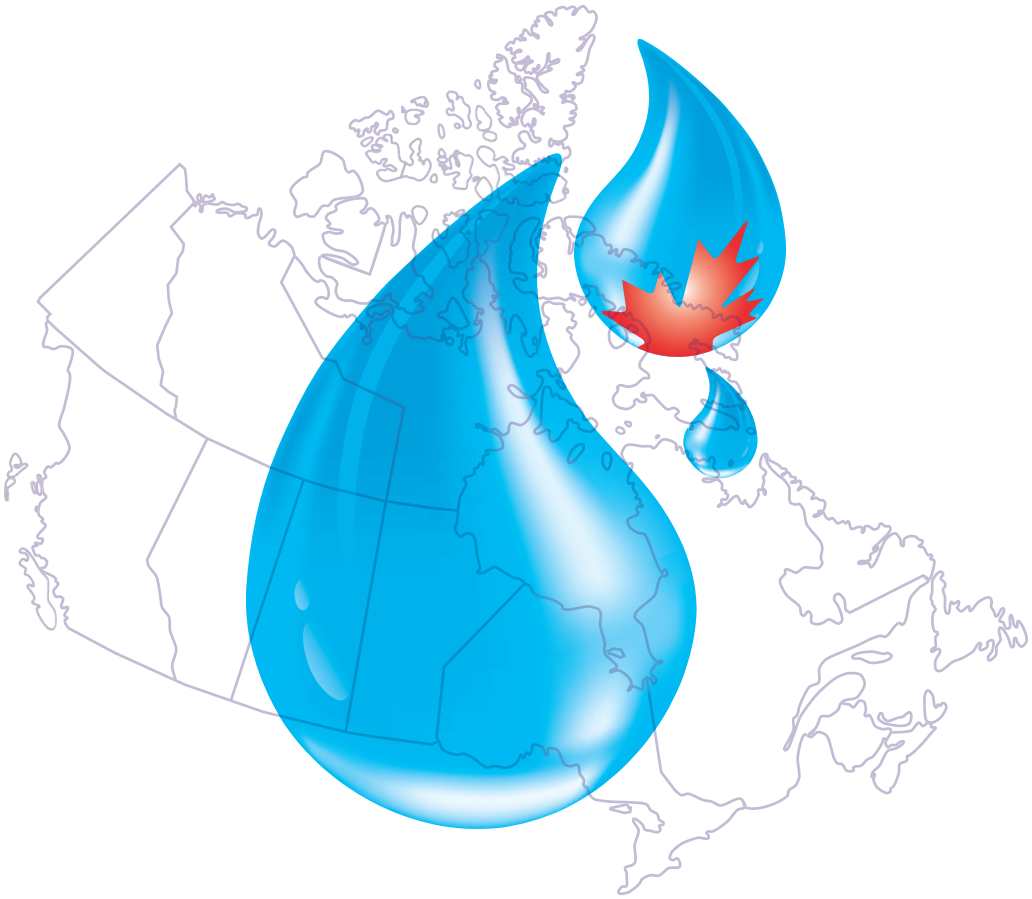
Health Canada Santé Canada

Your health and safety… our priority. *Votre santé et votre sécurité… notre priorité.*

Guidelines for Canadian Drinking Water Quality

Guideline Technical Document

2-Methyl-4-chlorophenoxyacetic Acid (MCPA)



Canada

Health Canada is the federal department responsible for helping the people of Canada maintain and improve their health. *We assess the safety of drugs and many consumer products, help improve the safety of food, and provide information to Canadians to help them make healthy decisions. We provide health services to First Nations people and to Inuit communities. We work with the provinces to ensure our health care system serves the needs of Canadians.*

Published by authority of the
Minister of Health

Guidelines for Canadian Drinking Water Quality: Guideline Technical Document 2-Methyl-4-chlorophenoxyacetic Acid (MCPA)
is available on Internet at the following address: www.healthcanada.gc.ca

Également disponible en français sous le titre :
Recommandations pour la qualité de l'eau potable au Canada : document technique Acide (4-chloro-2-méthylphénoxy) acétique (MCPA)

This publication can be made available on request on
diskette, large print, audio-cassette and braille.

For further information or to obtain additional copies, please contact:
Publications
Health Canada
Ottawa, Ontario K1A 0K9
Tel.: 613-954-5995
Fax: 613-941-5366
Email: info@hc-sc.gc.ca

Cat.: H128-1/10-620E-PDF
ISBN: 978-1-100-17194-4

Guidelines for Canadian Drinking Water Quality

Guideline Technical Document

2-Methyl-4-chlorophenoxyacetic Acid (MCPA)

Prepared by the
Federal-Provincial-Territorial Committee on Drinking Water
of the
Federal-Provincial-Territorial Committee on Health and the Environment

Ottawa, Ontario

February 2010

This document may be cited as follows:

Health Canada (2010) Guidelines for Canadian Drinking Water Quality: Guideline Technical Document—2-Methyl-4-chlorophenoxyacetic Acid (MCPA). Water, Air and Climate Change Bureau, Healthy Environments and Consumer Safety Branch, Health Canada, Ottawa, Ontario. (Catalogue No. H128-1/10-620E-PDF)

The document was prepared by the Federal-Provincial-Territorial Committee on Drinking Water of the Federal-Provincial-Territorial Committee on Health and the Environment.

Any questions or comments on this document may be directed to:

Water, Air and Climate Change Bureau
Healthy Environments and Consumer Safety Branch
Health Canada
269 Laurier Avenue West, Address Locator 4903D
Ottawa, Ontario
Canada K1A 0K9

Tel.: 613-948-2566
Fax: 613-952-2574
Email: water_eau@hc-sc.gc.ca

Other Guideline Technical Documents for the Guidelines for Canadian Drinking Water Quality can be found on the following web page: www.healthcanada.gc.ca/waterquality

Table of Contents

February 2010

2-Methyl-4-chlorophenoxyacetic Acid (MCPA)

Part I. Overview and Application

1.0 Guideline

The maximum acceptable concentration (MAC) for 2-methyl-4-chlorophenoxyacetic acid (MCPA) in drinking water is 0.1 mg/L (100 µg/L).

2.0 Executive summary

2-Methyl-4-chlorophenoxyacetic acid (MCPA) is a phenoxyacetic acid herbicide, registered in Canada for use on agricultural sites, fine turf and lawns, in forestry and at industrial sites. It is among the top 10 pesticides sold in Canada and is used across the country, most extensively in the Prairie provinces. Herbicide formulations can use various forms of MCPA, including the free acid, salts and esters, but all release the acid as the active ingredient.

This Guideline Technical Document reviews the health risks associated with MCPA in drinking water. It assesses all identified health risks, taking into account available studies and approaches, as well as the limitations of available treatment technology. It considers exposure to MCPA through drinking water only from ingestion, as exposure through inhalation and skin contact is not considered to be significant. From this review, a maximum acceptable concentration (MAC) of 0.1 mg/L (100 µg/L) for MCPA in drinking water is established, based on health effects.

2.1 Health effects

Some studies have been conducted on the impacts of chlorophenoxy herbicides, including MCPA, on human health. However, because the subjects were exposed to several pesticides, as well as to other organic compounds, these studies cannot be used to assess the toxicity of MCPA to humans. The MAC is established based on kidney effects observed in the rat.

Health Canada classifies MCPA as unclassifiable with respect to carcinogenicity in humans, based on inadequate data from human studies and a lack of adequate animal studies. This is consistent with the classification of the International Agency for Research on Cancer.

2.2 Exposure

There are limited data available on human exposure to MCPA. Based on these data, drinking water is not expected to be a significant route of exposure. Low levels of MCPA in sources of drinking water have been found in many Canadian provinces. In specific situations, MCPA can be found in water as a result of spills, deliberate dumping of tank residues or equipment washing operations.

2.3 Analysis and treatment

The establishment of a drinking water guideline must take into consideration the ability to both measure the contaminant and remove it from drinking water supplies. MCPA can be detected at levels well below the MAC of 0.1 mg/L.

MCPA can be effectively treated in municipal-scale treatment facilities to below the MAC through a number of well-documented methods. At the residential scale, no drinking water treatment devices available on the market are currently certified for the removal of MCPA; however, certified devices capable of reducing the concentration of organic compounds may be suitable for MCPA removal.

3.0 Application of the guideline

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

The guideline for MCPA is based on a lifetime exposure to MCPA from drinking water and is protective against health effects from lifetime exposure. Short-term exceedances above the guideline value are unlikely to have an impact on health, unless these exceedances are due to massive contamination or spills. However, in the event that monitoring results show elevated levels on a regular basis, it is suggested that a plan be developed and implemented to address the situation.

MCPA, a phenoxyacetic acid herbicide registered for use in Canada, is not a concern for the majority of Canadians. Although MCPA is used everywhere in Canada, it is used most extensively in the Prairie provinces for agriculture, in the production of cereals, canary seeds, legumes and grasses, asparagus, field corn and sweet corn. Therefore, its application is limited to the growing season. As a result, in these high-use areas, MCPA can be introduced into surface water and possibly groundwater through runoff or as the result of spills, deliberate dumping of tank residues or equipment washing operations. MCPA is not persistent in water or soil because of its biological degradation (under aerobic conditions), an important degradation pathway. However, in oxygen-deprived environments such as groundwater or during periods of cold weather and low light, the degradation of MCPA via biological degradation or photodecomposition is rather limited.

3.1 Monitoring

MCPA is registered in Canada for various uses, with the major one being on agricultural sites, where it is used most extensively in the Prairie provinces during the growing season.

Frequent monitoring of treated surface water is recommended in areas of high use such as the Prairies and other agricultural areas during periods of peak use, which occur from May to early fall, and for treatment plants located downstream of these areas. This frequency will provide a complete picture of runoff contamination, especially after rainfall has occurred. Monitoring of groundwater from areas of high use is also recommended for MCPA, but at a reduced frequency.

Part II. Science and Technical Considerations

4.0 Identity, use, sources and fate in the environment

MCPA is a phenoxyacetic acid herbicide, with various formulations: as the free acid, as a dimethylamine salt (MCPA-DMAS), as a sodium salt (MCPA sodium salt) and as an ester (MCPA 2-ethylhexyl ester, or MCPA-EHE) (U.S. EPA, 2004b,d). Although MCPA may be applied in various forms, a single common functional group (the parent acid) is the active portion of the herbicide formulation (U.S. EPA, 2004c,e; PMRA, 2006). Diethanolamine MCPA, another amine salt formulation, is not discussed in this document, as there is no information available on its toxicology and Health Canada's Pest Management Regulatory Agency (PMRA) is proposing that it be phased out (PMRA, 2006).

MCPA acts as a plant growth regulator and is used to control broadleaf weeds in post-emergence in agriculture and in urban, forestry and aquatic environments (IARC, 1983; Weed Science Society of America, 1989; HSDB, 2003). MCPA is absorbed through both leaves and roots and is translocated throughout the plant. By stimulating nucleic acid and protein synthesis, MCPA affects enzyme activities, respiration and cell division. As a result, treated plants exhibit malformed leaves, stems and roots (U.S. EPA, 1990).

Those physicochemical properties of MCPA acid and its related forms that are relevant to their behaviour in the environment are summarized in Table 1.

The physicochemical properties of these other forms of MCPA vary widely according to the formulation. In general, the salts are water soluble, whereas the esters are lipophilic and less water soluble (U.S. EPA, 2004d,e). Based on its Henry's law constant, MCPA is not expected to volatilize from water or moist surfaces. Its vapour pressure also indicates a low potential to volatilize, and its dissociation constant indicates that it will dissociate rapidly at environmental pH (PMRA, 2006). As available environmental fate data show that all forms of MCPA will revert to MCPA acid, the physicochemical characteristics of MCPA in the environment will be those associated with MCPA acid (U.S. EPA, 2004a).

It should be noted that MCPA is usually applied along with other phenoxy herbicides, such as 2,4-dichlorophenoxyacetic acid (2,4-D), 4-(2,4-dichlorophenoxy)butyric acid (2,4-DB), (R)(+)-2-(4-chloro-2-methylphenoxy)propanoic acid (also known as mecoprop-p or MCPP-p) and 4-(2-methyl-4-chlorophenoxy)butyric acid (MCPB) (U.S. EPA, 2004b).

MCPA is registered for use in Canada for agricultural sites, for fine turf (parks, play-grounds, golf courses, zoos, botanical gardens and athletic playing fields), for lawns (residences, public and commercial buildings) and sod (grown in sod farms harvested for transplanting), in forestry (spruce seedlings for reforestation) and at industrial sites (vegetation control) (PMRA, 2005a). In Canada, the major applications of MCPA are in agriculture, where it is used in the production of cereals (barley, oats, rye, wheat and flax) and in the production of canary seeds, legumes and grasses, asparagus, field corn and sweet corn. MCPA is also applied to stubble/ summerfallow fields and pastures/rangeland (PMRA, 2005a). MCPA is used everywhere in Canada, particularly in the Prairies (PMRA, 2005a).

Table 1: Physicochemical properties[a]

Property	MCPA	MCPA-EHE	MCPA-DMAS	MCPA sodium salt
Form	Solid, flakes or crystalline powder	Liquid	Liquid	n.a.[b]
Melting point	120°C	260–265°C	111°C	n.a.
Henry's law constant	7.46×10^{-5} Pa·m^3/mol	2.56 Pa·m^3/mol	n.a.	n.a.
Density at 20°C	1.18–1.21 g/mL	1.06 g/mL	1.181 g/mL	n.a.
Vapour pressure at 20°C	8.18×10^{-5} to 1.36×10^{-4} Pa at 20°C	3.43×10^{-6} to 1.63×10^{-3} Pa at 20°C	n.a.	n.a.
Water solubility	Very soluble[c] 26.2 g/L at pH 5 293 g/L at pH 7 320 g/L at pH 9	Slightly soluble (0.1%, w:w)	Soluble; dissociates quickly to form the free phenoxy acid moiety and dimethylammonium	Soluble; reverts to the acid form under acidic conditions
Octanol/water partition coefficient (log K_{ow})	1.43–2.82	5.37	1.415 at 25°C	n.a.
Organic carbon partition coefficient (log K_{oc})	0.98-2.07	n.a.	n.a.	n.a.
Dissociation constant (pK_a)	3.07	n.a.	n.a.	n.a.

[a] From Worthing and Hance (1991); USDA (2001); Struger et al. (2004); U.S. EPA (2004a,d); PMRA (2006; 2007).
[b] n.a. = not available.
[c] Solubility as reported in PMRA (2006). It should be noted, however, that other literature sources report "practically insoluble." As these sources do not provide the pH at which the values were measured, these values are not reported in the table, as solubility changes with pH.

MCPA is among the top 10 pesticides sold in Canada. Table 2 presents the limited data available on the sales/use of MCPA from recent years. Brimble et al. (2005) reported that Saskatchewan is responsible for approximately 36% of all pesticide sales in Canada, making it the largest pesticide user in Canada. Although sales data for Saskatchewan are not currently available, a database to collect this information is under development. In Quebec, legislation bans the application of MCPA (and other specific pesticides) around all daycare facilities, schools, some public lands and private green spaces (Gouvernement du Québec, 2006).

Table 2: Sales/use of MCPA (active ingredient) in Canada[a]

Province	Year	Sales/use (active ingredient, in kg)	% of use based on top 20 active ingredients
British Columbia	2003	23 598	0.51
Alberta	1998	885 239	9.52
Manitoba[b]	2003	450 091	12.48
Ontario[b]	2003	129 337	3.07
Quebec[c]	2002	80 000 (approx.)	31 (approx.)
New Brunswick	2003	17 053	2.18
Nova Scotia[b]	2003	6 109	1.38
Prince Edward	2001	28 999	n.a.[d]

[a] Adapted from Brimble et al. (2005).
[b] MCPA values include MCPB.
[c] Ministère du Développement durable, de l'Environnement et des Parcs du Québec (2007).
[d] n.a. = not available.

4.1 Environmental fate

4.1.1 Soil

MCPA is not persistent in soil (U.S. EPA, 2004a), with a half-life varying between 15 and 50 days (Soderquist and Crosby, 1975; Sattar and Paasivirta, 1980). The rate of degradation depends upon several factors, such as soil type, soil pH, soil moisture, concentration of MCPA, climatic conditions and organic matter content (Sattar and Paasivirta, 1980). Degradation of MCPA occurred within 5–9 weeks in acidic soil compared with 1 week in neutral soil (pH 6.3 and above) (Sattar and Paasivirta, 1980).

Microbial degradation is the most important transformation process for MCPA in soil (Caux et al., 1995); the presence of both oxygen and proper moisture is important for its biodegradation (Sattar and Paasivirta, 1980). In the absence of oxygen, the biotransformation of MCPA in soil is negligible (PMRA, 2006). Photodecomposition and hydrolysis in soil are not important degradation processes for MCPA (U.S. EPA, 2004a,b; PMRA, 2006). When MCPA was applied to soil surfaces and irradiated with natural sunlight, its calculated half-life was 67 days, demonstrating that MCPA photodegraded very slowly (U.S. EPA, 2004a,b).

MCPA was shown to be mobile in soil in laboratory studies (U.S. EPA, 2004a). However, field studies indicate that MCPA does not leach appreciably below soil depths of 15 cm (PMRA, 2007). Its mobility seems to be related to the soil's organic matter content, increasing as the organic matter content decreases (WHO, 2003). Surface water may be contaminated via spray drift and runoff, whereas groundwater can be potentially contaminated because MCPA is mobile in soil and, as a result, may have a potential for leaching (U.S. EPA, 2004a). The mobility and leaching of the non-acid forms of MCPA (i.e., amine and sodium salts, esters) have not been determined.

Field studies with MCPA-EHE have shown that, under normal conditions, a large proportion converts to MCPA acid on the day of application, and the MCPA-EHE is nearly completely converted by day 3 (U.S. EPA, 2004a). However, under dry conditions, MCPA-EHE has been found to persist for days, with greater than 90% present after 48 hours (Smith and Hayden, 1980). In a non-sterile soil:calcium chloride system at pH 5.6 and pH 6.8, MCPA-EHE adsorbed to the soil particles but was available for degradation to MCPA, with a half-life of $\leq$ 12 hours (U.S. EPA, 2004a).

4.1.2 Water

Agricultural herbicides such as MCPA have been detected in lakes, rivers and reservoirs (dugouts), which may serve as sources for drinking water. Their migration from soil to water is the result of direct or indirect transport mechanisms, including non-target drift from aerial or ground boom spraying (vaporization in air), deposition in rain, erosion of soil particles by wind or water, surface runoff and leaching. In specific situations, MCPA can be found in water as a result of spills, deliberate dumping of tank residues or equipment washing operations (Caux et al., 1995; Murray et al., 2004). MCPA is not expected to volatilize from water based on its vapour pressure (8.18×10^{-5} to 1.36×10^{-4} Pa) and its Henry's law constant (7.46×10^{-5} Pa·cm^3/mol). By contrast, MCPA-EHE is expected to volatilize from water based on its low to intermediate vapour pressure (3.43×10^{-4} to 1.63×10^{-3} Pa) and its Henry's law constant (2.56 Pa·m^3/mol) (PMRA, 2007).

In water, biological degradation (under aerobic conditions) is an important process affecting MCPA's environmental fate (Soderquist and Crosby, 1975; Sattar and Paasivirta, 1980; Smith and Hayden, 1981; PMRA, 2006). MCPA in rice paddy water under dark conditions is totally degraded by aquatic microorganisms in 13 days (Soderquist and Crosby, 1975). However, in anaerobic aquatic systems (sediment/water), the biodegradation of MCPA was negligible (PMRA, 2006). Hydrolysis and photodegradation are not important routes in the degradation of MCPA in water (PMRA, 2006). In an aqueous solution (pH 8.3), MCPA had a photolytic half-life of 20–24 days in sunlight. Photolysis of dilute aqueous MCPA solutions yielded 4-chloro-2-methylphenol as the major by-product; *o*-cresol and 4-chloro-2-formylphenol were also identified (Soderquist and Crosby, 1975). During periods of cold weather and low light, the degradation of MCPA via biological degradation or photolysis is rather limited (Byrtus et al., 2004). MCPA acid does not readily hydrolyse in sterile buffer solution at pH 5–9 (U.S. EPA, 2004a). MCPA has not been shown to bind significantly to sediments (Caux et al., 1995).

The derivatives of MCPA have been shown to dissociate in water to MCPA acid. In deionized water, MCPA-DMAS completely dissociated to MCPA acid and dimethylammonium ion within 1.5 min (U.S. EPA, 2004a). In sterile buffers, the hydrolysis of MCPA-EHE to MCPA acid was pH dependent (half-life < 117 hours at pH 9, but no hydrolysis at pH 5 and pH 7).

4.1.3 Atmosphere

Pesticides can enter the atmosphere via application drift, evaporation, sublimation or erosion of treated soil. Once in the air, pesticides can be transported and redistributed, degraded or returned to the earth's surface via wet deposition (dissolved in rain) and dry deposition (as gases or aerosols or sorbed to solid macro-particles) (Hill et al., 2002; Waite et al., 2005). However, little information on the fate of MCPA is available. Waite et al. (2005) demonstrated,

by high-volume air sampling at various heights above ground level in the Canadian Prairies, that atmospheric concentrations of MCPA are strongly influenced by regional atmospheric transport and that its primary transport mechanism is via adsorption to solid particles in the atmosphere. The volatilization of MCPA in the acid or salt form is low (Weed Science Society of America, 1989; Caux et al., 1995). The half-life of MCPA due to photooxidation was estimated to be 2.2 days (Caux et al., 1995).

5.0 Exposure

Canadians can be exposed to MCPA through its presence in drinking water, air and food. In addition, certain segments of the population can be exposed through the use of specific consumer products or in occupational settings related to pesticide use and application. Although some exposure data are available, they are considered insufficient to justify modifying the default allocation factor for drinking water (i.e., the proportion of the total daily intake of MCPA allocated to drinking water) of 20%.

5.1 Air

During 1989 and 1990, MCPA was detected in only 4% of atmospheric samples at two dugout sites near Regina, Saskatchewan, where it was being applied locally, with a maximum concentration of 0.39 ng/m^3 (Waite et al., 2004). It was detected in 24% of bulk (dry plus wet) atmospheric deposits at these same sites, with a mean deposition rate of 129 ng/m^3 per day.

In a small southern Manitoba watershed, MCPA was detected at concentrations up to 13 ng/m^3 in atmospheric samples between 1993 and 1996 (Rawn et al., 1999).

In a province-wide survey of herbicide concentrations in rainfall conducted in Alberta between April and September (1999–2000), MCPA was detected in less than 50% of samples taken (Hill et al., 2002). Among the major pesticides, MCPA was detected in the second highest total amount, with maximum concentrations ranging from 38 to 84 µg/m^2 (based on an amount basis). The total amount of MCPA deposited in rainfall varied over the season, with levels highest during June and July (spraying season), and varied with the region sampled: the highest levels were observed in central rural Alberta, the second highest in southern rural Alberta and the lowest in remote regions and city locations.

In Alberta in 2000, MCPA was detected in 7 of 68 samples (10%) at four sites across Alberta in ambient air samples (Kumar, 2001). Concentrations ranged from 0.03 to 0.46 ng/m^3. MCPA was detected at relatively low concentrations and detection frequencies compared with other pesticides that had higher volatility.

5.2 Water

5.2.1 Drinking water

In Alberta, MCPA was seldom detected (11%) in a treated water survey program during the period 1995–2003 (Byrtus et al., 2004). MCPA was detected in 190 of a total of 1788 water samples collected for analysis throughout this period. MCPA was detected more at treatment facilities with surface water sources (13.7%) than at facilities with groundwater sources (2%); the maximum concentrations detected were 571 ng/L and 5 ng/L, respectively. The data showed no overall or seasonal trend over the 9 years in detection frequency or concentration, suggesting that MCPA could be detected in treated water supplies all year round.

MCPA was detected in 2 of 403 samples of municipal drinking water in surveys conducted in Manitoba from 1981 to 1999 (Manitoba Conservation, 2000). The maximum concentration found was 49 µg/L.

In various towns in Ontario, MCPA was detected in 4 of 29 raw water samples for 2004, at concentrations ranging from 27 to 49 ng/L, and in 2 of 132 treated water samples for the year 2004 and January 2005, at concentrations ranging from 27 to 66 ng/L (Ontario Ministry of the Environment, 2005). The detection limit was 20 ng/L.

In Nova Scotia, MCPA was not detected in raw or treated water from Dartmouth (detection limit 2 µg/L) or Stellarton (effective quantification limit 50 µg/L) during sampling done in June 2003 (Nova Scotia Department of Environment and Labour, 2005).

In Newfoundland and Labrador, MCPA was not detected in two wells sampled in 1982 (detection limit 2 µg/L) (Newfoundland and Labrador Department of Environment and Conservation, 2005).

MCPA was not detected in any of the 10 groundwater samples taken in Prince Edward Island in 1998 (Blundell and Harman, 2000).

5.2.2 Potential sources of drinking water

In British Columbia, MCPA was detected in 1 of 13 samples of runoff in the Lower Fraser Valley in 2003. The maximum concentration was 110 ng/L (Tuominen et al., 2005).

In Alberta, MCPA was detected in 1150 of 3062 samples (37.6%) collected from surface waters (rivers, streams, lakes, etc.) between 1995 and 2002 (Anderson, 2005). Concentrations ranged up to 8.5 µg/L, with the median concentration at 0.02 µg/L (detection limit 0.005 µg/L).

In Saskatchewan, runoff water from flood-irrigated fields enters a system of drainage ditches, which then drain into the South Saskatchewan River, potentially affecting downstream water quality. The concentrations of MCPA and other herbicides in the drainage water from two drainage ditches in an irrigation district that emptied into the South Saskatchewan River were sampled during the 1994–1996 growing seasons (Cessna et al., 2001). The maximum concentration of MCPA in the drainage water was 2.8 µg/L. Input of MCPA into the river was approximately 0.06% of the amounts applied; in all 3 years, MCPA was applied to flood-irrigated land irrigated by both drainage ditches. No significant increase in herbicide concentration was seen in the river as a result of herbicide input, because of the large flows seen in the river.

In a preliminary 2003 spring/summer pesticide surveillance study, MCPA was detected in all of 15 small reservoirs (dugouts) sampled in the three Prairie provinces (Murray et al., 2004). Mean MCPA concentrations in most of the dugouts ranged from 13 to 108 ng/L. The detection limit was 0.58 ng/L. Two reservoirs had higher levels, ranging from 200 to 320 ng/L, possibly a result of commercial formulations (which include MCPA) being applied in the watershed or catchment (Murray et al., 2004).

MCPA was detected in 10 of 49 samples of surface water taken from three of the Great Lakes—Lake Ontario (1998–1999), Lake Erie (1994, 1998, 2000) and Lake Huron (1999–2000)—with a maximum concentration of 5.4 ng/L, whereas it was not detected in nine samples from Lake Superior (1996–1997) (Struger et al., 2004). The detection limit was between 0.27 and 0.30 ng/L. Spatial and seasonal variations observed were related to MCPA's use patterns.

In sampling around the Great Lakes Areas of Concern in 2004, MCPA was detected in 127 out of 217 samples, with a maximum concentration of 350 ng/L (Struger et al., 2005). The detection limit was 5.8 ng/L. MCPA was detected in 120 out of 171 samples of surface water

around the Great Lakes Areas of Concern and small streams in the Niagara and Burlington areas in 2003; the maximum concentration was 1.23 µg/L, with a mean of 0.0139 µg/L. MCPA was detected in 27 out of 59 samples of surface water in Great Lakes Areas of Concern and connecting channels in 2002, with a maximum concentration of 40 ng/L (mean 2.9 ng/L). In Lake Huron tributaries sampled in 2002, MCPA was detected in 11 out of 47 samples, with a maximum concentration of 80 ng/L (Struger et al., 2005). MCPA was not detected in all 133 samples taken in 1998–2000 in the area of the Don and Humber river watersheds (detection limit 100 ng/L) (Struger et al., 2002).

In Quebec, MCPA was seldom detected (11%) during the summer of 2003 in the tributaries of the St. Lawrence River; the maximum concentration seen was 120 ng/L (Murray et al., 2004). These tributaries drain from agricultural areas where MCPA is used in the cultivation of cereals, vegetables and grassland.

MCPA was detected in 37% of 481 samples of surface water taken from four rivers in the corn and soy growing areas of Quebec between 2002 and 2004; the maximum concentration found was 4.9 µg/L, and the detection limit was 0.01 µg/L (Giroux et al., 2006). This same percentage (37% of 1447 samples) was also seen in these same four rivers during previous sampling years (1993–2001); the maximum concentration found was slightly higher, 7.0 µg/L, and the detection limit varied from 0.02 to 0.05 µg/L (Giroux et al., 1997; Giroux, 1999, 2002). MCPA was also detected in 69 out of 122 samples from five other surface waters in agricultural areas in Quebec surveyed in 1996 and 1997, with a maximum concentration of 2.6 µg/L; the detection limit was 0.05 µg/L (Giroux, 1998).

In the Maritime provinces, MCPA was not detected in any of the 60 surface water samples taken in New Brunswick (2003 and 2004), Nova Scotia (2004) and Prince Edward Island (2003 and 2004); the detection limit was 1 µg/L (Murphy and Mutch, 2005). Nor was MCPA detected in the rivers of eight different municipalities with agricultural or urban activities in New Brunswick in 2004 (New Brunswick Department of Health, 2005).

5.3 Food

There are limited Canadian data available on the concentration of MCPA in food. Between 1980 and 1985, 354 composite vegetable samples representing nine vegetable commodities were collected from Ontario farm deliveries. MCPA was detected in one of six samples of asparagus, at a concentration of 0.06 mg/kg, below the maximum residue limit (MRL) of 0.1 mg/kg (Frank et al., 1987a). Monitoring studies in 1980–1982 in Ontario found MCPA levels of 0.01 mg/kg in peaches and 0.02 mg/kg in strawberries, both below the MRL (Frank et al., 1987b).

No current U.S. data were identified. Historically, during monitoring of pesticides in foods in the Total Diet Study program, in which ready-to-eat foods were sampled (June 1964–April 1969), MCPA was found very infrequently at low levels (maximum concentration 0.4 mg/kg) in products such as dairy products, grains, cereals and sugars (Bovey, 1980a). MCPA was not detected in any food composites collected from June 1969 to 1976 (IARC, 1983; HSDB, 2003).

MCPA-DMAS was not detected in grain 56 days after application to wheat treated in the tillering stage (Chow et al., 1971).

6.0 Analytical methods

The only U.S. Environmental Protection Agency (EPA)-approved method for measuring MCPA in drinking water is EPA Method 555 (Rev. 1.0). This method employs high-performance liquid chromatography (HPLC) with a photodiode array ultraviolet detector (PDA-UV). Samples are hydrolysed, acidified, filtered and extracted prior to separation and analysis using HPLC with a PDA-UV. The method detection limit is 0.8 µg/L (U.S. EPA, 1992).

The World Health Organization (WHO) recognizes liquid–liquid extraction with dichloromethane and derivatization with diazomethane using gas chromatography (GC) with either mass spectrometry (MS) or an electron capture detector. The method detection limit is approximately 0.1 µg/L (WHO, 2003). It is considered a very common method of analysis for MCPA (Hernandez et al., 1993; Tekel and Kavacicová, 1993).

The Centre d'expertise en analyse environnementale du Québec (CEAEQ, 1999) reported a method (MA.403-P.Chlp 2.0) for measuring MCPA in drinking water with a detection limit of 0.01 µg/L. The method employs solid-phase extraction (SPE) of an acidified sample on a C-18 column, followed by esterification and purification of the dried extract. The sample is analysed using a GC system equipped with a mass spectrometer (GC-MS).

7.0 Treatment technology

7.1 Municipal scale

Treatment technologies reported to be effective for the reduction of MCPA in drinking water include activated carbon adsorption and/or ozonation, membrane filtration, UV irradiation and advanced oxidation processes (AOPs). Full-scale and pilot-scale studies have demonstrated that effluent concentrations of MCPA well below the MAC of 0.1 mg/L (100 µg/L) are achievable using the methods described below. The selection of an appropriate treatment process for a specific water supply will depend on many factors, including the characteristics of the raw water supply and the operational conditions of the specific treatment method.

7.1.1 Conventional treatment

Limited scientific literature has been published on the effectiveness of conventional surface water treatment techniques for the reduction of MCPA in drinking water. Conventional treatment techniques are reported to be ineffective in reducing the concentration of a variety of classes of pesticides in drinking water, in particular hydrophilic or lipophobic compounds (Robeck et al., 1965; Miltner et al., 1989; Foster et al., 1991, 1992; Haiste-Gulde et al., 1993). The concentrations of organic compounds, such as pesticides, may be reduced through coagulation/flocculation if they are hydrophobic or have low molecular weight acidic functional groups (Randtke, 1988). The chemical properties of MCPA (moderately lipophilic; substituted acetic acid) may result in limited removal by conventional water treatment.

Operational data collected from a conventional water treatment process demonstrated a 50% reduction of MCPA to levels below 0.033 µg/L (Byrtus et al., 2004). Foster et al. (1992) observed some reduction of low levels of chlorophenoxy acid in a conventional surface water treatment plant. Similarly, Lambert and Graham (1995) reported a reduction of influent MCPA concentration (level not provided) to below 1 µg/L using slow sand filtration.

7.1.2 Adsorption

Activated carbon adsorption has been widely used to reduce the concentration of pesticides in drinking water and is recognized by WHO as a suitable treatment technology for the removal of MCPA to levels below 0.1 µg/L (Robeck et al., 1965; Miltner et al., 1989; Foster et al., 1992; Duguet et al., 1994; WHO, 2004). The capacity of activated carbon to remove pesticides by adsorption is affected by a variety of factors, such as concentration, pH, competition from other contaminants or natural organic matter, contact time and the physicochemical properties of the pesticide. The effectiveness of granular activated carbon (GAC) filtration is also a function of the empty bed contact time (EBCT), flow rate and filter run time. The effectiveness of powdered activated carbon is also a function of the carbon dosage.

Operational data from a municipal-scale treatment plant using conventional treatment with a GAC filter-adsorber demonstrated that this type of treatment system can reduce low influent MCPA levels of 0.47 µg/L to below 0.02 µg/L (Frick and Dalton, 2005). No information was provided on the operational conditions of the GAC adsorber used in this study. Pilot-scale study results indicated that post-filtration GAC adsorbers can reduce influent MCPA levels of 2 µg/L to below 0.1 µg/L. No breakthrough of MCPA was observed over a period greater than 400 days using an EBCT of 20 minutes (Schippers et al., 2004). Other pilot-scale studies also found that GAC filtration was capable of reducing influent MCPA concentrations of 1 µg/L to below 0.1 µg/L; however, the bed life was not determined, as MCPA was only periodically present in the water supply (Hart, 1989; Hart and Chambers, 1991).

7.1.3 Ozonation and ozonation/adsorption

WHO (2004) also recognizes ozonation as a suitable treatment technology for the reduction of MCPA to levels below 0.1 µg/L. Bonné et al. (2000) observed a 65% reduction of MCPA from influent levels of 20 µg/L to below 7 µg/L using ozonation alone and a reduction to effluent levels below 0.1 µg/L using combined ozonation and biological activated carbon filtration treatment. Additional pilot-scale studies using ozonation followed by GAC found 100% removal at ozone doses of 2–4 mg/L and contact times of less than 15 minutes (Foster et al., 1992). The potential presence of aliphatic acids, aldehydes, ketones and other ozonation by-products such as bromate and assimilable organic carbon (AOC) may require additional treatment following ozonation and/or process optimization to minimize by-product formation. Camel and Bermond (1998) reported that mineralization of pesticides using ozonation or other oxidation techniques is generally incomplete; as a result, water treatment process design using this method should include sand or GAC filtration following oxidation. It has also been suggested that the use of ozonation prior to GAC adsorption increases the biological activity of the filter bed and may extend the bed life for pesticide removal (Lambert and Graham, 1995).

7.1.4 Ultraviolet

Pilot-scale studies evaluating the effectiveness of UV treatment for the removal of pesticides from groundwater achieved a removal efficiency of 94% to effluent levels below 0.1 µg/L for MCPA with UV energy inputs of 300 Wh/m^3. Removal efficiency was found to be dependent on the energy dose and was not affected by the initial pesticide concentration. In addition, it was reported that the formation of by-products from the UV irradiation of MCPA may include organics as well as nitrite (Bourgine et al., 1997). Bench-scale experiments examining the effectiveness of UV irradiation observed complete degradation of MCPA using

a low-pressure lamp and a wavelength of 254 nm. Removals of 90% and 100% of the initial reaction concentrations (50 mg/L) of MCPA following 20 and 40 minutes of reaction time, respectively, were observed (Benitez et al., 2004).

7.1.5 Ultraviolet and hydrogen peroxide oxidation

Full-scale AOPs such as UV and hydrogen peroxide oxidation treatment have been assessed for the reduction of different classes of pesticides (Kruithof et al., 2002a,b). Although MCPA was not studied specifically, other chlorophenoxy herbicides were studied. Results indicated that a variety of UV doses (< 1200 mJ/cm^2) and hydrogen peroxide doses (< 15 g/m^3) resulted in an 80% or greater degradation of several chlorophenoxy herbicides (e.g., 2,4-D) to effluent levels below 0.1 µg/L. Formation of bromate and metabolites was reported to be insignificant; however, GAC filtration was required following UV/hydrogen peroxide oxidation to remove AOC and residual hydrogen peroxide. This study also noted that the UV doses required for oxidation of pesticides were much higher than those needed for disinfection (Kruithof et al., 2002a,b).

Laboratory-scale studies found that the degradation of MCPA is accelerated using UV/hydrogen peroxide when compared with UV treatment alone. Within 12 minutes, 90% degradation was observed; however, initial concentrations were relatively high (50 mg/L), and the results did not include information on the final effluent levels (Benitez et al., 2004).

7.1.6 Membrane filtration

Various membrane filtration techniques, including ultrafiltration, nanofiltration and reverse osmosis, have been shown to be effective methods for the reduction of MCPA in drinking water (Taylor et al., 1995, 2000; Hofman et al., 1997; Schippers et al., 2004). Pilot-scale studies of ultrafiltration membranes have reported average MCPA removals of ≥ 99% to effluent levels below 0.1 µg/L (Schippers et al., 2004). Similarly, pilot-scale studies of reverse osmosis membranes demonstrated average MCPA removals ranging from 97% to 99%, resulting in effluent concentrations below 0.2 µg/L. Results of this study also indicated that pesticide removal did not decrease with increasing membrane age (Bonné et al., 2000). Taylor et al. (2000) conducted reverse osmosis pilot-scale studies to evaluate various factors affecting pesticide removal. An average MCPA removal of 97.5% was observed under varying flux, recovery and source water quality conditions, to produce effluent concentrations below 0.3 µg/L. Pesticide rejection was found to be dependent on a variety of system components, including type of membrane system, flux, recovery, pesticide solubility, charge and molecular weight. Results from this study also indicated that representative influent water quality and bench- or pilot-scale membrane units should be used for the selection of membranes for full-scale application.

7.1.7 Emerging treatment technologies

Several drinking water treatment technologies for MCPA are being developed but are still primarily in the experimental stage or do not have published information on the effectiveness of pilot- or large-scale application. Some of the emerging technologies include the following:

- *Other AOPs*—Experiments examining the degradation pathways of MCPA using ozone and UV indicate that the addition of UV results in a more rapid degradation of MCPA than with ozone alone (Benoit-Guyod et al., 1986). Other AOPs, such as ozone combined with hydrogen peroxide, have been effective for the removal of several

classes of pesticides, including other chlorophenoxy herbicides; however, no information was found on the removal of MCPA specifically (Ijpelaar et al., 2002; Kruithof et al., 2002b; Benitez et al., 2004). Laboratory studies have shown that the Fenton process is also an effective AOP for the degradation of MCPA (Fdil et al., 2003).

- *Electrochemical degradation*—A variety of electrochemical degradation techniques have been examined. Laboratory studies found electrochemical degradation by peroxi-coagulation and photoperoxi-coagulation was effective for the removal of MCPA (Boye et al., 2003). Electrochemical degradation by anodic oxidation and electro-Fenton using a boron-doped diamond electrode was also found to be effective for MCPA removal (Brillas et al., 2004).
- *Alternative adsorbents*—Adsorption of MCPA from aqueous solutions has also been demonstrated using acid-activated spent bleaching earth, organo-clays and an adsorbent produced from elutrilithe (Akçay and Yurdakoç, 2003; Mahramanlioglu and Güçlü, 2003; Mahramanlioglu et al., 2003).

7.2 Residential scale

Municipal treatment of drinking water is designed to reduce contaminants to levels at or below their guideline value. As a result, the use of residential scale treatment devices on municipally treated water is generally not necessary but primarily based on individual choice. In cases where an individual household obtains its drinking water from a private well, a private residential drinking water treatment device may be an option for reducing MCPA concentrations in drinking water.

Health Canada does not recommend specific brands of drinking water treatment devices, but it strongly recommends that consumers use devices that have been certified by an accredited certification body as meeting the appropriate NSF International (NSF)/American National Standards Institute (ANSI) drinking water treatment unit standards. These standards have been designed to safeguard drinking water by helping to ensure the material safety and performance of products that come into contact with drinking water. Certification organizations provide assurance that a product conforms to applicable standards and must be accredited by the Standards Council of Canada (SCC). In Canada, the following organizations have been accredited by the SCC to certify drinking water devices and materials as meeting NSF/ANSI standards:

- Canadian Standards Association International (www.csa-international.org);
- NSF International (www.nsf.org);
- Water Quality Association (www.wqa.org);
- Underwriters Laboratories Inc. (www.ul.com);
- Quality Auditing Institute (www.qai.org);
- International Association of Plumbing & Mechanical Officials (www.iapmo.org).

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

Although no certified treatment devices are currently available for the reduction of MCPA from untreated water (such as a private well), treatment devices using activated carbon filters or reverse osmosis may be effective. Treatment devices certified under NSF International/American National Standards Institute (NSF/ANSI) Standard 53 (Drinking Water Treatment Units—Health Effects) for the reduction of the concentration of volatile organic compounds or NSF/ANSI Standard 58 (Reverse Osmosis Drinking Water Treatment Systems)

for the reduction of the concentration of organic compounds may be suitable alternatives for the reduction of MCPA. Before a treatment device is installed, the well water should be tested to determine general water chemistry and to select the type of device that is appropriate.

Periodic testing by an accredited laboratory should be conducted on both the water entering the treatment device and the finished water to verify that the treatment device is effective. Devices can lose removal capacity through usage and time and need to be maintained or replaced. Consumers should verify the expected longevity of the components in their treatment device as per the manufacturer's recommendations and service it when required.

8.0 Kinetics and metabolism

MCPA is rapidly absorbed following ingestion, is not extensively metabolized and is eliminated primarily in the urine, mostly as unchanged MCPA, in rats, dogs and humans. However, dogs have a longer plasma half-life and slower elimination than other species, including humans. MCPA-DMAS and MCPA-EHE were rapidly converted to MCPA in rat studies, and the metabolism and toxicokinetics were similar to those of MCPA.

8.1 Absorption

MCPA is readily absorbed from the gastrointestinal tract (via gavage and following direct gastric intubation) in rats, dogs and humans (Elo, 1976; Fjeldstad and Wannag, 1977; Kolmodin-Hedman et al., 1983a,b; Jahanshahi and Stow, 1995; Hardwick, 1999, 2000; Lappin et al., 2002).

Oral administration of single MCPA doses of 5 or 100 mg/kg bw resulted in peak plasma concentrations being attained within 2–4 hours of dosing in rats and within 4.5–7 hours in beagle dogs (Lappin et al., 2002). Similar peak plasma concentrations were attained (within 2–3 hours of dosing) in rats with a single dose of 5 mg/kg bw of either MCPA-DMAS or MCPA-EHE (van Ravenzwaay et al., 2004). Human volunteers given an MCPA dose of 0.015 mg/kg bw per day exhibited a peak plasma concentration after 1 hour (Kolmodin-Hedman et al., 1983a). Timchalk (2004), in a comparison review of these metabolism studies in rats, dogs and humans, showed that dogs had a longer plasma half-life than rats and humans. At a dosage of 5 mg/kg bw, the plasma half-life was 63 hours in dogs, which was considerably higher than that in rats (6 hours) or humans (11 hours), but humans received a lower dose of MCPA (0.015 mg/kg bw).

8.2 Distribution

Once absorbed, MCPA diffuses readily across biological membranes and is widely distributed to various tissues and organs via the circulatory system. Concentrations decline rapidly; in rats, MCPA is rapidly excreted, mainly unchanged, in the urine (Elo, 1976; Jahanshahi and Stow, 1995; van Ravenzwaay et al., 2004). No significant accumulation of MCPA is observed in the tissues.

In rats administered [^{14}C]MCPA by direct gastric intubation at a single dose of 11.5 mg/kg bw, the peak concentration in tissues was reached between 2 and 8 hours after dosing, after which the concentrations declined rapidly (Elo, 1976). The tissues/organs with the highest concentrations were the blood, kidney, suprarenal gland, lung, heart, liver, thyroid gland and bone marrow. In contrast, the brain, adipose tissue, testis and muscle contained the lowest concentrations.

In rats administered [^{14}C]MCPA at single oral dose of 5 or 100 mg/kg bw, the radioactivity in the tissues and carcasses accounted for $\leq$ 2.3% of the dose at sacrifice (Jahanshahi and

Stow, 1995; van Ravenzwaay et al., 2004). In sacrificed rats receiving the low-dose regimens (sacrificed on day 4), MCPA was non-detectable in most tissues, except in fat, skin and kidneys. In sacrificed rats receiving the higher dose (sacrificed on day 7), the level of radioactivity was also highest in fat, skin and kidneys, but MCPA was detected at higher concentrations and in more organs than at the lower dose. In addition, females had higher levels of radioactivity than males. The authors observed that small amounts of residual activity found in kidneys were consistent with continued excretion of the compound (van Ravenzwaay et al., 2004).

8.3 Metabolism

The metabolism and toxicokinetics of MCPA-DMAS and MCPA-EHE were investigated in rats administered single doses of 5 mg/kg bw each and compared with MCPA (van Ravenzwaay et al., 2004). Toxicokinetics and metabolism were indistinguishable from those of MCPA. MCPA, MCPA-DMAS and MCPA-EHE were not extensively metabolized in rats after oral administration.

In the fatal intoxication of a 23-year-old male, the forensic autopsy found 4-chloro-2-methylphenol in the body fluids and organ tissues, suggesting a metabolite of MCPA (Takayasu et al., 2008). In a study where five healthy human volunteers were given 15 µg/kg body weight of MCPA, the further investigation of free or conjugated MCPA in one individual showed that conjugation varied between 56–73% within the 72 hour collection period (Kolmodin-Hedman et al., 1983b).

Lappin et al. (2002) reported that rats orally exposed to 5 and 10 mg/kg/day MCPA excreted the parent compound mainly in the urine (approximately 65% of the dose). The only significant metabolite in the rat urine was the hydroxymethylphenoxyacetic acid (HMCPA); a trace of the glycine conjugate of MCPA was also detected, however, in an amount too small to reliably quantify. The dog urine contained a smaller proportion of MCPA (2–29%) than that seen in the rat, however, the glycine conjugate of MCPA was detected at much higher levels (up to 37% of the dose, and the taurine conjugate, which was not detected in the rat urine, was also detected (up to 7% of the dose).

8.4 Excretion

Renal excretion is reported as the major route of MCPA elimination in rats and dogs dosed orally with MCPA (Elo, 1976; Jahanshahi and Stow, 1995; Lappin et al., 2002; van Ravenzwaay et al., 2004). Dogs and rats have different recovery patterns. Studies showed that renal clearance in dogs was slower and less extensive than in rats (Lappin et al., 2002) or humans (Fjeldstad and Wannag, 1977; Kolmodin-Hedman et al., 1983a,b).

In rats, 75–80% of the administered dose was excreted in the urine over 24 hours, irrespective of the dose. In dogs, after oral administration of MCPA in single doses of 5 or 100 mg/kg bw, elimination was not complete at the end of 120 hours (Lappin et al., 2002).

In rats, the parent compound (MCPA) was the major compound excreted in the urine, along with lower levels of an oxidation product (4-chloro-2-hydroxymethyl-phenoxyacetic acid [HMCPA]) and trace amounts of the glycine conjugate (Lappin et al., 2002). In dogs, the parent compound was also present in the urine, but at lower levels than in the rat. In addition, three metabolites were recovered in the urine: the glycine conjugate, at higher levels than in the rat, and, to a lesser extent, HMCPA and a taurine conjugate (Lappin et al., 2002).

Faecal elimination was a minor route for both species; however, dogs had a higher proportion of MCPA in the faeces compared with rats. Radioactivity was not detected in expired air of rats orally dosed with [^{14}C]MCPA at 5 mg/kg bw (van Ravenzwaay et al., 2004).

In human volunteers given MCPA at 0.015 mg/kg bw, an average of 40% of the given dose was excreted in the urine during the first 24 hours (Kolmodin-Hedman et al., 1983b). In another study, volunteers given 5 mg of MCPA excreted 50% in the urine within 48 hours and 55% within 96 hours; by the fifth day, the concentration in the urine was below the detection limit (Fjeldstad and Wannag, 1977). No attempt to analyse metabolites was seen in either human study, nor were the doses radiolabelled using [^{14}C]MCPA.

In a comparison review of metabolism studies in rats, dogs and humans, Timchalk (2004) showed that dogs had a longer plasma half-life and slower elimination than rats and humans, which resulted in a substantially higher body burden of MCPA, at comparable doses, than in other species. In previous studies with organic acids with similar pharmacokinetic properties, the dog had a more limited capacity than other species to excrete organic acids via the kidney. The authors suggested that the following two mechanisms may be responsible for this decrease in renal clearance: saturation of renal secretion and increased renal tubule reabsorption. These differences in the pharmacokinetics of MCPA and other related organic acids between dogs and other species suggest that the use of dog toxicity data for determining human health risk may not be appropriate.

9.0 Health effects

9.1 Effects in humans

The lowest published lethal oral dose for MCPA in humans is 814 mg/kg bw (RTECS, 2005). Symptoms of acute exposure to large doses of MCPA have been reported as a result of poisoning from accidental ingestion and accidental exposure during manufacturing or application in the field. The symptoms include fatigue, weakness, anoxia, nausea, vomiting, diarrhoea, lowering of the blood pressure, body temperature disturbance, progressive hypotension, ataxia, neuromuscular irritability and convulsion (Popham and Davis, 1964; Johnson and Koumides, 1965; Jones et al., 1967; Palva et al., 1975; Bovey, 1980b; Timonen and Palva, 1980; U.S. EPA, 1984).

Various epidemiological studies have been conducted with phenoxy herbicides in Canada, the United States, Australia, New Zealand and several European countries. Most epidemiological studies conducted to date have dealt with multiple exposures to various chlorophenoxy herbicides, including principally 2,4-D and 2,4,5-trichlorophenoxyacetic acid (2,4,5-T), and to other pesticides, raw materials, intermediates and processing chemicals. It has been reported that some phenoxy herbicides, such as 2,4,5-T, were contaminated by dioxins and furans during production, but MCPA was not shown to be contaminated with dioxin (Wiklund et al., 1988; Eriksson et al., 1990; Mannetje et al., 2005). Controversy exists as to whether the presence of dioxin increased the risk of certain cancers. Cases of soft tissue sarcoma (STS), non-Hodgkin's lymphoma (NHL) and Hodgkin's disease have been associated with phenoxy herbicides, including those contaminated with dioxin; however, results were not consistent (Mannetje et al., 2005).

Some of these epidemiological studies have included MCPA as part of the repertoire of herbicides examined (Hardell and Sandström, 1979; Eriksson et al., 1981; Hardell et al., 1981; Vineis et al., 1986, 1991; Wiklund et al., 1987, 1988, 1989; Eriksson et al., 1990; Saracci et al., 1991; Bueno de Mesquito et al., 1993; Becher et al., 1996; Lynge, 1998); however, very few studies report outcomes specific to MCPA (and related compounds), and it is therefore difficult to isolate exposure to MCPA alone. These studies, as reported below, are limited, since the sample sizes were small, co-exposure to other pesticides likely occurred, and there was no detailed information on dose used and amount of time spent applying pesticides. More definitive studies with accurate assessment of MCPA-specific exposure are needed.

A population-based case–control study in northern and central Sweden investigated the potential association between exposure to a group of several classes of pesticides including MCPA and the risk of NHL. Male cases (404) with NHL were selected during 1987–1990, along with twice as many controls. The authors found that among the pesticides, herbicide use was marginally associated with NHL, with an odds ratio (OR) of 1.6 and a 95% confidence interval (CI) of 1.0–2.5; however, the sample size was small (61 cases and 81 controls). Further analysis, looking at subjects exposed to specific classes of herbicides, showed that the phenoxyacetic acids group predominated, with an OR of 1.5 (CI = 0.9–2.4), which was not significant. However, among the phenoxyacetic acid group, MCPA showed an OR of 2.7 (CI = 1.0–6.9). Because of the small number of exposed cases and controls for MCPA (12 cases and 11 controls), not much reliance can be placed on the results (Hardell and Eriksson, 1999).

Two nested case–control studies looking at STS and NHL were conducted within an international cohort of workers exposed to phenoxy herbicides, chlorophenols and dioxin, as well as other pesticides in the workplace (Kogevinas et al., 1995). Results showed an excess risk of STS for exposure to any phenoxy herbicide (OR = 10.3; CI = 1.2–90.6; 10 exposed cases of STS were observed vs. 30 controls) and to each of the three major classes of phenoxy herbicides, including the class of MCPA (including MCPA, MCPP [(±)-2-(4-chloro-2-methylphenoxy)-propanoic acid or mecoprop] and MCPB; OR = 11.3; CI = 1.3–98; 10 exposed cases vs. 29 controls). The association for NHL was weaker than those observed for STS; no excess risk was strongly associated with any of the exposures. According to the authors, it is complicated to evaluate the independent effect of each herbicide or contaminant on cancer risk, since workers are rarely exposed to a single herbicide. The authors found no specific association between risk and those herbicides contaminated with dioxin.

A cohort study was conducted in Denmark on the health effects related to potential herbicide exposure in 4461 workers (3390 males and 1071 females) working between 1947 and 1993 in two phenoxy herbicide production facilities. MCPA, 2-(2,4-dichlorophenoxy)propanoic acid (2,4-DP or dichlorprop) and MCPP were the main herbicides produced in these facilities, but other compounds, such as dyes and pigments, were also manufactured (Lynge, 1993, 1998). A non-significant twofold risk of STS was observed in persons potentially exposed to phenoxy herbicides compared with the Danish population; four cases were observed compared with 1.68 expected cases (standardized incidence ratio = 2.38; CI = 0.7–6.1). No excess of NHL was observed among workers potentially exposed to phenoxy herbicides compared with the Danish population. The overall cancer risk was found to be similar for both the Danish population and workers. However, the contribution of MCPA could not be determined due to exposure to multiple herbicides. The authors suggested that their findings (although based on small numbers) continue to suggest a possible association between exposure to MCPA and exposure to other related phenoxy herbicides, such as MCPP and 2,4-DP, and the risk of STS. Previous Swedish

case–control studies with phenoxy herbicides by Eriksson et al. (1981) and Hardell et al. (1981) suggested a possible association (i.e., an increased risk) between STS and exposure to phenoxy herbicides as well as chlorophenols and their contaminants.

In another cohort study (1947–1975), mortality and cancer incidences were examined in 5754 workers from a British factory that manufactured, formulated and sprayed principally MCPA, but also other agricultural chemicals during that same period (Coggon et al., 1986). The overall mortality as well as mortality from cancer were less than expected from national rates; however, when the rural correction factor was applied, the deficit of deaths from cancer became a slight excess, but was not statistically significant. Only one death from STS was observed in this study, compared with the expected number of 0.9 in the complete cohort and 0.6 in workers potentially exposed to phenoxy acids. Mortalities from Hodgkin's disease and NHL were less than expected from the national rates. The authors concluded that "if there is a hazard of STS due to MCPA, then the risk is less than suggested by earlier studies of 2,4,5-T and 2,4,5-trichlorophenol, and it is small in absolute terms."

Because of the small size of most of the cohorts, not much reliance could be placed on the results, whether positive or negative.

Although several epidemiological studies were conducted on the reproductive and developmental outcomes of pesticide exposures, only a few included MCPA and are reported below.

A study was conducted to analyse the effect of pesticide exposure on the risk of spontaneous abortion in an Ontario farm population (Arbuckle et al., 1999). A questionnaire was used to obtain information from 2110 women on 3936 pregnancies, including 395 spontaneous abortions. Preconception (4-month period from 3 months before conception to the calendar month of conception) and post-conception (4-month period from calendar month of conception to the end of the first trimester) exposure windows were examined separately, in addition to differentiating between early (< 12 weeks) and late (12–19 weeks) spontaneous abortions for these same windows of exposure. Results showed a weak association between the risk of early spontaneous abortion and preconception exposure to any phenoxyacetic acid herbicides (adjusted OR = 1.1; CI = 0.6–1.9). However, when restricted to early abortions, the adjusted OR increased to 2.5 (CI = 1.0–6.4); in contrast, the adjusted OR for late abortions decreased to 0.4 (CI = 0.2–1.0). When the analysis accounted for the use of protective equipment or clothing in male applicators exposed to a phenoxy herbicide, the OR (for all spontaneous abortions or for early abortions subgroup) was less than 1 in males reporting the use of such equipment/clothing. In contrast, it was considerably higher in the early spontaneous abortion subgroup when males failed to use the protective equipment/clothing while being exposed. When the analysis was restricted to exposure to MCPA, the results showed no elevated risk of spontaneous abortion from preconception exposure for all gestational ages; the adjusted OR was 0.8 (CI = 0.4–1.7). In contrast, the adjusted OR for MCPA for early abortions increased to 2.3 (CI = 0.8–6.5), whereas the adjusted OR for late abortions decreased to 0.4 (CI = 0.1–1.2). Further analysis suggested that if preconception exposure to MCPA occurred for 1 month or more, the adjusted OR increased to 5.4 (CI = 1.7–17.3) for early abortions; the OR was less than 1 for late abortions for MCPA, as well as for all the other phenoxy herbicides analysed.

Limitations of the study (Arbuckle et al., 1999) include small sample size (e.g., the unexposed group and the MCPA subgroup), use of memory recall (quality of information limited by the memory of the respondents and the length of recall for pesticide usage generally greater than 10 years) and the lack of detailed information on dose used and amount of time spent applying pesticides. According to the authors, the findings of the study suggest that there may

be a preconceptual effect with MCPA and phenoxy herbicides in adverse pregnancy outcomes, particularly early spontaneous abortions (which may suggest a male-mediated effect due to the higher risk seen as a result of not using protective equipment or clothing). However, given the limitations of the study, additional studies are needed to confirm these findings.

In order to evaluate the possibility that offspring of agricultural pesticide applicators might have increased risks of birth anomalies, Garry et al. (1996) compared the births (n = 4935) of state-licensed, private pesticide applicators (n = 34 772) in Minnesota between 1989 and 1992 with those of the state's birth registry (containing 210 723 live births within the same period). The birth defect rate for all birth anomalies was significantly increased in children born to private applicators. The pattern of excess frequency of birth anomalies was analysed by region, pesticide use, season and male/female sex ratio. Analyses of the various regions showed western Minnesota, a major growing region for wheat, sugar beet and potato, as having the highest rate of birth anomalies per 1000 live births. Data for MCPA and 2,4-D were pooled because of their similarities of chemical structure, spectrum of biocidal activity and crop use, although 2,4-D was used more than MCPA. In the case of 2,4-D and MCPA, the frequency of anomalies in high-use areas was not significantly increased (OR = 1.86; CI = 0.69–2.05) for combined births with central nervous system, circulatory/respiratory, urogenital and muscular anomalies; however, a significant increase was reported when all anomalies were combined (OR = 1.51; CI = 1.40–1.62). No individual data were available for MCPA in this cohort study (Garry et al., 1996).

Very few epidemiological studies have been conducted with regards to reproductive and developmental outcomes with MCPA, and those that have been conducted are limited by small sample sizes. Because workers may be exposed to multiple phenoxy herbicides and other compounds, as well as possibly to contaminants such as dioxin, it is difficult to isolate exposure to MCPA alone.

Another key limitation of the studies above was that there was only potential for exposure to have occurred, and none of the studies had any direct measurements of exposure for the individuals in the study.

9.2 Effects on laboratory animals and *in vitro* test systems

9.2.1 Acute toxicity

Details on the available acute oral toxicity studies are provided in Table 3.

Table 3: Summary of acute oral toxicity studies

	Oral LD_{50} (mg/kg bw)[a]		
Forms of MCPA	**Rats**	**Mice**	**Guinea pigs**
MCPA acid	700–1383[1,2,3,4]	439–800[5,6]	700[5]
MCPA-EHE	2235[3]		
MCPA-DMAS	1200–1867[2,3]	550[7]	
MCPA sodium salt	3500[3]	560[7]	

[a] References are as follows: 1. Ben-Dyke et al. (1979); 2. Rowe and Hymas (1954); 3. U.S. EPA (2003); 4. U.S. EPA (1990); 5. RTECS (2005); 6. Weed Science Society of America (1989); 7. Gurd et al. (1965).

9.2.2 Short-term exposure studies

Short-term studies were conducted on the effects of MCPA, MCPA-DMAS and MCPA-EHE in mice, rats and dogs. Adverse health effects were noted in the liver and kidney. In general, dogs appear to be more sensitive than rats to the adverse effects of MCPA after repeated exposure. According to the U.S. EPA (2003, 2004e), this increased sensitivity appears to be a consequence of reduced capacity in the elimination of MCPA in dogs relative to rats.

In a 28-day oral range-finding toxicity study, MCPA (94.8%) was administered to mice (4–6 per sex per dose) in the diet at concentrations of 0, 100, 300, 900 or 2700 ppm (equivalent to doses of 0, 19.1–22.0, 56.3–67.7, 173.4–184.8 and 453.7–820.1 mg/kg bw per day for males and 0, 20.7–26.2, 69.2–73.9, 193.4–223.9 and 442.3–956.3 mg/kg bw per day for females). Observed effects at the highest dose in both sexes included motor disturbances, significant cumulative body weight loss, hepatotoxicity (increased serum alanine aminotransferase [ALT] and alkaline phosphatase [ALP] activities, increased liver weight and related histopathological findings), spleen effects (decreased mean spleen weights, gross observation of involution, increased neutrophil counts and decreased lymphocyte counts) and decreased kidney weights. High-dose males had decreased mean testicular weight with histopathological findings of testicular atrophy, whereas females had atrophy of the ovaries and uterine glands. At necropsy, high-dose animals were shown to be cachectic (state of general ill health characterized by malnutrition, weakness and emaciation). Liver effects (cloudy swelling) were observed in one mid-dose female. In female mice, the lowest-observed-adverse-effect level (LOAEL) is 900 ppm (193.4–223.9 mg/kg bw per day) based on cloudy swelling in the liver, and the no-observed-adverse-effect level (NOAEL) is 300 ppm (69.2–73.9 mg/kg bw per day). In male mice, the LOAEL is 2700 mg/kg (453.7–820.1 mg/kg bw per day), and the NOAEL is 900 ppm (173.4–184.8 mg/kg bw per day) (Kirsch, 1985a). The highest dose used in this study was within range of the LD_{50} for mice, which may explain the significant effects at this dose.

Effects on the kidney were also noted in 90-day studies in rats. Technical-grade MCPA (94.8%) was administered to rats (15 per sex per dose) at dietary concentrations of 0, 50, 150 or 450 ppm (equivalent to doses of 0, 3.6, 10.9 and 32.6 mg/kg bw per day for males and 0, 4.0, 12.1 and 35.8 mg/kg bw per day for females). At 450 ppm, an increase in creatinine values in the plasma of females was observed. At the same level, decreases in cholesterol and calcium values in the males were observed. The authors mentioned that these effects are difficult to evaluate, as they occur only in males. Also, an increase in absolute and relative kidney weights in males was observed. At 150 ppm, increased absolute kidney weights (108% of controls) were noted ($p < 0.05$). No changes were observed at the lowest level (50 ppm). The authors concluded that the NOAEL lies between 50 and 150 ppm and is based on renal impairment related to calcium and kidney weight changes, but no histopathological alterations were detected that correlated with this increase in kidney weight (Kirsch, 1985b). In this same study, PMRA (2007) established a NOAEL of 3.6 mg/kg bw per day and a LOAEL of 10.9 mg/kg bw per day based on kidney effects (increased absolute and relative weights, urinary bilirubin, crystals and pH).

In a combined subchronic toxicity and neurotoxicity study, MCPA (94.2%) was administered to groups of 15 male and 15 female Wistar rats for 3 months at dietary concentrations of 0, 50, 500 or 2500 ppm (equivalent to doses of 0, 3, 34 or 177 mg/kg bw per day for males and 0, 4, 42 or 188 mg/kg bw per day for females) (Mellert et al., 1994). At the highest dose, a significant decrease in body weight was observed in both sexes beginning on day 7 of the administration period and continuing until the end of the study. At the highest dose, in both sexes, a significant decrease in haematological parameters (red blood cells, haemoglobin and

haematocrit), a significant increase in liver enzymes (ALT, ALP and aspartate aminotransferase [AST]) and alteration of hepatocytes, characterized by cytoplasmic eosinophilia and granular cytoplasm in the liver, were observed. In addition, a higher incidence/grading of foam cell accumulations in the lung and myeloid atrophy of the haematopoietic marrow were seen in both sexes. In high-dose males, a decrease in testes weights, testicular atrophy and atrophy of the seminal vesicles and prostate, aspermia or oligospermia in the epididymides were observed. For the neurotoxicity evaluation, functional observational battery and motor activity assessments were performed on 10 animals per sex per group prior to the treatment and on treatment days 22, 50 and 85. Effects observed at 2500 ppm were a decreased value of hindlimb grip strength in females on day 85, decreased foot splay test values ($p < 0.02$) in males on day 22 and reduced values ($p < 0.02$) of forelimb grip strength in males on day 50. No significant treatment-related changes were seen at the two lowest doses. The U.S. EPA set the NOAEL at 500 ppm (34 and 42 mg/kg bw per day for males and females, respectively) and the LOAEL at 2 500 ppm (177 and 188 mg/kg bw per day for males and females, respectively), based on decreased body weight and body weight gains, liver pathology, changes in clinical chemistry and haematological parameters, testicular atrophy and changes in motor activity.

U.S. EPA (2004e) considered MCPA "a neurotoxicant based on clinical signs of neurotoxicity" based on the study by Mellert et al. (1994) and an acute neurotoxicity study conducted with rats (U.S. EPA, 2003). Additional studies (acute and subchronic oral studies) conducted with MCPA-DMAS and MCPA-EHE and rats also showed adverse neurotoxic effects, with MCPA-EHE being the most toxic of the three forms of MCPA (U.S. EPA, 2004e). Neurotoxic effects seen in these studies included impaired coordination and gait, reduced motor activity, ataxia (muscle incoordination), decrease in arousal and reduced hind grip strength.

MCPA was administered in the diet to Charles River rats (10 per sex per dose) at dose levels of 0, 4, 8 or 16 mg/kg bw per day for 90 days. No treatment-related effects were observed other than a significant increase in both relative and absolute kidney weights for males at the high dose, with moderate increases at the other two treatment levels in males. There were no treatment-related histopathological alterations in either sex at any dose level tested. The no-observed-effect level (NOEL) for increased kidney weights in rats was 8 mg/kg bw per day (Holsing and Kundzin, 1970).

In two separate 90-day studies, technical MCPA (94.8%) was given in the diet to beagle dogs (four per sex per dose) at dose levels of 0, 3, 12 or 48 mg/kg bw per day and at dose levels of 0, 0.3, 1 or 12 mg/kg bw per day, respectively. Severe toxicity and mortality were seen at the highest dose (48 mg/kg bw per day): one female died during week 5, and the remaining three females and three out of four males were sacrificed moribund during weeks 7–8. A decrease in kidney and liver function, characterized by an increase in blood urea, ALT and creatinine levels, was noted at 3 mg/kg bw per day and above. A NOAEL of 1 mg/kg bw per day was reported in this study, and a LOAEL of 3 mg/kg bw per day based on impaired renal function, without histopathological change, was also reported. This lack of histopathological change probably indicates that the effects are reversible (Reuzel and Hendriksen, 1980).

In a 1-year study, male and female beagle dogs (six per sex per dose) were administered technical-grade MCPA (94.8%) in the diet at concentrations of 0, 6, 30 or 150 ppm (equivalent to doses of 0, 0.22, 1.02 or 5.32 mg/kg bw per day in males and 0, 0.21, 1.02 or 5.12 mg/kg bw per day in females) (Hellwig, 1986). No treatment-related clinical signs or deaths were seen during the study. In the high-dose males, mean cumulative body weight gain was 77% of controls for the 1- to 364-day interval. At the high dose (both sexes), statistically significant

increases were observed in serum creatinine concentration (at 13, 26 and 52 weeks) and serum ALT and AST activities at most sampling intervals. Gross necropsy showed dark brown discoloration of the kidney in four of six mid-dose females, in four of six high-dose males and in all high-dose females. Histopathological changes were observed in the kidney and included a dose-related increase in severity in kidney pigment deposition in the proximal tubular epithelium in all females and three of the six males at the highest dose and in four females at the middle dose. No treatment-related effects were seen at the low dose (Hellwig, 1986). Based on this study, the U.S. EPA (2003) established a NOAEL of 6 ppm (0.22 and 0.21 mg/kg bw per day for males and females, respectively) and a LOAEL of 30 ppm (1.02 mg/kg bw per day in both sexes) based on nephrotoxicity (evident as gross necropsy and hispathological changes).

Two subchronic studies were also conducted with the other forms of MCPA. MCPA-DMAS (99.9% active ingredient) was administered in beagle dogs at dietary concentrations of 0, 20, 80 or 360 ppm (equivalent to doses of 0, 0.6, 2.4 and 10.9 mg/kg bw per day in the males and to 0, 0.7, 2.9 and 12.8 mg/kg bw per day in the females) for a period of 110–118 days (Hellwig et al., 1995a). At the highest dose, both sexes had increases in creatinine, urea and ALT levels, whereas males had increases in partial thromboplastin times. At 80 ppm, increases in creatinine and urea levels were observed in both sexes, whereas increases in ALT levels and partial thromboplastin times were observed in females. Increases in ALT levels correlated with a subacute to chronic interstitial inflammation of the liver. No significant changes were observed at the lowest doses in either sex. The U.S. EPA (2003) set the LOAEL at 80 ppm (2.4 mg/kg bw per day in males and 2.9 mg/kg per day in females) based on histopathology changes (increases in a subacute to chronic interstitial inflammation of the liver), haematology and clinical chemistry and the NOAEL at 20 ppm (0.6 mg/kg bw per day in males and 0.7 mg/kg bw per day in females). No statistical details were provided in the review.

Beagle dogs were administered MCPA-EHE (93.5% active ingredient) at dietary concentrations of 0, 20, 80 or 360 ppm (equivalent in the males to 0, 0.6, 2.5 and 11.1 mg/kg bw per day and in the females to 0, 0.7, 2.8 and 12.7 mg/kg bw per day) for a period of 110–118 days. The administered doses are equivalent to 0, 0.4, 1.6 and 7.1 mg/kg bw per day in males and 0, 0.4, 1.8 and 8.1 mg/kg bw per day in females as MCPA acid. At 360 ppm, both sexes had increases in clinical chemistry parameters (creatinine, urea and ALT levels), partial thromboplastin times, relative and absolute thyroid weights and relative ovary weights (females). Increases in ALT levels correlated with a subacute to chronic interstitial inflammation of the liver. At 80 ppm, both sexes had increases in creatinine and urea levels, whereas females had increases in ALT levels. No treatment-related changes were observed at the lowest dose in either sex. The U.S. EPA (2003) set the LOAEL for systemic toxicity in beagle dogs at 80 ppm (1.6 mg/kg bw per day as MCPA acid in males and 1.8 mg/kg bw per day in females) based on changes in clinical chemistry parameters (increases in creatinine, and urea and ALT levels). The NOAEL is 20 ppm (0.4 mg/kg bw per day as MCPA acid in both sexes) (Hellwig et al., 1995b). No statistical details were provided in the review.

9.2.3 Long-term exposure (chronic toxicity) and carcinogenicity

Long-term exposure and/or carcinogenicity studies with MCPA were conducted in rats and mice. No evidence of carcinogenicity was seen in either species; however, both rats and mice showed evidence of adverse effects in the liver and kidney similar to those observed in the subchronic studies, and at comparable dose levels. No long-term study in dogs was located.

Wistar rats (50 per sex per dose) received MCPA (94.8%) in their diet for 2 years at 0, 20, 80 or 320 ppm (corresponding to doses of 0, 1.1, 4.4 or 17.6 mg/kg bw per day in males and 0, 1.4, 5.7 or 23 mg/kg bw per day in females) (Kirsch, 1988; Bellet et al., 1999). Two satellite groups (n = 10–15 per sex per dose per group) were also studied. No treatment-related effects were seen at 20 ppm. Changes in clinical chemistry in the absence of histopathology were seen at 80 ppm in both sexes. Effects at the high dose included a minimal decrease in body weight in males (day 14 and beyond; $p < 0.05$) and a small but sporadic increase in body weight in females ($p < 0.05$). Clinical chemistry parameters showed a significant decrease in triglycerides in males at weeks 78 and 104 and an elevation of ALT levels in females at weeks 52, 78 and 104. At the high dose, gross and microscopic pathological changes in male rats indicated a chronic progressive nephropathy, as seen by an increase in the retraction and glandular surface of the kidney. At the doses tested, there was no treatment-related increase in tumour incidence when compared with controls. The authors reported the systemic NOEL at 20 ppm (1.1 mg/kg bw per day in males and 1.4 mg/kg bw per day in females). However, the U.S. EPA (2003) in their review set the NOAEL for systemic toxicity at 80 ppm (4.4 mg/kg bw per day in males and 5.7 mg/kg bw per day in females) and the LOAEL at 320 ppm (17.6 mg/kg bw per day in males and 23 mg/kg bw per day in females) based on hepatotoxicity (increased ALT levels) in females and kidney effects in males. However, PMRA (2005b, 2006) found that this study did not test high enough doses to reach a maximum tolerated dose (MTD) and, as a result, was not adequate to fully assess the overall oncogenic potential of MCPA.

B6C3F1 mice (50 per sex per dose) received MCPA (94.6%) for 2 years in the diet at 0, 20, 100 or 500 ppm, corresponding to doses of 0, 3.2, 15.7 or 79.5 mg/kg bw per day in males and 0, 3.9, 19.5 or 97.2 mg/kg bw per day in females (Kuhborth et al., 1988; Bellet et al., 1999). One satellite group (n = 10 per sex per dose) was used for haematological examination. Body weight changes were observed in both sexes during the course of the study; however, the final body weights in males and females were not statistically different from those of the control group. The kidney was the only organ with treatment-related lesions. Kidney weights were statistically significantly higher in high-dose females. The kidney lesions included increased incidences of intratubular calcification and tubular hyaline-proteinaceous casts in high-dose males and females. In the mid- and high-dose females, there was a non-dose-related increase in the incidence of slight renal hyperplasia (7/50 and 4/50, respectively) compared with controls and the low dose, at which none was observed. In addition, there was an increased incidence of renal tubular epithelial focal hyperplasia in high-dose males (not specified if statistically significant). The authors reported the systemic NOEL at 100 ppm (15.7 mg/kg bw per day in males and 19.5 mg/kg bw per day in females) (Kuhborth et al., 1988; Bellet et al., 1999). However, the U.S. EPA (2003) set the systemic NOAEL in males at 100 ppm (15.7 mg/kg bw per day) and the LOAEL in males at 500 ppm (79.5 mg/kg bw per day) based on histopathological changes in the kidneys. In female mice, U.S. EPA (2003) set the systemic NOAEL at 20 ppm (3.9 mg/kg bw per day) and the LOAEL at 100 ppm (19.5 mg/kg bw per day), based on renal hyperplasia, which was considered toxicologically significant at that dose.

9.2.4 Mutagenicity/genotoxicity

Based on the weight of evidence, MCPA acid and its other forms are not considered to be of genotoxic concern *in vivo*. As outlined below, MCPA was not mutagenic in the majority of

bacterial and mammalian cell gene mutation assays reported and did not induce DNA damage in the SOS chromotest. In addition, no *in vivo* evidence was found to suggest clastogenicity in bone marrow, and sister chromatid exchange tests gave negative or weakly positive results.

With the exception of one positive and two weakly positive results (reviewed in Elliott, 2005), MCPA acid was negative in *in vitro* bacterial assays using *Salmonella typhimurium* (several strains) (Räsänen et al., 1977; Nishimura et al., 1982; Moriya et al., 1983; Kappas, 1988; Jones et al., 1993a), and both MCPA-DMAS and MCPA-EHE were also negative (Jones et al., 1992, 1993b; Elliott, 2005).

Negative results with MCPA acid, MCPA-DMAS and MCPA-EHE were observed in mammalian cell mutation assays (Chinese hamster ovary HPRT with and without S9) (Adams et al., 1993a,b,c; Elliott, 2005).

One positive result was obtained with MCPA acid in a mitotic recombination assay with *Aspergillus nidulans* (Kappas, 1988). A weakly positive result was found in the yeast mutagenicity test in *Saccharomyces cerevisiae* with MCPA acid (Zetterberg, 1978, 1979).

Negative results with MCPA acid were observed in an SOS chromotest (*Escherichia coli* PQ37 with and without S9) (Mersch-Sundermann et al., 1989).

Chromosomal aberrations *in vitro* were detected in human peripheral lymphocytes (with and without S9) at high cytotoxic concentrations with MCPA acid and MCPA-DMAS, but not with MCPA-EHE (Akhurst et al., 1993a,b,c; Elliott, 2005).

In vivo chromosomal aberration assays with MCPA acid were negative in the Chinese hamster for doses up to 1200 mg/kg bw administered by oral gavage (Gelbke and Engelhardt, 1985a,d), whereas sister chromatid exchange assays were either negative or weakly positive at the same dose level and for the same route of exposure (Linnainmaa, 1984; Gelbke and Engelhardt, 1985b,c; Mustonen et al., 1989). Negative results were observed in *in vivo* bone marrow micronucleus assays with MCPA acid, MCPA-DMAS and MCPA-EHE in which mice were given a 384 mg/kg bw dose by oral gavage (Proudlock et al., 1993a,b,c).

This overall lack of genotoxicity following MCPA exposure is consistent with the lack of carcinogenicity in animals (Elliott, 2005).

9.2.5 Reproductive and developmental toxicity

Developmental effects in the presence of maternal toxicity were seen with rats when dosed with MCPA, MCPA-DMAS and MCPA-EHE. No developmental effects in the presence of maternal toxicity were seen in the rabbit. No reproductive effects were seen in a two-generation study involving rats.

MCPA (94.22%) was administered daily by gavage to pregnant female Wistar rats on days 6–15 of gestation at dose levels of 0, 15, 60 or 120 mg/kg bw per day (Hellwig and Hildebrand, 1993a). The LOAEL for maternal toxicity was 120 mg/kg bw per day, based on treatment-related decreases in body weight, body weight gain and food consumption during treatment and for the remainder of the gestation period. The LOAEL for development toxicity was 120 mg/kg bw per day, based on decreased placental and fetal body weights and on an increase in the number of fetuses with skeletal retardation. The NOAEL for maternal and developmental toxicity was 60 mg/kg bw per day.

MCPA (94.22%) was administered once daily by gavage to Himalayan rabbits on days 7–19 of gestation at dose levels of 0, 15, 30 or 60 mg/kg bw per day (Hellwig and Hildebrand, 1993b). At 60 mg/kg bw per day, treatment-related decreases were noted in maternal body weight, body weight gain and food consumption. The LOAEL for maternal toxicity was

60 mg/kg bw per day based on significant decreases in body weight, body weight gain and food consumption during the treatment period. The NOAEL for maternal toxicity was 30 mg/kg bw per day. The NOAEL for developmental toxicity was equal to or greater than the highest dose tested, 60 mg/kg bw per day. No developmental LOAEL was determined.

MCPA-DMAS (78.2%) was administered to 17–25 pregnant CD rats per group by gavage in 0.5% methylcellulose at doses of 0, 18.5, 62 or 185 mg/kg bw per day (equivalent to doses of 0, 15, 50 and 150 mg MCPA free acid/kg bw per day) on gestation days 6–19, inclusive (Cappon, 1999b). Maternal toxicity, consisting of clinical signs and mortality of one rat, was observed in high-dose females. When adjusted to account for gravid uterine weights, the body weight in high-dose females was comparable to the controls. Gravid uterine weights were significantly reduced in the high-dose group compared with the controls. Complete litter resorption occurred in five high-dose dams; this post-implantation loss was significantly higher than in controls (41.8% compared with 3.8% for the controls). The mean fetal body weight in the high-dose group was significantly less than the controls (2.1 g compared with 3.5 g for the controls). An increase in the incidence of major external and/or skeletal malformations was seen in the fetuses of the 150 mg/kg bw per day groups (11/17 litters) compared with controls (3/25 litters). In addition, there was an increase in the incidence of skeletal variations at the high dose compared with controls. The LOAEL for maternal toxicity was 150 mg MCPA acid/kg bw per day based on mortality and clinical signs, with a NOAEL of 50 mg/kg bw per day as MCPA acid. U.S. EPA (2003) set the LOAEL for developmental toxicity as 150 mg/kg bw per day as MCPA acid based on increased resorptions, decreased fetal body weight and external and skeletal malformations/variations. The NOAEL for developmental toxicity was set at 50 mg/kg bw per day as MCPA acid (U.S. EPA, 2003).

MCPA-EHE (99.9%) was administered to 25 pregnant CD rats per group by gavage in 0.5% methylcellulose at doses of 0, 23.5, 62.7 or 188 mg/kg bw per day (equivalent to 0, 15, 40 and 120 mg/kg bw per day as MCPA acid) on gestation days 6–19, inclusive (Cappon, 1999a). Food consumption was significantly reduced in high-dose females during treatment (83–91% of control group values). As a result, mean net body weight and mean net body weight gain (when adjusted to account for gravid uterine weights) were statistically decreased by 5% and 28%, respectively, compared with controls. Complete litter resorption was seen in two high-dose dams, and there were corresponding slight (but not significant) increases in post-implantation loss, total resorptions and early resorption. At the highest dose, mean fetal weight was significantly decreased compared with controls (2.5 vs. 3.7 g for controls). Significant increases in the incidence of several skeletal variations, including unossified sternebrae and bent ribs, were observed at this dose. The incidence of an ossified cervical centrum number 1 was statistically decreased at 62.7 and 188 mg/kg bw per day (13.7, 12.2, 4.6 and 0.6% per litter for the control, low-, mid- and high-dose groups, respectively). U.S. EPA (2003) set the LOAEL for developmental toxicity at 188 mg/kg bw per day as MCPA-EHE (120 mg/kg bw per day for MCPA acid) based on total litter resorptions, decreased fetal weight and altered growth, and the NOAEL for developmental toxicity was 62.7 mg/kg bw per day as MCPA-EHE (40 mg/kg bw per day for MCPA acid). The LOAEL for maternal toxicity was 188 mg/kg bw per day as MCPA-EHE (120 mg/kg bw per day as MCPA acid) based on reduced body weight gains and reduced food consumption (U.S. EPA, 2003). The NOAEL for maternal toxicity was 62.7 mg/kg bw per day as MCPA-EHE (40 mg/kg bw per day as MCPA acid).

No reproductive effects were observed when male and female albino rats (n = 25 per sex per dose per generation) were exposed to MCPA (94.8%) in the diet at concentrations of 0, 50,

150 or 450 ppm (corresponding to doses of 0, 2.5, 7.5 or 22.5 mg/kg bw per day) for two generations (MacKenzie, 1986; Bellet et al., 2001). There were no treatment-related effects on mean live litter sizes, sex ratios at birth or pup survival of either litter of the treated groups of either generation. At the high dietary level (450 ppm), statistically significant differences were noted in body weight gain for both male pups (F_{1a}) and female pups (F_{1a} and F_{1b}) and in body weight and body weight gains for both male and female pups from F_{2a} and $F_{2b.}$ No significant effects on the reproductive function for either generation (both sexes) were observed (MacKenzie, 1986; Bellet et al., 2001).

In this study, the NOEL for reproductive function in rats administered MCPA was determined to be 450 ppm (approximately 22.5 mg/kg bw per day). The NOEL for general systemic toxicity based on body weight in adult animals in the F_{1b} generation and for effects on the offspring of the F_{1b} generation (based on reduced pup weight and pup weight gains) was 150 ppm (approximately 7.5 mg/kg bw per day). Based on the results of the study, MCPA is not a reproductive toxicant for rats, which was confirmed by the U.S. EPA (2003). However, PMRA (2006) determined that the MTD had not been achieved in this study. According to PMRA (2006), MCPA showed a potential for increased sensitivity of the young in the absence of maternal toxicity due to decreases seen in body weight and body weight gain of the pups from both generations during lactation. As a result of the evaluation of this two-generation study, the MCPA Task Force Three submitted two additional one-generation confidential studies to PMRA (2007), where they administered either the acid or MCPA-EHE using higher doses than in the above two-generation study. No adverse effects were seen on pup body weight until the time of weaning, indicating that there was no increased sensitivity of the young relative to maternal animals.

The U.S. EPA (2004e), in its Hazard Identification Assessment Review Committee report, reported that because of its concerns with neurotoxicity in the acute and subchronic studies with the various forms of MCPA, the currently available data supported the need to perform a developmental neurotoxicity study.

10.0 Classification and assessment

Based on inadequate data from epidemiological studies and the lack of adequate animal studies, Health Canada classifies MCPA as Group VIA (unclassifiable with respect to carcinogenicity in humans), as defined in Health Canada (1994). IARC (1983) evaluated MCPA and concluded that “no adequate data were available to evaluate the carcinogenicity of MCPA to experimental animals. The data on humans were also considered to be inadequate. The available data are insufficient to evaluate the carcinogenicity to humans of MCPA alone.” IARC (1986) also evaluated the family of chlorophenoxy herbicides and concluded that “there is limited evidence that occupational exposures to chlorophenoxy herbicides are carcinogenic to humans.” The U.S. EPA (2003, 2004c,e) has classified MCPA as “not likely to be carcinogenic to humans,” based on the lack of evidence of carcinogenicity in mice and rats.

Although a limited number of epidemiological studies have been conducted on the effects of MCPA and related chlorophenoxy compounds, the evidence for carcinogenicity and reproductive effects remains inconclusive. Available studies have dealt with multiple exposures to mixtures of chlorophenoxy herbicides, other pesticides as well as other organic compounds. The results were difficult to interpret, and the studies were considered limited for several reasons, such as the lack of consideration of confounding factors and small sample size.

There was no evidence of carcinogenicity in the long-term mouse or rat studies using MCPA acid. However, PMRA (2005b, 2006, 2007) indicated that the long-term rat study did not reach the maximum tolerated dose and that it was not considered adequate for assessing the overall potential for carcinogenicity. Tests for genotoxicity and mutagenicity were largely negative.

Subchronic studies have shown that dogs are more sensitive than rats or mice to the effects of MCPA and related compounds, with effects seen at levels at least 10 times lower in dogs than in rats or mice based on chronic and subchronic studies. Allometric scaling of data from rats, dogs and humans indicates that the renal clearance of MCPA in dogs is approximately 10 times slower than in humans (Timchalk, 2004). The unique sensitivity of dogs to MCPA-mediated effects observed in the literature, therefore, may be attributed to the reduced renal clearance of organic acids (e.g., MCPA) leading to higher concentrations in blood compared to humans and other species. This evidence suggests that the dog is not an appropriate indicator species for MCPA-mediated toxicity in humans (Timchalk, 2004). Based on the results of the allometric scaling across species, reported by Timchalk (2004), and the available animal database for MCPA, the PMRA (2007) deemed the rat as the most appropriate model for the human health risk assessment for agricultural and other non-turf uses of MCPA. No long-term studies on dogs were located in the literature.

PMRA (2006, 2007, 2008) has derived a chronic (lifetime) dietary reference dose, or acceptable daily intake (ADI), for MCPA of 0.012 mg/kg bw per day using the NOAEL of 3.6 mg/kg bw per day from the 90-day study in rats by Kirsch (1985b). The NOAEL was based on kidney effects (increased absolute and relative weights, urinary bilirubin, crystals and pH).

A TDI is established as follows, using the NOAEL and uncertainty factors identified by PMRA in their ADI calculation:

$$\text{TDI} = \frac{\text{3.6 mg/kg bw per day}}{300}$$

$$= \text{0.012 mg/kg bw per day}$$

where:

- 3.6 mg/kg bw per day is the NOAEL in the Kirsch (1985b) 90-day study in rats,
- 300 is the uncertainty factor: × 10 for interspecies variability; × 10 for intraspecies variability; × 3 for database deficiencies - inadequate carcinogenicity assessment, since the MTD was not achieved in the two-year rat study (Bellet, 1999).

Although the NOAEL is obtained from a sub-chronic study, a × 10 uncertainty factor to account for database deficiencies (use of a sub-chronic study instead of a chronic study) is not warranted, since the kidney effects noted after 90 days of dosing were not evident after 2 years of exposure to higher levels of MCPA, suggesting that the rat may be able to adapt to these effects. However, the 2-year rat study by Bellet (1999) did not achieve the MTD, and the effects at 90 days were considered to be indicative of an initial toxic insult to the kidney, because the kidney is the target organ in all species tested. Since the NOAEL for kidney effects in the 90-day rat study is the lowest NOAEL reported in the animal toxicity database for MCPA (excluding the

dog), the TDI for MCPA is also protective of all other adverse effects reported in the sub-chronic and chronic rat studies, including systemic, kidney, liver, testicular, reproductive/developmental and nervous system effects.

Using the TDI of 0.012 mg/kg bw per day, the Maximum Acceptable Concentration (MAC) for MCPA in drinking water is derived as follows:

$$MAC = \frac{TDI \times BW \times AF}{WC}$$

$$= \frac{0.012 \text{ mg/kg bw per day} \times 70 \text{ kg} \times 0.20}{1.5 \text{ L/day}}$$

$$= 0.112 \text{ mg/L (0.1 mg/L rounded)}$$

where:

TDI = the tolerable daily intake derived above;

BW = body weight; the mean adult body weight estimated for a Canadian is 70 kg;

WC = water consumption; 1.5 L/day is the daily volume of tap water consumed by an adult;

AF = allocation factor; the proportion of the total daily intake of MCPA estimated to originate from exposure via drinking water, compared to other sources (food, soil, air and consumer products). In the absence of comprehensive or appropriate exposure data for all relevant environmental media, a default allocation factor of 20% is used.

10.1 International Considerations

The U.S. EPA has not established a maximum contaminant level (MCL) for MCPA in drinking water. It did establish a life-time health advisory in 1988, to serve as informal technical guidance to assist federal, state and local officials responsible for protecting public health when emergency spills or contamination situations occur. They are not to be construed as legally enforced standards (U.S. EPA, 1987; 2006).

The WHO (1996) established a drinking water guideline for MCPA of 0.002 mg/L based on the one-year feeding study in dogs indicating a NOAEL of 0.15 mg/kg/day for renal and liver toxicity published by Hellwig (1986). The derivation of the guideline used an uncertainty factor of 300 to account for interspecies (× 10) and intraspecies (× 10) variation, and the inadequacy of the database (× 3), as well as an allocation of 10% of the TDI for drinking water exposure (WHO, 1996, 2003).

11.0 Rationale

MCPA is a commonly used herbicide in Canada. It is registered for use in Canada for agricultural sites, for fine turf, lawns and sod, in forestry and at industrial sites. MCPA is used everywhere in Canada, particularly in the Prairies, and is among the top 10 pesticides sold in Canada. Although MCPA is used widely in Canada, exposure data do not indicate significant levels in drinking water.

Health Canada classifies MCPA as unclassifiable with respect to carcinogenicity in humans, based on inadequate data from epidemiological studies and the lack of adequate animal studies. This is consistent with the classifications established by IARC and the U.S. EPA. The Maximum Acceptable Concentration for MCPA in drinking water was established based on kidney effects in the rat.

A MAC of 0.1 mg/L (100 µg/L) is established for MCPA in drinking water. This MAC is achievable by available treatment technology, and measurable by available analytical methods. As part of its ongoing guideline review process, Health Canada will continue to monitor new research in this area and recommend any change to the guideline that it deems necessary.

12.0 References

Akçay, G. and Yurdakoç, K. (2003). Removal of various phenoxyalkanoic herbicides from water by organo-clays. Acta Hydrochim. Hydrobiol., 28: 300–304.

Adams, K., Kirkpatrick, D., Godfrey, A. , Anderson, A., and Dawe, I.S. (1993a). Chinese hamster ovary/HGPRT locus assay: MCPA acid: Final report: Lab Project No.: JEL 29/921115. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK. 42 pp. [cited in Cal-EPA, 2000; U.S. EPA, 2003].

Adams, K., Ransome, S., Anderson, A., and Dawe, I.S. (1993b). Chinese hamster ovary/HGPRT locus assay: MCPA DMAS: Final report: Lab Project No.: JEL 27/921113. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK. 42 pp. [cited in Cal-EPA, 2000; U.S. EPA, 2003].

Adams, K., Henly, S., Anderson, A. et al. (1993c). Chinese hamster ovary/HGPRT locus assay: MCPA 2-EHE: Lab Project No.: JEL 28/921114. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK [cited in U.S. EPA, 2003].

Akhurst, L.C., King, J., Anderson, A., and Dawe, I.S. (1993a). MCPA DMAS: Metaphase chromosome analysis of human lymphocytes cultured *in vitro*: Lab Project No.: JEL 30/921176. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK [cited in Cal-EPA, 2000; U.S. EPA, 2003].

Akhurst, L.C., King, J., Anderson, A., and Dawe, I.S. (1993b). MCPA acid: Metaphase chromosome analysis of human lymphocytes cultured *in vitro*: Lab Project No.: JEL 32/921190. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK [cited in Cal-EPA, 2000; U.S. EPA, 2003].

Akhurst, L.C., King, J., Anderson, A., Dawe, I.S. et al. (1993c). MCPA 2-EHE: Metaphase chromosome analysis of human lymphocytes cultured *in vitro*: Lab Project No.: JEL 31/921188. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK [cited in U.S. EPA, 2003].

Anderson, A.-M. (2005). Review of pesticide data in Alberta surface waters since 1995. Environmental Monitoring and Evaluation Branch, Alberta Environment, November. 172 pp.

Arbuckle, T.E., Savitz, D.A., Mery, L.S. and Curtis, K.M. (1999). Exposure to phenoxy herbicides and the risk of spontaneous abortion. Epidemiology, 10(6): 752–760.

Becher, H., Flesch-Janys, D., Kauppinen, T., Steindorf, K., Manz, A. and Wahrendorf, J. (1996). Cancer mortality in German male workers exposed to phenoxy herbicides and dioxins. Cancer Causes Control, 7: 312–321.

Bellet, E.M., van Ravenzwaay, B., Pigott, G. and Leemings, N. (1999). Chronic dietary toxicity and oncogenicity evaluations of MCPA (4-chloro-2-methylphenoxyacetic acid) in rodents. Regul. Toxicol. Pharmacol., 30: 223–232.

Bellet, E.M., van Ravenzwaay, B., Hellwig, J. and Pigott, G. (2001). Reproductive toxicity of MCPA (4-chloro-2-methylphenoxyacetic acid) in the rat. Int. J. Toxicol., 20: 29–38.

Ben-Dyke, R., Sanderson, D.M. and Noakes, D.N. (1979). Acute toxicity data for pesticides. World Rev. Pestic. Control, 9: 119–127.

Benitez, F.J., Acero, J.L., Real, F.J. and Roman, S. (2004). Oxidation of MCPA and 2,4-D by UV radiation, ozone, and the combinations UV/H_2O_2 and O_3/H_2O_2. J. Environ. Sci. Health, B39(3): 393–409.

Benoit-Guyod, J.L., Crosby, D.G. and Bowers, J.B. (1986). Degradation of MCPA by ozone and light. Water Res., 20: 67–72.

Blundell, G. and Harman, J. (2000). A survey of the quality of municipal supplies of drinking water from ground-water sources in Prince Edward Island. Sierra Club of Canada, Eastern Canada Chapter, and Department of Earth Sciences, University of Waterloo, Waterloo, Ontario.

Bonné, P.A.C., Beerendonk, E.F., van der Hoek, J.O. and Hofman, J.A.M.H. (2000). Retention of herbicides and pesticides in relation to aging of RO membranes. Desalination, 132: 189–193.

Bourgine, F., Chapman, J. and Martin, S. (1997). Traitement des pesticides par photolyse UV. Tech. Sci. Meth. Genie Urbain Genie Rural, 7–8: 23–29.

Bovey, R.W. (1980a). Residues and fate of phenoxy herbicides in the environment. In: The science of 2,4,5-T and associated herbicides. John Wiley and Sons, New York, NY. pp. 301–356.

Bovey, R.W. (1980b). Toxicology of phenoxy herbicides in animals and man — General considerations. In: The science of 2,4,5-T and associated herbicides. John Wiley and Sons, New York, NY. pp. 71–132.

Boye, B., Brillas, E. and Dieng, M. (2003). Electrochemical degradation of the herbicide 4-chloro-2-methylphenoxy-acetic acid in aqueous medium by peroxi-coagulation and photoperoxi-coagulation. J. Electroanal. Chem., 540: 25–34.

Brillas, E., Boye, B., Sirés, I., Garrido, J.A., Rodriguez, R.M., Arias, C., Cabot, P.-L. and Comninellis, C. (2004). Electrochemical destruction of chlorophenoxy herbicides by anodic oxidation and electro-Fenton using a boron doped diamond electrode. Electrochim. Acta, 49: 4487–4496.

Brimble, S., Bacchus, P. and Caux, P.-Y. (2005). Pesticide utilization in Canada: A compilation of current sales and use data; prepared in fulfilment of a requirement of the Environment Canada Pesticide Program Coordinating Committee. Environment Canada. 142 pp.

Bueno de Mesquito, H.B., Doornbos, G., van der Kuip, D.A.M., Kogevinas, M. and Winkelmann, R. (1993). Occupational exposure to phenoxy herbicides and chlorophenols and cancer mortality in The Netherlands. Am. J. Ind. Med., 23: 289–300.

Byrtus, G., Pongar, K., Browning, C., Burland, R., McGuinness, E. and Humphries, D. (2004). A summary of pesticide residue data from Alberta Treated Water Survey, 1995–2003. Environmental Assurance Service, Alberta Environment, Edmonton, Alberta. 57 pp.

Cal-EPA (2000). Summary of toxicology data: MCPA (MCPA-acid). Medical Toxicology Branch, Department of Pesticide Regulation, California Environmental Protection Agency, Sacramento, CA. Available at: www.cdpr.ca.gov/docs/toxsums/pdfs/786.pdf

Camel, V. and Bermond, A. (1998). The use of ozone and associated oxidation processes in drinking water treatment. Water Res., 32(11): 3208–3222.

Cappon, G.D. (1999a). A prenatal developmental toxicity study of MCPA-EHE in rats. Unpublished report, WIL Research Laboratories, Ashland, OH, October 12 (Laboratory Study No. WIL-325004; MRID 44954101) [cited in U.S. EPA, 2003].

Cappon, G.D. (1999b). A prenatal developmental toxicity study of MCPA-DMA in rats. Unpublished report, WIL Research Laboratories, Ashland, OH, October 12 (Laboratory Study No. WIL-325003; MRID 44954102) [cited in U.S. EPA, 2003].

Caux, P.-Y., Kent, R.A., Bergeron, V., Fan, G.T. and Macdonald, D.D. (1995). Environmental fate and effects of MCPA: a Canadian perspective. Crit. Rev. Environ. Sci. Technol., 25(4): 313–376.

CEAEQ (1999). Détermination des pesticides de type aryloxyacide; extraction avec C-18 suivie d'une esterification: dosage per chromatographie en phase gazeuse couplée à un spectromètre de masse. Centre d'expertise en analyse environnementale du Québec. Available at: www.ceaeq.gouv.qc.ca/methodes/pdf/MA403Pchlp20.pdf

Cessna, A.J., Elliot, J.A., Tollefson, L. and Nicholaichuk, W. (2001). Herbicide and nutrient transport from an irrigation district into the South Saskatchewan River. J. Environ. Qual., 30: 1796–1807.

Chow, C., Montgomery, M.L. and Yu, T.C. (1971). Methodology and analysis for residues of MCP and 2,4,5-T in wheat. Bull. Environ. Contam. Toxicol., 6: 576–580 [cited in Bovey, 1980a].

Coggon, D., Pannett, B., Winter, P., Acheson, E.D. and Bonsall, J. (1986). Mortality of workers exposed to 2-methyl-4-chlorophenoxyacetic acid. Scand. J. Work Environ. Health, 12: 448–454.

Duguet, J.P., Bernazeau, F. and Bruchet, P. (1994). Occurrence of pesticides in natural water and removal during drinking water processes. Water Supply, 12(1–2): 111–115.

Elliott, B. (2005). Review of the genotoxicity of 4-chloro-2-methylphenoxyacetic acid. Mutagenesis, 20(1): 3–13.

Elo, H. (1976). Distribution and elimination of 2-methyl-4-chlorophenoxyacetic acid (MCPA) in male rats. Acta Pharmacol. Toxicol., 39(1): 58–64.

Eriksson, M., Hardell, L., Berg, N.O., Möller, T. and Axelson, O. (1981). Soft-tissue sarcomas and exposure to chemical substances: a case–referent study. Br. J. Ind. Med., 38: 27–33.

Eriksson, M., Hardell, L. and Adami, H.-O. (1990). Exposure to dioxins as a risk factor for soft tissue sarcoma: a population-based case–control study. J. Natl. Cancer Inst., 82(6): 486–490.

Fdil, F., Aaron, J.J., Oturan, N., Chaouch, A. and Oturan, M.A. (2003). Photochemical degradation of chlorophenoxy alkanoic herbicides in aqueous media. Rev. Sci. Eau, 16(10): 123–142.

Fjeldstad, P. and Wannag, A. (1977). Human urinary excretion of the herbicide 2-methyl-4-chlorophenoxyacetic acid. Scand. J. Work Environ. Health, 3: 100–103.

Foster, D.M., Rachwal, A.J. and White, S.L. (1991). New treatment processes for pesticides and chlorinated organics control in drinking water. J. Inst. Water Environ. Manage., 5: 466–476.

Foster, D.M., Rachwal, A.J. and White, S.L. (1992). Advanced treatment for the removal of atrazine and other pesticides. Water Supply, 10: 133–146.

Frank, R., Braun, H.E. and Ripley, B.D. (1987a). Residues of insecticides, fungicides, and herbicides on Ontario-grown vegetables 1980–1985. J. Assoc. Off. Anal. Chem., 70: 1081–1086.

Frank, R., Braun, H.E. and Ripley, B.D. (1987b). Residues of insecticides, fungicides, and herbicides in fruit produced in Ontario, Canada, 1980–1984. Bull. Environ. Contam. Toxicol., 39: 272–279.

Frick, E.A. and Dalton, M.S. (2005). Characterization of anthropogenic organic compounds in the source water and finished water for the City of Atlanta, October 2002–September 2004. Proceedings of the 2005 Georgia Water Resources Conference, April 25–27, 2005, University of Georgia, Athens, GA. Available at: http://ga.water.usgs.gov/pubs/other/gwrc2005/pdf/GWRC05_Frick.pdf

Garry, V.F., Schreinemachers, D., Harkins, M.E. and Griffith, J. (1996). Pesticide appliers, biocides, and birth defects in rural Minnesota. Environ. Health Perspect., 104(4): 394–399.

Gelbke, H.P. and Engelhardt, G. (1985a). Cytogenetic investigations in Chinese hamsters after a single oral administration of MCPA: bone marrow chromosome analysis. BASF Aktiengesellschaft, Ludwigshafen, Germany (Report No. 10M0046/8304) [cited in Elliott, 2005].

Gelbke, H.P. and Engelhardt, G. (1985b). Cytogenetic investigations in Chinese hamsters after a single oral administration of MCPA: sister chromatid exchange (SCE). BASF Aktiengesellschaft, Ludwigshafen, Germany (Report No. 16M0046/8305) [cited in Elliott, 2005].

Gelbke, H.P. and Engelhardt, G. (1985c). Cytogenetic investigations in Chinese hamsters after a single oral administration of MCPA: sister chromatid exchange (SCE). BASF Aktiengesellschaft, Ludwigshafen, Germany (Report No. 16M0046/8356) [cited in Elliott, 2005].

Gelbke, H.P. and Engelhardt, G. (1985d). Cytogenetic investigations in Chinese hamsters after a single oral administration of MCPA: bone marrow chromosome analysis. BASF Aktiengesellschaft, Ludwigshafen, Germany (Report No. 10M0046/8367) [cited in Elliott, 2005].

Giroux, I. (1998). Impact de l'utilisation des pesticides sur la qualité de l'eau des bassins versants des Rivières Yamaska, L'Assomption, Chaudière et Boyer. Volet assainissement agricole. Direction des écosystèmes aquatiques, Ministère de l'Environnement et de la Faune du Québec [cited in PMRA, 2005c].

Giroux, I. (1999). Contamination de l'eau par les pesticides dans les régions de culture de maïs et soya au Québec. Campagnes d'échantillonnage de 1996, 1997 et 1998. Ministère de l'Environnement et de la Faune du Québec.

Giroux, I. (2002). Contamination de l'eau par les pesticides dans la région de culture de maïs et de soya au Québec. Résultats des campagnes d'échantillonnage 1999, 2000 et 2001, et évolution temporelle de 1992 à 2001. Ministère de l'Environnement du Québec.

Giroux, I., Duchemin, M. and Roy, M. (1997). Contamination de l'eau par les pesticides dans les régions de culture intensive du maïs au Québec. Campagne d'échantillonnage de 1994 et 1995. Direction des écosystèmes aquatiques, Ministère de l'environnement et de la Faune du Québec.

Giroux, I., Robert, C. and Dassylva, N. (2006). Présence de pesticides dans l'eau au Québec : bilan dans des cours d'eau de zones en culture de maïs et de soya en 2002, 2003 et 2004, et dans les réseaux de distribution d'eau potable. Ministère du Développement durable, de l'Environnement et des Parcs, Direction du suivi de l'état de l'environnement, Direction des politiques de l'eau et Centre d'expertise en analyse environnementale du Québec. 57 pp. + 5 annexes (ISBN 2-550-46504-0; Envirodoq No. ENV/2006/013; Collection No. QE/00173). Available at: www.mddep.gouv.qc.ca/pesticides/mais_soya/P1-pesticides-mais-soya-2002-2004.pdf

Gouvernement du Québec. Règlement modifiant le Code de gestion des pesticides. *Loi sur les pesticides*. (L.R.Q., c. P-9.3, a.101, 104, 105, 107 and 109, par. 11.1˚ to 13˚). Éditeur officiel du Québec. Gazette officielle du Québec. April 26. p 1747. Available at: www2.publicationsduquebec.gouv.qc.ca/dynamicSearch/telecharge.php?type=3&file=/P_9_3/P9_3R0_01.HTM

Gurd, M.R., Harmer, G.L.M. and Lessel, B. (1965). Acute toxicity and 7-month feeding studies with mecoprop and MCPA. Food Cosmet. Toxicol., 3: 883–885 [cited in IARC, 1983].

Haiste-Gulde, B., Baldauf, G. and Brauch, H.-J. (1993). Removal of pesticides from raw waters. Water Supply, 11: 187–196.

Hardell, L. and Eriksson, M. (1999). A case–control study of non-Hodgkin lymphoma and exposure to pesticides. Cancer, 85(6): 1353–1360.

Hardell, L. and Sandström, A. (1979). Case–control study: soft tissue sarcomas and exposure to phenoxyacetic acids or chlorophenols. Br. J. Cancer, 39: 711–717.

Hardell, L., Eriksson, M., Lenner, P. and Lundgren, E. (1981). Malignant lymphoma and exposure to chemicals, especially organic solvents, chlorophenols and phenoxy acids: a case–control study. Br. J. Cancer, 43: 169–176.

Hardwick, T. (1999). ^{14}C-MCPA: Absorption and excretion in the beagle dog. Unpublished report, Covenance Laboratories Ltd., North Yorkshire, UK, December (Final Report No. 729/D1141; MRID 4559301) [cited in U.S. EPA, 2003].

Hardwick, T. (2000). ^{14}C-MCPA: Metabolite profiles in the beagle dog. Unpublished report, Covenance Laboratories Ltd., North Yorkshire, UK, June (Amended Final Report No. 729/201-D1141; MRID 4559302) [cited in U.S. EPA, 2003].

Hart, J. (1989). Survey of the effectiveness of granular activated carbon in reducing the concentration of pesticides in drinking water. Final report prepared by WRc for the Department of the Environment, London, UK (Report No. DoE 2229-M).

Hart, J. and Chambers, V.K. (1991). Consultancy: Removal of pesticides by GAC and GAC/oxidants. Final report to the Drinking Water Inspectorate, Department of the Environment, London, UK.

Health Canada (1994). *Canadian Environmental Protection Act*. Human health risk assessment for priority substances. Minister of Supply and Services Canada, Ottawa, Ontario.

Hellwig, J. (1986). Report on the toxicity of MCPA in beagle dogs after 12 month administration in the diet: Project No. 33D0046/8341. Unpublished study prepared by BASF Institute. 691 pp. (microfiche) [also cited in U.S. EPA, 2003].

Hellwig, J. and Hildebrand, B. (1993a). Study of the prenatal toxicity of MCPA-acid in rats after oral administration (gavage): Lab Project No. 30R0374/91096. Unpublished study prepared by BASF Aktiengesellshaft, Ludwigshafen, Germany. 302 pp. [cited in U.S. EPA, 2003].

Hellwig, J. and Hildebrand, B. (1993b). Study of the prenatal toxicity of MCPA-acid in rabbits after oral administration (gavage): Lab Project No. 40R0374/91095. Unpublished study prepared by BASF Aktiengesellshaft, Ludwigshafen, Germany. 230 pp. [cited in U.S. EPA, 2003].

Hellwig, J., Bachmann, S., Deckardt, K., et al. (1995a). MCPA-DMA salt—Subchronic oral toxicity study in beagle dogs: administration in the diet: Lab Project No.: 31D0385/91115. Unpublished study prepared by BASF Aktiengesellschaft, Ludwigshafen, Germany. 407 pp. [cited in U.S. EPA, 2003].

Hellwig, J. et al. (1995b). MCPA-EH-ester—Subchronic oral toxicity study in beagle dogs—Administration in diet. Unpublished report, Department of Toxicology, BASF, Ludwigshafen/Rhine, Germany, January 9 (Report No. 31D0385/91115; MRID 43556801) [cited in U.S. EPA, 2003].

Hernandez, F., Beltran, J. and Sancho, J.V. (1993). Study of multi-residue methods for the determination of selected pesticides in groundwater. Sci. Total Environ., 132: 297–312.

Hill, B.D., Harker, K.N., Haselback, P., Inaba, D.J., Byers, S.D. and Moyer, J.R. (2002). Herbicides in Alberta rainfall as affected by location, use and season: 1999 to 2000. Water Qual. Res. J. Can., 37(3): 515–542.

Hofman, J.A.M.H., Beerendonk, E.F., Folmer, H.C. and Kruithof, J.C. (1997). Removal of pesticides and other micropollutants with cellulose-acetate, polyamide and ultra-low pressure reverse osmosis membranes. Desalination, 113: 209–214.

Holsing, G.C. and Kundzin, M. (1970). Final report: three-months dietary administration—rats. BASF Aktiengesellschaft, Ludwigshafen, FRG [cited in U.S. EPA, 1984; WHO, 2003].

HSDB (2003). Hazardous Substances Data Bank Number 1127. MCPA CAS # 94-74-6. U.S. National Library of Medicine, Bethesda, MD. Last revision date: 20030214. Available at: http://toxnet.nlm.nih.gov/

IARC (1983). (4-Chloro-2-methylphenoxy)acetic acid (MCPA). In: Miscellaneous pesticides. International Agency for Research on Cancer, Lyon, France. IARC Monogr. Eval. Carcinog. Risks Hum., 30: 255–269.

IARC (1986). Occupational exposures to chlorophenoxy herbicides. In: Some halogenated hydrocarbons and pesticide exposures. International Agency for Research on Cancer, Lyon, France. IARC Monogr. Eval. Carcinog. Risk Chem. Hum., 41: 357–407.

Ijpelaar, G.F., Groenendijk, M., Hopman, R. and Kruithof, J.C. (2002). Advanced oxidation technologies for the degradation of pesticides in ground water and surface water. Water Sci. Technol. Water Supply, 2(1): 129–138.

Jahanshahi, M. and Stow, R. (1995). ^{14}C-MCPA: absorption, distribution, metabolism, and excretion in the rats. Unpublished report, Corning Hazelton (Europe), North Yorkshire, UK, June 20 (Laboratory Report No. 1149/5-1011; MRID 43755202) [cited in U.S. EPA, 2003].

Johnson, J.R.M. and Koumides, O. (1965). A further case of MCPA poisoning. Br. Med. J., 2: 629–630.

Jones, D.J.R., Knight, A.G. and Smith, A.J. (1967). Attempted suicide with herbicide containing MCPA. Arch. Environ. Health, 14: 363–367.

Jones, E., Kitching, J., Anderson, A. and Dawe, I.S. (1992). Ames *Salmonella typhimurium* bacterial reverse mutation assay on MCPA-DMAS. Huntingdon Research Centre Ltd., Huntingdon, UK (HRC Study No. JEL/26/921053) [cited in Cal-EPA, 2000].

Jones, E., Kitching, J., Anderson, A. and Dawe, I.S. (1993a). Ames *Salmonella typhimurium* bacterial reverse mutation assay on MCPA acid. Huntingdon Research Centre Ltd., Huntingdon, UK (HRC Study No. JEL 26/920957) [cited in Cal-EPA, 2000].

Jones, E., Kitching, J., Anderson, A. and Dawe, I.S. (1993b). Ames *Salmonella typhimurium* bacterial reverse mutation assay on MCPA-2-EHE. Unpublished study prepared by Huntingdon Research Centre Ltd., Huntingdon, UK (Report No. JEL 25/921054) [cited in U.S. EPA, 2003].

Kappas, A. (1988). On the mutagenic and recombinogenic activity of certain herbicides in *Salmonella typhimurium* and in *Aspergillus nidulans*. Mutat. Res., 204: 615–621 [cited in Elliott, 2005].

Kirsch, P. (1985a). Study of the toxicity of MCPA in mice after 4 weeks administration in the diet. Unpublished study, Department of Toxicology, BASF Aktiengesellschaft, Ludwigshafen, FRG, April 4 (Laboratory Study No. 50S0046; MRID 00165470) [cited in U.S. EPA, 2003].

Kirsch, P. (1985b). Report on the study of the toxicity of MCPA in rats after 3-months' administration in the diet. Department of Toxicology, BASF Aktiengesellschaft, Ludwigshafen, FRG, April 1 (Laboratory Study No. 3150046/8302; MRID 00165471; microfiche) [also cited in U.S. EPA, 2003].

Kirsch, P. (1988). Study on the chronic toxicity and oncogenic potential of MCPA in rats. Unpublished report, Department of Toxicology, BASF Aktiengesellschaft, Ludwigshafen/Rhein, FRG, May 18 (Study No. 71S0045/8345; MRID No. 40634101) [cited in U.S. EPA, 2003].

Kogevinas, M., Kauppinen, T., Winkelmann, R., Becher, H., Bertazzi, P.A., Bueno-de-Mesquita, H.B., Coggon, D., Green, L., Johnson, E., Littorin, M., Lynge, E., Marlow, D.A., Mathews, J.D., Neuberger, M., Benn, T., Pannett, B., Pearce, N., and Saracci, R. (1995). Soft tissue sarcoma and non-Hodgkin's lymphoma in workers exposed to phenoxy herbicides, chlorophenols, and dioxins: 2 nested case–control studies. Epidemiology, 6: 396–402.

Kolmodin-Hedman, B., Höglund, S. and Åkerblom, M. (1983a). Studies on phenoxy acid herbicides. I. Field study. Occupational exposure to phenoxy acid herbicides (MCPA, dichlorprop, mecoprop and 2,4-D) in agriculture. Arch. Toxicol., 54(4): 257–265.

Kolmodin-Hedman, B., Hoglund, S., Swensson, A., Akerblom, M. (1983b), Studies on phenoxy acid herbicides. II. Oral and dermal uptake and elimination in urine of MCPA in humans, Arch. Toxicol., 54(4), 267-273.

Kruithof, J.C., Kamp, P.C. and Belosevic, M. (2002a). UV/H_2O_2 treatment for inactivation of pathogenic micro-organisms and pesticide degradation: From challenge to full scale application. In: American Water Works Association Annual Conference Proceedings. American Water Works Association, Denver, CO.

Kruithof, J.C., Kamp, P.C. and Belosevic, P.C. (2002b). UV/H_2O_2 treatment: the ultimate solution for pesticide removal and disinfection. Water Sci. Technol. Water Supply, 2(1):113–122.

Kuhborth, B., Deckaidt, K., Mirea, D. Schilling, K., and Hildebrand, B. (1988). Study on the oncogenic potential of MCPA in mice. Unpublished report, BASF Aktiengesellschaft, Ludwigshafen, FRG, July 26 (Project No. 80S0046/8358; MRID No. 40792301) [cited in U.S. EPA, 2003 and Bellet et al. 1999].

Kumar, Y. (2001). Pesticides in ambient air in Alberta. Prepared for Science and Standards Division, Alberta Environment, Edmonton, Alberta, August. Available at: www3.gov.ab.ca/env/protenf/pesticide/publications/info/Pesticides_in_Ambient_Air_Report.pdf

Lambert, S.D. and Graham, N.J.D. (1995). A comparative evaluation of the effectiveness of potable water filtration processes. J. Water Supply Res. Technol. (SRT) – Aqua, 44(1): 38–51.

Lappin, G.J., Hardwick, T.D., Stow, R., Pigott, G.H. and van Ravenzwaay, B. (2002). Absorption, metabolism and excretion of 4-chloro-2-methylphenoxyacetic acid (MCPA) in rat and dog. Xenobiotica, 32(2): 153–163.

Linnainmaa, K. (1984). Induction of sister chromatid exchanges among workers occupationally exposed to phenoxy acid herbicides 2,4-D and MCPA. Teratog. Carcinog. Mutagen., 3: 269–279.

Lynge, E. (1993). Cancer in phenoxy herbicide manufacturing workers in Denmark, 1947–87 — an update. Cancer Causes Control, 4: 261–272.

Lynge, E. (1998). Cancer incidence in Danish phenoxy herbicide workers, 1947–1993. Environ. Health Perspect., 106(2): 683–688.

MacKenzie, K.M. (1986). Two-generation reproductive study with MCPA in rats. Final report. Unpublished study, Hazelton Laboratories America Inc., Madison, WI, November 3 (Laboratory Study No. 6148-100; MRID 40041701) [cited in U.S. EPA, 2003].

Mahramanlioglu, M. and Güçlü, K. (2003). Removal of MCPA from aqueous solutions using adsorbent produced from elutrilithe. Energy Sources, 25:1–13.

Mahramanlioglu, M., Kizilcikli, I., Biçer, I. and Tuncay, M. (2003). Removal of MCPA from aqueous solutions by acid-activated spent bleaching earth. J. Environ. Sci. Health, B38(6): 813–827.

Manitoba Conservation (2000). Detections of pesticides in Manitoba municipal water. Water Quality Management Section, Manitoba Conservation, Winnipeg, Manitoba [cited in PMRA, 2005c].

Mannetje, A.'t., McLean, D., Cheng, S., Boffetta, P., Colin, D. and Pearce, N. (2005). Mortality in New Zealand workers exposed to phenoxy herbicides and dioxins. Occup. Environ. Med., 62: 34–40.

Mellert, W., Deckardt, K., Kaufmann, W. and Hildebrand, B. (1994). MCPA acid: Subchronic oral dietary and neurotoxicity study in Wistar rats. Unpublished study, Department of Toxicology, BASF Aktiengesellschaft, Ludwigshafen/Rhein, Germany, December 27 (Laboratory Project ID No. 50C0374/91133; MRID 43562601) [cited in U.S. EPA, 2003].

Mersch-Sundermann, V., Hofmeister, A., Mueller, G. and Hof, H. (1989). [Examination of mutagenicity of organic microcontaminations of the environment. III. Communication: The mutagenicity of selected herbicides and insecticides with the SOS chromotest.] Zentrabl. Hyg., 189: 135–146 (in German).

Miltner, R.J., Baker, D.B., Speth, T.F. and Fronk, C.A. (1989). Treatment of seasonal pesticides in surface waters. J. Am. Water Works Assoc., 1: 43–52.

Ministère du Développement durable, de l'Environnement et des Parcs du Québec (2007). Personal communication from I. Gorse, Direction des politiques en milieu terrestre.

Moriya, M., Ohta, T., Watanabe, K., Miyazawa, T., Kato, K. and Shirasu, Y. (1983). Further mutagenicity studies on pesticides in bacterial reversion assay system. Mutat. Res., 116: 185–216.

Murphy, C. and Mutch, J. (2005). Unpublished water monitoring data from the Environment Canada Atlantic Region. Collected as part of the Environment Canada Pesticide Science Fund [cited in PMRA, 2005d].

Murray, J., Andersen, D. and Kent, R. (2004). Presence, levels and relative risks of priority pesticides in selected Canadian aquatic ecosystems. An Environment Canada Pesticides Science Fund Project. Year 1 (2003–2004) annual report. National Water Research Institute, Environment Canada, Burlington, Ontario.

Mustonen, R., Elovaara, E., Zitting, A., Linnainmaa, A. and Vainio, H. (1989). Effects of commercial chlorophenolate, 2,3,7,8-TCDD, and pure phenoxyacetic acids on hepatic peroxisome proliferation, xenobiotic metabolism and sister chromatid exchange in the rat. Arch. Toxicol., 63: 203–208.

New Brunswick Department of Health (2005). Personal communication from R. Albert.

Newfoundland and Labrador Department of Environment and Conservation (2005). Personal communication from M. Goebel.

Nishimura, N., Nishimura, H. and Oshima, H. (1982). Survey on mutagenicity of pesticides by the *Salmonella*-microsome test. J. Aichi Med. Univ. Assoc., 10: 305–312 [cited in Elliott, 2005].

Nova Scotia Department of Environment and Labour (2005). Personal communication from J.A. MacDonald.

Ontario Ministry of the Environment (2005). Personal communication from P. Lachmaniuk.

Palva, H.L.A., Koivisto, O. and Palva, I.P. (1975). Aplastic anaemia after exposure to a weed killer, 2-methyl-4-chlorophenoxyacetic acid. Acta Haematol., 53: 105–108.

PMRA (2005a). Internal report. MCPA use profile for Water Quality and Health Bureau, Health Canada. Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario, September 7.

PMRA (2005b). Internal report. Comments submitted to Water Quality and Health Bureau, Health Canada. Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario, March 24.

PMRA (2005c). Internal report. Concentration of MCPA in drinking water. Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario, September 1.

PMRA (2005d). Internal report. Additional data on MCPA in drinking water. Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario, October 27.

PMRA (2006). Re-evaluation of the lawn and turf uses of the herbicide 4-chloro-2-methylphenoxy acetic acid (MCPA). Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario, April 28 (PACR2006-05). Available at: www.pmra-arla.gc.ca/english/pubs/pacr-e.html

PMRA (2007). Proposed re-evaluation decision. The agricultural, forestry and industrial site uses of the herbicide (4-chloro-2-methylphenoxy)acetic acid (MCPA). Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario. Consultation document of July 2007 (PRVD2007-01). Available at: www.pmra-arla.gc.ca/english/pubs/prvd-e.html

PMRA (2008). Re-evaluation Decision. (4-chloro-2-methylphenoxy)acetic acid (MCPA). Pest Management Regulatory Agency, Health Canada, Ottawa, Ontario. (RVD2008-20). Available at: www.pmra-arla.gc.ca/english/pdf/rvd/rvd2008-20-eng.pdf

Popham, R.D. and Davis, D.M. (1964). A case of MCPA poisoning. Br. Med. J., 1: 677–678.

Proudlock, R.J., Taylor, K., Anderson, A. and Dawe, I.S. (1993a). MCPA DMAS micronucleus test. Huntingdon Research Centre Ltd., Huntingdon, UK, April 2 (HRC Study No. JEL 33/921197) [cited in Cal-EPA, 2000; Elliott, 2005].

Proudlock, R.J., Elmore, E.A., Anderson, A. and Dawe, I.S. (1993b). MCPA acid micronucleus test. Huntingdon Research Centre Ltd., Huntingdon, UK, April 23 (HRC Study No. JEL 35/921198) [cited in Cal-EPA, 2000; Elliott, 2005].

Proudlock, R.J., Goodenough, A.J., Anderson, A. and Dawe, I.S. (1993c). MCPA 2-EHE micronucleus test. Huntingdon Research Centre Ltd., Huntingdon, UK, April 22 (HRC Study No. JEL 33/921197) [cited in Elliott, 2005].

Randtke, S.J. (1988). Organic contaminant removal by coagulation and related process combinations. J. Am. Water Works Assoc., 80(5): 40–56.

Räsänen, L., Hattula, M.L. and Arstila, A.U. (1977). The mutagenicity of MCPA and it soil metabolites, chlorinated phenols, catechols and some widely used slimicides in Finland. Bull. Environ. Contam. Toxicol., 18(5): 565–571.

Rawn, D.F.K., Halldorson, T.H.J., Lawson, B.D., and Muir, D.C.G. (1999). A multi-year study of four herbicides in air and precipitation from a small prairie watershed. J. Environ. Qual. 28: 898-906.

Reuzel, P.G.J. and Hendriksen, C.F.M. (1980). Subchronic (13-week) oral toxicity study of MCPA in beagle dogs: final report. Unpublished study, BASF Aktiengesellschaft, Ludwigshafen, FRG [cited in WHO, 2003; U.S. EPA 2003].

Robeck, G., Dostal, K.A., Cohen, J.M. and Kreissl, J.F. (1965). Effectiveness of water treatment processes in pesticide removal. J. Am. Water Works Assoc., 57: 181–199.

Rowe, V.K. and Hymas, T.A. (1954). Summary of toxicological information on 2,4-D and 2,4,5-T type herbicides and an evaluation of the hazards to livestock associated with their use. Am. J. Vet. Res., 15: 622–629.

RTECS (2005). Registry of Toxic Effects of Chemical Substances: MCPA. CAS # 94-74-6. RTECS No.: AG1575000. Chemical profiles created by Canadian Centre for Occupational Health and Safety, Hamilton, Ontario. Available at: www.ccohs.ca

Saracci, R., Kogevinas, M., Bertazzi, P.-A., Bueno de Mesquita, B.H., Coggon, D., Green, L.M., Kauppinen, T., L'Abbé, K.A., Littorin, M., Lynge, E., Mathews, J.D., Neuberger, M., Osman, J., Pearce, N. and Winkelmann, R. (1991). Cancer mortality in workers exposed to chlorophenoxy herbicides and chlorophenols. Lancet, 338(8774): 1027–1032.

Sattar, M.A. and Paasivirta, J. (1980). Fate of chlorophenoxy acetic acids in acid soil. Chemosphere, 9: 745–752.

Schippers, J.C., Kruithof, J.C., Nederlof, M.M., Hofman, J.A.M.H. and Taylor, J.S. (2004). Integrated membrane systems. American Water Works Association Research Foundation and American Water Works Association, Denver, CO (Report No. 90899).

Smith, A.E. and Hayden, B.J. (1980). Hydrolysis of MCPA esters and the persistence of MCPA in Saskatchewan soils. Bull. Environ. Contam. Toxicol., 25: 369–373.

Smith, A.E. and Hayden, B.J. (1981). Relative persistence of MCPA, MCPB and mecoprop in Saskatchewan soils, and the identification of MCPA in MCPB-treated soils. Weed Sci., 21: 179–183.

Soderquist, C.J. and Crosby, D.G. (1975). Dissipation of 4-chloro-2-methylphenoxyacetic acid (MCPA) in a rice field. Pestic. Sci., 6: 17–33.

Struger, J., Fletcher, T., Martos, P., Ripley, B. and Gris, G. (2002). Pesticide concentrations in the Don and Humber river watersheds (1998–2000). Interim report. Environment Canada and the Ontario Ministry of the Environment, December [cited in PMRA, 2005c].

Struger, J., L'Italien, S. and Sverko, E. (2004). In-use pesticide concentrations in surface waters of the Laurentian Great Lakes, 1994–2000. J. Great Lakes Res., 30(3): 435–450.

Struger, J., Marvin, C., Sveko, E., Dove, A., Palace, V., Todd, A. and Fletcher, T. (2005). Unpublished water monitoring data from the Environment Canada Ontario Region. Collected as part of the Environment Canada Pesticide Science Fund [cited in PMRA, 2005d].

Taylor, J., Mulford, L.A., Chen, S.S. and Hofman, J.A.M. (1995). Membrane filtration of pesticides. American Water Works Association Annual Conference Proceedings. American Water Works Association, Denver, CO.

Taylor, J., Chen, S.S., Mulford, L.A. and Norris, D. (2000). Flat sheet, bench and pilot testing for pesticide removal using reverse osmosis. American Water Works Association Research Foundation and American Water Works Association, Denver, CO (Report No. 90808).

Tekel, J. and Kavacicová, J. (1993). Chromatographic methods in the determination of herbicide residues in crops, food and environmental samples. J. Chromatogr., 643: 291–303.

Timchalk, C. (2004). Comparative inter-species pharmacokinetics of phenoxyacetic acid herbicides and related organic acids. Evidence that the dog is not a relevant species for evaluation of human health risk. Toxicology, 200(1): 1–19.

Timonen, T.T. and Palva, I.P. (1980). Acute leukemia after exposure to a weed killer, 2-methyl-4-chlorophenoxy-acetic acid. Acta Haematol., 63: 170–171.

Tuominen, T., Pasternak, J., Sekela, M., Ryan, A., Hii, B., Strub, R., McPherson, B., Wan, M., Kuo, J. and Hamilton, C. (2005). Unpublished water monitoring data from the Environment Canada Pacific and Yukon Region. Collected as part of the Environment Canada Pesticide Science Fund [cited in PMRA, 2005d].

USDA (2001). Agricultural Research Service (ARS) Pesticide Properties Database on MCPA (94-74-6). U.S. Department of Agriculture. MCPA last updated May 1999. Available at: www.ars.usda.gov/SP2UserFiles/ad_hoc/12755100DatabaseFiles/PesticidePropertiesDatabase/Allchemicals/listallchemicals.doc

U.S. EPA (1984). Health and environmental effects profile for MCPA and MCPB. Environmental Criteria and Assessment Office, Office of Research and Development, U.S. Environmental Protection Agency (NTIS/PB88-162391; microfiche).

U.S. EPA (1990). Registration on standard for pesticide products containing MCPA as the active ingredient. Government Reports Announcement and Index (GRA & I), Issue 07. U.S. Environmental Protection Agency (NTIS/PB90-146556).

U.S. EPA (1992). Methods for the determination of organic compounds in drinking water—supplement II. Environmental Monitoring Systems Laboratory, Office of Research and Development, U.S. Environmental Protection Agency, August (EPA-600-R-92-192).

U.S. EPA (2003). MCPA: Toxicology chapter for RED (Reregistration Eligibility Decision). Office of Prevention, Pesticides, and Toxic Substances, U.S. Environmental Protection Agency, Washington, DC, July 1 (Document ID: EPA-HQ-OPP-2004-0239-0019). Available at: www.regulations.gov/fdmspublic/component/main

U.S. EPA (2004a). Environmental Fate and Effects Division's risk assessment for the reregistration eligibility document for 2-methyl-4-chlorophenoxyacetic acid (MCPA). U.S. Environmental Protection Agency (Document ID: EPA-HQ-OPP-2004-0239-0006). Available at: www.regulations.gov/fdmspublic/component/main

U.S. EPA (2004b). R.E.D. Facts: MCPA. Office of Prevention, Pesticides and Toxic Substances, U.S. Environmental Protection Agency, September (7508C; Document ID: EPA-HQ-OPP-2004-0239-0002). Available at www.epa.gov/oppsrrd1/REDs/factsheets/mcpa_red_fs.pdf; www.regulations.gov/fdmspublic/component/main

U.S. EPA (2004c). MCPA summary. U.S. Environmental Protection Agency (Document ID: EPA-HQ-OPP-2004-0156-0003). Available at: www.regulations.gov/fdmspublic/component/main

U.S. EPA (2004d). Reregistration Eligibility Decision for MCPA (2-methyl-4-chlorophenoxyacetic acid). List A Case 0017. Office of Prevention, Pesticides, and Toxic Substances, U.S. Environmental Protection Agency, Washington, DC, September 30 (Document ID: EPA-HQ-OPP-2004-0239-0003). Available at: www.epa.gov/oppsrrd1/REDs/mcpa_red.pdf; www.regulations.gov/fdmspublic/component/main

U.S. EPA (2004e). MCPA — Corrected first report of the Hazard Identification Assessment Review Committee. Office of Prevention, Pesticides, and Toxic Substances, U.S. Environmental Protection Agency, Washington, DC (Document ID: EPA-HQ-OPP-2004-0239-0018). Available at: www.regulations.gov/fdmspublic/component/main

U.S. EPA (2006). Drinking Water Health Advisories. Available at: www.epa.gov/waterscience/criteria/drinking/dwstandards.html#defn

van Ravenzwaay, B., Pigott, G. and Leibold, E. (2004). Absorption, distribution, metabolism and excretion of 4-chloro-2-methylphenoxyacetic acid (MCPA) in rats. Food Chem. Toxicol., 42(1): 115–125.

Vineis, P., Terracini, B., Ciccone, G., Cignetti, A., Colombo, E., Donna, A., Maffi, D.A., Pisa, R., Ricci, P., Zanini, E. and Comba, P. (1986). Phenoxy herbicides and soft-tissue sarcomas in female rice-weeders: a population-based case control study. Scand. J. Work Environ. Health, 13(1): 9–17.

Vineis, P., Faggiano, F., Tedeschi, M. and Ciccone, G. (1991). Incidence rates of lymphomas and soft-tissue sarcomas and environmental measurements of phenoxy herbicides. J. Natl. Cancer Inst., 83(5): 362–363.

Waite, D.T., Cessna, A.J., Grover, R., Kerr, L.A. and Snihura, A.D. (2004). Environmental concentrations of agricultural herbicides in Saskatchewan, Canada: bromoxil, dicamba, diclofop, MCPA and trifluralin. J. Environ. Qual., 33(5): 1616–1628.

Waite, D.T., Bailey, P., Sproull, J.F., Quiring, D.V., Chau, D.F., Bailey, J. and Cessna, A.J. (2005). Atmospheric concentrations and dry and wet deposits of some herbicides currently used on the Canadian Prairies. Chemosphere, 58: 693–703.

Weed Science Society of America (1989). Herbicide handbook. 6th edition. Weed Science Society of America, Champaign, IL. pp. 171–173.

WHO (1996). Guidelines for drinking-water quality, 2nd edition, vol. 2. Health criteria and other supporting documentation. World Health Organization, Geneva. ISBN 9241544805. Available at: www.who.int/water_sanitation_health/dwq/gdwq2v1/en/index1.html

WHO (2003). MCPA in drinking-water. Background document for development of WHO Guidelines for drinking-water quality. World Health Organization, Geneva, Switzerland (WHO/SDE/WSH/03.04/38). Available at: www.who.int/water_sanitation_health/dwq/chemicals/mcpa/en/

WHO (2004). Guidelines for drinking-water quality. Chapter 8. World Health Organization, Geneva, Switzerland Available at: www.who.int/water_sanitation_health/dwq/GDWQ2004web.pdf

Wiklund, K., Dich, J. and Holm, L.-E. (1987). Risk of malignant lymphoma in Swedish pesticide appliers. Br. J. Cancer, 56: 505–508.

Wiklund, K., Dich, J. and Holm, L.-E. (1988). Soft tissue sarcoma risk in Swedish licensed pesticide applicators. J. Occup. Med., 30(10): 801–804.

Wiklund, K., Dich, J. and Holm, L.-E. (1989). Risk of soft tissue sarcoma, Hodgkin's disease and non-Hodgkin lymphoma among Swedish licensed pesticide applicators. Chemosphere, 18(1–6): 395–400.

Worthing, C.R. and Hance, R.J. (eds.). (1991). The pesticide manual. 9th edition. British Crop Protection Council, Farnham, UK.

Zetterberg, G. (1978). Genetic effects of phenoxy acids on microorganisms. Ecol. Bull., 27: 193–204.

Zetterberg, G. (1979). Mechanism of the lethal and mutagenic effects of phenoxyacetic acids in *Saccharomyces cerevisiae*. Mutat. Res., 60: 291–300.

Appendix A: List of acronyms

2,4-D	2,4-dichlorophenoxyacetic acid
2,4-DB	4-(2,4-dichlorophenoxy)butyric acid
2,4-DP	2-(2,4-dichlorophenoxy)propanoic acid (dichlorprop)
2,4,5-T	2,4,5-trichlorophenoxyacetic acid
ALP	alkaline phosphatase
ALT	alanine aminotransferase
ANSI	American National Standards Institute
AOC	assimilable organic carbon
AOP	advanced oxidation process
AST	aspartate aminotransferase
bw	body weight
CI	confidence interval
DNA	deoxyribonucleic acid
DOC	dissolved organic carbon
EBCT	empty bed contact time
EPA	Environmental Protection Agency (United States)
GAC	granular activated carbon
GC	gas chromatography
HMCPA	4-chloro-2-hydroxymethyl-phenoxyacetic acid
HPLC	high-performance liquid chromatography
IARC	International Agency for Research on Cancer
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
MAC	maximum acceptable concentration
MCPA	2-methyl-4-chlorophenoxyacetic acid
MCPA-DMAS	MCPA dimethylamine salt
MCPA-EHE	MCPA 2-ethylhexyl ester
MCPB	4-(2-methyl-4-chlorophenoxy)butyric acid
MCPP	(±)-2-(4-chloro-2-methylphenoxy)propanoic acid (mecoprop)
MCPP-p	(R)(+)-2-(4-chloro-2-methylphenoxy)propanoic acid (mecoprop-p)
MRL	maximum residue limit
MS	mass spectrometry
MTD	maximum tolerated dose
NHL	non-Hodgkin's lymphoma
NOAEL	no-observed-adverse-effect level
NOEL	no-observed-effect level
NSF	NSF International
OR	odds ratio
PDA	photodiode array
PMRA	Pest Management Regulatory Agency
S9	metabolic activation (9000 × *g* supernatant)
SCC	Standards Council of Canada
SPE	solid-phase extraction
STS	soft tissue sarcoma

TDI	tolerable daily intake
U.S. EPA	United States Environmental Protection Agency
UV	ultraviolet
WHO	World Health Organization