The use of PAC offers the advantage of providing virgin carbon when required (e.g., during the pesticide application season) (Miltner et al., 1989). The removal efficiency of PAC depends on the PAC type and dose, the contact time, the PAC characteristics (type, particle size), the adsorbability of the contaminant and the presence of NOM (Gustafson et al., 2003; Summers et al., 2010; Haist-Gulde and Happel, 2012; Chowdhury et al., 2013). In addition to the adsorption capacity of the GAC, the maximum operation time for GAC adsorbers to remove pesticides depends on the filter velocity, empty bed contact time, the GAC characteristics (type, particle size), the adsorbability of the contaminant and the organic background matrix (Haist-Gulde and Happel, 2012). Because GAC fixed bed adsorbers are typically operated on a continuous basis, the GAC can become fouled (or preloaded) with NOM and it 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).

When bromoxynil is oxidized, degradation by-products can be formed as discussed further in Section 4.2.1.5. One bench-scale study evaluated the adsorption of bromoxynil to PAC as well as one of the ozone degradation by-products, 3-bromo-4,5-dihydroxybenzonitrile (Br-DHBN) (Schoutteten et al., 2016). Separate adsorption tests with initial bromoxynil or Br-DHBN concentration of 5 mg C/L were conducted by mixing 0–18 mg PAC to 80 mL solution on a shaker for three days at 25°C. The authors stated that the results showed better adsorption of the degradation by-product, Br-DHBN, to PAC than bromoxynil.

Activated carbon is expected to be effective for the removal of bromoxynil based on the limited published literature. As such, it is important to perform appropriate testing prior to full-scale implementation with source water under the proposed operating conditions to ensure that adequate bromoxynil removal is occurring.

Table 5. Adsorption study for bromoxynil

Initial (mg/L)	Activated Carbon	Adsorption Capacity (mg/m^2)	pH	Overall Description	Reference
35.6	Darco G-60	0.62	2.47	Bench-scale study Mixed for 24 hours at room temperature (T ~ 25°C) Darco G-60 (surface area = 776 m^2/g; mass = 1.5–6.0 mg)	Yang et al. (2004)
		0.45	4.53		
		0.28	6.58		

4.2.1.3 Membrane filtration

In general, nanofiltration (NF) and RO are effective pressure-driven membrane processes for the removal of pesticides from drinking water (Van der Bruggen and Vandecasteele, 2003; US EPA, 2011). The effectiveness of NF and RO for pesticide removal 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. In choosing a membrane, the molecular weight of bromoxynil (> 276 Da) should be considered. In addition to the sieving effect, retention of small pesticide molecules by larger pore size membranes can be influenced by the physicochemical interactions between the pesticide and the membrane surface (Plakas and Karabelas, 2012). 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 (e.g., MWCO, pore size) to determine the potential for removal by membrane filtration. Bromoxynil is somewhat hydrophobic (log K_{ow} > 2) and has a fairly low p*K*a, indicating potential for further removal through hydrophobic bonding to the membrane surface and

electrostatic exclusion (Bellona et al., 2004; Plakas and Karabelas, 2012). Based on these physiochemical properties, it is expected that bromoxynil can be removed through membrane processes.

As there is no published literature on the removal of bromoxynil using 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 bromoxynil removal is occurring.

4.2.1.4 Oxidation

Pilot-scale and bench-scale oxidation studies of bromoxynil using ozone (O_3) and ultraviolet (UV) photolysis can be effective treatment methods for removing bromoxynil from water depending on a variety of factors including contact time, oxidant dose and water matrix (pH, alkalinity and organic matter) (Bourgine et al., 1997; Chelme-Ayala et al., 2010a, 2010b; Chelme-Ayala et al., 2011). Bourgine et al. (1997) reported limited data from a pilot-scale test using UV photolysis to reduce the concentrations of several pesticides in groundwater including bromoxynil. The authors indicated that bromoxynil was easily degraded and that the UV photolysis achieved a greater than 85% removal. A bench-scale study conducted by Chelme-Ayala et al. (2010a) investigated degradation of bromoxynil using direct UV photolysis in natural water. The water samples were collected from the North Saskatchewan River, upstream of the City of Edmonton (W1) and from an irrigation return flow discharging into Redwater River (W2). The quality of natural waters is discussed in Table 6. The results indicated that 30 minutes and 56 minutes were required to achieve 50% degradation of bromoxynil in samples W1 and W2, respectively. In addition, higher UV doses were needed for degradation of bromoxynil in water samples with higher total organic carbon concentration (TOC) and higher alkalinity (see Table 6). The reported UV doses are much higher than those typically required for inactivation of microorganisms (Health Canada, 2019c, 2019d).

A bench-scale ozonation study reported an increase in degradation efficiency of bromoxynil with an increase in pH level (from 2.0 to 7.0) in buffered ultrapure water (Chelme-Ayala et al., 2010b). The different reactivity of bromoxynil was due to the higher reactivity of the deprotonated bromoxynil species formed when pH increased. The reaction rate constants ranged from 2.3×10^2 to 4.6×10^2 $M^{-1}s^{-1}$ at a pH level of 2.0 and from 6.0×10^2 to 6.4×10^2 $M^{1}s^{1}$ at a pH level of 7.0 for the reaction of ozone with bromoxynil using a different kinetic method (see Table 6). Overall, ozone oxidation reactions may proceed through two pathways. In reactions conducted under acidic conditions direct molecular ozonation is the dominant process, while an indirect mechanism by hydroxyl radicals ($^{\bullet}OH$) controls the reactions at pH greater than 10.0 (Hoigné and Bader, 1976). Gottschalk et al. (2000) indicated that both oxidation pathways, direct ozonation and hydroxyl radical oxidation, may proceed at pH levels greater than 7.0.

Bench-scale ozonation tests examined the effect of pH, alkalinity and humic acid levels on the degradation of bromoxynil in ultrapure and natural waters (sampling discussed above) (Chelme-Ayala et al., 2011) (see Table 7). An increase of the degradation rate of bromoxynil was observed with an increase in pH level from 7.0 to 9.0. Due to the scavenging effect on bicarbonate ions in the ozone radical chain reactions and the reaction of ozone with humic acids, higher degradation efficiency of bromoxynil was reported in water samples with lower levels of organic matter and alkalinity. The scavenging effect of carbonate and bicarbonate ions and sodium nitrite on photolytic degradation of bromoxynil was also reported by Kochany et al. (1990b) and Kochany (1992).

When bromoxynil is oxidized, degradation by-products can be formed as discussed further in Section 4.2.1.5.

Table 6. Removal of bromoxynil via oxidation

Oxidant	Influent (M)	Oxidant Dose	Removal %	Process Description	References
UV	Not available	Energy 100–500 Wh/m^3	66.6%—100 Wh/m^3 87.9%—200 Wh/m^3 93.1%—300 Wh/m^3 93.3%—500 Wh/m^3	Pilot scale: groundwater; pH 7.1–7.2; turbidity 0.1–0.2 NTU; TOC 0.5–1.54 mg/L; nitrate 35–40 mg/L; sulphate 50–60 mg/L; A medium pressure mercury lamp.	Bourgine et al. (1997)
	3.6 x 10^{-6} M	483 mJ/cm^2 574 mJ/cm^2	90%—W1[a] 90%—W2[b]	Bench scale: Natural water spiked with bromoxynil; W1: alkalinity 136 mg/L as $CaCO_3$; TOC 2.8 mg/L; pH 8.1; W2: alkalinity 230 mg/L as $CaCO_3$; TOC 20.6 mg/L; pH 8.4.	Chelme-Ayala et al. (2010a)
Oxidant	**Influent (M)**	**Oxidant Dose**	**Removal %**	**Process Description**	**References**
O_3	9 x 10^{-6} M	0.1–0.5 mM	98% at pH 7.0 in 2 minutes	Bench-scale: buffered ultrapure water; pHs 2.0 and 7.0; room T°: 20°C; tert-butyl alcohol 10 mM ($^{\bullet}OH$ scavenger).	Chelme-Ayala et al. (2010b)

TOC—total organic carbon concentration.

[a] W1: Samples collected from the North Saskatchewan River, upstream of the City of Edmonton.

[b] W2: Samples collected from an irrigation return flow discharging into Redwater River.

Table 7. Bench-scale ozonation tests conducted with spiked ultra-pure buffered water and natural water

Oxidant	Influent (M)	Oxidant Dose	Removal %	Process Description	Reference
O_3	3.6×10^{-6} M	1.7×10^{-5} M	87% at pH 7.0 99% at pH 9.0	Ultrapure water: pHs 7.0 and 9.0.	Chelme-Ayala et al. (2011)
			89%—0.0 mM 47%—5.0 mM	Ultrapure water: Alkalinity 0.0 and 5.0 mM as $CaCO_3$; pH 7.0.	
			88%—8.8×10^{-6} M 72%—22.0×10^{-6} M	Ultrapure water: Humic acid 8.8×10^{-6} and 22.0×10^{-6} M; alkalinity 1.0 mM.	
		2.1×10^{-5} M	60%—W1[a] 39%—W2[b]	Natural water spiked with bromoxynil; W1: alkalinity 136 mg/L as $CaCO_3$; TOC 2.8 mg/L; pH 8.1; W2: alkalinity 230 mg/L as $CaCO_3$; TOC 20.6 mg/L; pH 8.4.	

TOC—total organic carbon concentration.

[a] W1: Samples collected from the North Saskatchewan River, upstream of the City of Edmonton.

[b] W2: Samples collected from an irrigation return flow discharging into Redwater River.

4.2.1.5 Advanced Oxidation Processes

Bench-scale tests reported a high reactivity of bromoxynil toward •OH generated by ozone decomposition at basic conditions (pH > 10) (Chelme-Ayala et al., 2010b; Chelme-Ayala et al., 2011). Chelme-Ayala et al. (2010b) calculated a reaction rate constant of 8.45×10^9 $M^{-1}s^{-1}$ of the reaction of ozone (0.015 mM) with bromoxynil concentration of 9.0 µM at pH 11.0.

Bench-scale removal of bromoxynil using two AOPs, UV/H_2O_2 and O_3/H_2O_2, was studied in natural water samples (sampling discussed in section 4.2.1.4) (Chelme-Ayala et al., 2010a; Chelme-Ayala et al., 2011). Both processes, UV/H_2O_2 and O_3/H_2O_2, reported an increase in the levels of degradation of bromoxynil compared to direct UV photolysis and molecular ozonation, respectively. The results in Table 8 showed that a higher degradation rate of bromoxynil was achieved in water samples having a lower TOC concentration and a lower alkalinity (samples W1). The presence of organic matter and bicarbonate ions in natural water reduced the concentration of •OH available to react with the pesticides (Chelme-Ayala et al., 2010a; Chelme-Ayala et al., 2011).

Studies identified several degradation by-products of bromoxynil oxidation after UV photolysis and/or ozonation in aqueous solution: 3-bromo-4-hydroxybenzonitrile, 4-hydroxybenzonitrile, 3-bromo-4-hydroxy-5-nitrobenzonitrile, 4-hydroxy-3-nitrobenzonitrile, 3,5-dibromo-2,4-dihydroxybenzonitrile, 3-bromo-4,5-dihydroxybenzonitrile (Kochany and Chaudhry, 1990a; Kochany et al., 1990b; Marchado et al., 1995; Chelme-Ayala et al., 2010b). Chelme-Ayala et al. (2010b) suggested that the degradation of bromoxynil occurs via hydroxylation and debromination. Studies reported that some pesticide degradation by-products are more persistent than the parent molecule. As such, the application of higher oxidant doses may be required to degrade the target molecule and the degradation by-products generated during the treatment (Chelme-Ayala et al., 2011; Beduk et al., 2012; Li et al., 2019). A H_2O_2/O_3 ratio in the range 0.4–0.6 was suggested as an optimum ratio for pesticide degradation (Glaze et al., 1987; Acero and von Gunten, 2001; Can and Cakir, 2010). Although oxidation and AOPs appear to be effective treatment processes for removal of bromoxynil, water utilities need to consider the formation of the degradation by-products, depending on the oxidant selected and water quality.

Table 8. Removal of bromoxynil via advanced oxidation processes

Process	Influent (M)	Oxidant Dose		Removal %	Process Description	References
UV/H_2O_2	3.6×10^{-6} M	333 mJ/cm^2 366 mJ/cm^2	H_2O_2—8.8×10^{-4} M	90%—W1[a] 90%—W2[b]	Bench-scale: natural water spiked with bromoxynil; W1: alkalinity 136 mg/L as $CaCO_3$; TOC 2.8 mg/L; pH 8.1; W2: alkalinity 230 mg/L as $CaCO_3$; TOC 20.6 mg/L; pH 8.4.	Chelme-Ayala et al. (2010a)
O_3/H_2O_2	3.6×10^{-6} M	O_3—2×10^{-5} M; H_2O_2—1×10^{-5} M (H_2O_2/O_3 = 0.5)		70%—W1 49%—W2		Chelme-Ayala et al. (2011)

TOC—total organic carbon concentration.

[a] W1: Samples collected from the North Saskatchewan River, upstream of the City of Edmonton.

[b] W2: Samples collected from an irrigation return flow discharging into Redwater River.

4.2.1.6 Biofiltration

Biological treatment involves targeting the removal of the biodegradable organic material fraction. The effectiveness of biological treatment depends 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, rapid granular media filtration without the maintenance of a disinfectant residual across the bed and slow sand filtration.

A laboratory batch study was conducted to observe the biodegradation of bromoxynil using groundwater added to a salt medium (Preuss et al. 1996). Under anaerobic conditions, biodegradation of bromoxynil was > 99% after 32 days. No biodegradation was observed under aerobic conditions.

4.2.2 Residential-scale

In cases where bromoxynil removal is desired at the household level, for example, when a household obtains its drinking water from a private well, a residential drinking water treatment unit may be an option for decreasing bromoxynil concentrations in drinking

water. Before a treatment unit is installed, the water should be tested to determine the general water chemistry and bromoxynil concentration in the source water. There is a lack of performance testing of treatment technologies; however, adsorption (activated carbon) and RO treatment units are expected to be effective for bromoxynil removal at the residential-scale. 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:

- CSA Group (www.csagroup.org);
- NSF International (www.nsf.org);
- Water Quality Association (www.wqa.org);
- UL LLC (www.ul.com);
- Bureau de Normalisation du Québec (www.bnq.qc.ca) (available in French only);
- International Association of Plumbing and Mechanical Officials (www.iapmo.org); and
- Truesdail Laboratories Inc. (www.truesdail.com).

An up-to-date list of accredited certification organizations can be obtained from the SCC (www.scc.ca).

Currently, bromoxynil is not included in the performance requirements of NSF/ANSI standards. However, consumers can use a treatment unit that is certified to the standards for adsorption or RO to ensure that the material safety has been tested. In addition, units that have been certified for the removal of atrazine are more likely to be effective for the removal of bromoxynil, as bromoxynil was shown to have better adsorption than atrazine (see Section 4.2.1.2).

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, 2011, 2012). These approaches require a system assessment to characterize the source water, describe the treatment barriers that prevent or reduce contamination, to identify the conditions that can result in contamination and to 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

Bromoxynil 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 bromoxynil to enter source water (e.g., raw water supply to the drinking water system) based on site-specific considerations.

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

Where treatment is required to remove bromoxynil, 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 bromoxynil removal.

Where treatment is in place for bromoxynil 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 and during periods of peak use. When routine operational monitoring indicates the potential for contaminant breakthrough, such as with GAC, monitoring should be conducted quarterly to plan for the regeneration or replacement of the media. When a degradation process is utilized, oxidation by-product formation should also be considered.

6.0 INTERNATIONAL CONSIDERATIONS

Other national and international organizations have drinking water guidelines, standards and/or guidance values for bromoxynil in drinking water. Variations in these values can be attributed to the age of the assessments or to differing policies and approaches, including the choice of key study and the use of different consumption rates, body weights and source allocation factors.

Australia has set a guideline value of 0.01 mg/L (10 µg/L) for bromoxynil in drinking water (NHMRC and NRMMC, 2011). This guideline value is based on a no-observed-effect level of 0.3 mg/kg bw per day from a 12-month dietary study in dogs which reported reduced bodyweight gain at 1.5 mg/kg bw per day and evidence of anemia at 7.5 mg/kg bw per day. The US EPA does not have a regulatory value for bromoxynil. It concluded that there are no chronic or acute risks of concern for any subpopulations from drinking water (US EPA, 1998). The World Health Organization has not set a specific guideline value for bromoxynil.

Bromoxynil is not approved for use in the European Union (European Commission, 2020).

7.0 RATIONALE

Bromoxynil is registered in Canada to control a wide spectrum of annual broadleaf weeds in food and feed crops. Despite its common use in Canada, data provided by provinces and territories that monitor for bromoxynil in source and drinking water indicate that, when detected, levels of bromoxynil are below the MAC. The liver is considered the target organ for bromoxynil toxicity. Although no human studies have investigated the effects of bromoxynil on the liver, animal studies conducted in several species (rats, mice and dogs) have consistently shown liver toxicity following bromoxynil exposure. Health Canada, in collaboration with the Federal-Provincial-Territorial Committee on Drinking Water, has established a MAC of 0.03 mg/L (30 µg/L) based on the following considerations:

- An HBV of 0.03 mg/L (30 µg/L) based on an increase in clinical signs and liver weight and decreases in body weight and body weight gain observed in dogs.
- Bromoxynil can be accurately measured at concentrations well below the MAC.
- Bromoxynil is expected to be removed at the municipal and residential scale.

The MAC is protective of potential health effects. As part of its ongoing guideline review process, Health Canada will continue to monitor new research in this area, including the outcomes of PMRA evaluations, and recommend any change to this guideline technical document that it deems necessary.

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APPENDIX A: LIST OF ABBREVIATIONS

ADI	Acceptable daily intake
AHS	Agricultural Health Study
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
ANSI	American National Standards Institute
AOP	Advanced oxidation process
Br-DHBN	3-bromo-4,5-dihydroxybenzonitrile
bw	Body weight
CAR	Constitutive androstane receptor
CAS	Chemical Abstracts Service
CD-1	Mouse strain
CHO	Chinese hamster ovary, cell line
CSA	CSA Group or Canadian Standards Association
DNA	Deoxyribonucleic acid
FNIHB	First Nations and Inuit Health Branch
GAC	Granulated activated carbon
GC/MS	Gas Chromatography with Mass Spectrometry Detection
GD	Gestation days
HBV	Health-based value
HGPRT	Hypoxanthine-guanine phosphoribosyltransferase
HPCL-UV	High Performance Liquid Chromatography with Ultraviolet Detection
HPLC-MS	High Performance Liquid Chromatography with Mass Spectrometry Detection

Kow	n-octanol:water partition coefficient
LC50	Median lethal concentration
LD50	Median lethal dose
LOAEL	Lowest-observed-adverse-effect level
MAC	Maximum acceptable concentration
MDL	Method detection limit
MOA	Mode of action
MRL	Method reporting limit
MWCO	Molecular weight cut-off
NF	Nanofiltration
NOAEL	No-observed-adverse-effect level
NOM	Natural organic matter
NSF	NSF International
NTU	Nephelometric turbidity unit
•OH	Hydroxyl radicals
PAC	Powdered activated carbon
PCPA	Pest Control Products Act
PMRA	Pest Management Regulatory Agency
PPARa	Peroxisome proliferator-activated receptor
RO	Reverse osmosis
SCC	Standards Council of Canada
TOC	Total organic carbon concentration
US EPA	United States Environmental Protection Agency
UV	Ultraviolet
WHO	World Health Organization

APPENDIX B: CANADIAN WATER QUALITY DATA

Table B1. Levels of bromoxynil 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)		25th percentile (ng/L)	Mean (ng/L)	Median (ng/L)	75th percentile (ng/L)
			Min	Max				
Tap Water								
AB, SK, MB—rural communities (2004–2005)	?/28	-	0.99	227.00	-	12.80	-	-
Surface Water								
BC—Lower Fraser Valley and Okanagan Basin (2003–2005)	0/83	0.25	< 0.25	-	-	-	-	-
ON (2003)	22/162	0.99	1.13	692	-	-	-	-
ON (2004)	81/228	0.99	1.00	110	-	-	-	-
ON (2005)	46/183	0.99	1	45.8	-	-	-	-
QC (2003)	1/51	20	< 20	50	-	-	-	-
QC (2004)	2/70	10–20	< 10	40	-	-	-	-
QC (2005)	1/59	20	< 20	270	-	-	-	-
Rivers								
AB, SK, MB—8 sites (2003)	22/64	0.99	< 0.99	63.3	-	-	1	-
Reservoir Water								
AB, SK, MB—15 sites (2003–2004)	111/206	0.99	0.5	384	0.99	-	0.99	3.68

Information adapted from Environment Canada (2011).

?—number of detects not given; MDL—method detection limit.