Screening Assessment for the Challenge

Methane, chloro-
(Methyl chloride)

Chemical Abstracts Service Registry Number
74-87-3

Environment Canada
Health Canada

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Synopsis

Pursuant to section 74 of the *Canadian Environmental Protection Act, 1999* (CEPA 1999), the Ministers of the Environment and of Health have conducted a screening assessment of methane, chloro- or methyl chloride, Chemical Abstracts Service Registry Number 74-87-3. This substance was identified in the categorization of the Domestic Substances List as a high priority for action under the Challenge. Methyl chloride was identified as a high priority as it was considered to pose the greatest potential for exposure of individuals in Canada and it had been classified by the European Commission on the basis of carcinogenicity. Although methyl chloride met the ecological categorization criterion for persistence, it did not meet the criteria for potential for bioaccumulation and inherent toxicity to aquatic organisms. Therefore, the focus of this assessment of methyl chloride relates primarily to human health risks.

According to information provided by Statistics Canada, 1,049,000 kg of methyl chloride were imported into Canada in 2006.

The most important industrial uses of methyl chloride are as a chemical intermediate in manufacturing processes in which methyl chloride is consumed. In Canada, the largest reported use of methyl chloride is as a solvent in the manufacture of butyl rubber and the next largest reported use is in the manufacture of quaternary ammonium compounds. Methyl chloride is not produced in Canada as a commercial product for sale.

Methyl chloride, a gas at room temperature, is ubiquitous in air. There are significant natural and anthropogenic sources of methyl chloride released principally to the atmosphere which include biomass burning, the open oceans, plants, fungi, coal and waste combustion, and industrial processes. Methyl chloride is a by-product of combustion when biomass and fossil fuels are burned. Industrial facilities that burn large quantities of coal such as coal-fired power generating plants and integrated steel mills, as well as kraft pulp mills operating recovery boilers are sources of release of methyl chloride to the atmosphere from combustion processes. A butyl rubber plant is the largest point source of release of methyl chloride in Canada.

Methyl chloride has been measured in indoor and ambient air, and detected in a small percentage of samples of groundwater, surface water and municipally-treated drinking water. Dietary intake and the use of consumer products except for tobacco are expected to make a negligible contribution to human exposure to this substance.

As methyl chloride was classified on the basis of carcinogenicity by a national agency, carcinogenicity was a key focus for this screening assessment. In a 2-year rodent inhalation bioassay, renal tumours were significantly increased in male mice from the high-concentration group. No tumours were observed in female mice or in rats of either sex. The tumours in male mouse kidney may be initiated by progression from hyperplasia due to regeneration following chronic high-concentration exposure, rather than by direct mutagenic activity of methyl chloride, and may not be relevant to humans, due to species differences in metabolism of methyl chloride.

The primary target organ for methyl chloride toxicity was identified in humans and in rodents as the central nervous system. The critical effect concentration was based on axonal swelling and degeneration in the spinal nerves of male and female mice exposed to methyl chloride for up to 2 years. Effects on male rat reproductive organs and male mouse kidney hyperplastic lesions and tumours were only observed at exposure concentrations well above the critical effect concentration. Comparison of the critical effect level in experimental animals with the upper bounding estimates of general population exposure from all sources results in acceptable margins of exposure for all age groups.

Methyl chloride meets the criteria for persistence in air, water, soil and sediment, but does not meet the bioaccumulation criteria set out in the *Persistence and Bioaccumulation Regulations*. It exhibits only a moderate to low potential for toxicity to aquatic organisms. On the basis of its relatively low ecological hazard, and the low concentrations measured in environmental media and effluents in Canada and elsewhere, it is concluded that methyl chloride is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Based on the available information on its potential to cause harm to human health, it is concluded that methyl chloride is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

This substance will be included in the upcoming *Domestic Substances List* inventory update initiative. In addition and where relevant, research and monitoring will support verification of assumptions used during the screening assessment.

Based on the information available, it is concluded that methyl chloride does not meet any of the criteria set out in section 64 of CEPA 1999.

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) (Canada 1999) requires the Minister of the Environment and the Minister of Health to conduct screening assessments of substances that have met the categorization criteria set out in the Act to determine whether these substances present or may present a risk to the environment or to human health.

Based on the information obtained through the categorization process, the Ministers identified a number of substances as high priorities for action. These include substances that

- met all of the ecological categorization criteria, including persistence (P), bioaccumulation potential (B) and inherent toxicity to aquatic organisms (iT), and were believed to be in commerce; and/or
- met the categorization criteria for greatest potential for exposure (GPE) or presented an intermediate potential for exposure (IPE) and had been identified as posing a high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The Ministers therefore published a notice of intent in the *Canada Gazette*, Part I, on December 9, 2006 (Canada 2006), which challenged industry and other interested stakeholders to submit, within specified timelines, specific information that may be used to inform risk assessment and to develop and benchmark best practices for the risk management and product stewardship of those substances identified as high priorities.

The substance methane, chloro- (methyl chloride) was identified as a high priority for assessment of human health risk because it was considered to present the greatest potential for exposure and it was classified by another agency on the basis of carcinogenicity.

The Challenge for methyl chloride was published in the *Canada Gazette* on May 31, 2008 (Canada 2008). A substance profile was released at the same time. The substance profile presented the technical information available prior to December 2005 that formed the basis for categorization of this substance. As a result of the Challenge, submissions of information were received.

Although methyl chloride was determined to be a high priority for assessment with respect to human health and also met the ecological categorization criteria for persistence, it did not meet the criteria for potential for bioaccumulation and inherent toxicity to aquatic organisms. Therefore, this assessment focuses principally on information relevant to the evaluation of risks to human health.

Screening assessments focus on information critical to determining whether a substance meets the criteria for defining a chemical as toxic as set out in section 64 of CEPA 1999. Screening assessments examine scientific information and develop conclusions by incorporating a weight of evidence approach and precaution.

This screening assessment includes consideration of information on chemical properties, hazards, uses and exposure, including the additional information submitted under the Challenge. Data relevant to the screening assessment of this substance were identified in original literature, review and assessment documents and stakeholder research reports and from recent literature searches, up to January 2009 for the human health section. Key studies were critically evaluated; modelling results may have been used to reach conclusions. Evaluation of risk to human health involves consideration of data relevant to estimation of exposure (non-occupational) of the general population, as well as information on health hazards (based principally on the weight of evidence assessments of other agencies that were used for prioritizing the substance). Decisions for human health are based on the nature of the critical effect and/or margins between conservative effect levels and estimates of exposure, taking into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. The final screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents a summary of the critical information upon which the conclusion is based.

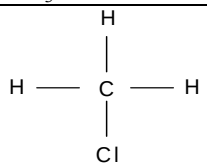
This screening assessment was prepared by staff in the Existing Substances Programs at Health Canada and Environment Canada and incorporates input from other programs within these departments. The human health and ecological portions of this assessment have undergone external written peer review/consultation. Comments on the technical portions relevant to human health were received from scientific experts selected and directed by Toxicology Excellence for Risk Assessment (TERA), including Dr. Michael Dourson (TERA), Dr. Pam Williams (E Risk Sciences) and Dr. Glenn Talaska (University of Cincinnati). Additionally, the draft of this screening assessment was subject to a 60-day public comment period. Although external comments were taken into consideration, the final content and outcome of the screening risk assessment remain the responsibility of Health Canada and Environment Canada.

The critical information and considerations upon which the assessment is based are summarized below.

Substance Identity

For the purposes of this document, this substance will be referred to as methyl chloride, derived from the common name. Its substance identity information is summarized in Table 1.

Table 1. Substance identity for methyl chloride

CAS RN	74-87-3
DSL name	Methane, chloro-
NCI names	Chloromethane (ECL, EINECS, ENCS, PICCS) Methane, chloro- (AICS, ASIA-PAC, NZloC, PICCS, SWISS, TSCA) Methyl chloride (ECL, ENCS, PICCS)
Other names	Artic; F 40; Freon 40; HCC 40; Monochloromethane; R 40; R 40 (refrigerant); UN 1063; UN 1063 (DOT)
Chemical group (DSL stream)	Discrete organics
Major chemical class or use	Chlorocarbons
Major chemical subclass	Haloalkanes
Chemical formula	CH_3Cl
Chemical structure	
SMILES	ClC
Molecular mass	50.49 g/mol

Abbreviations: AICS, Australian Inventory of Chemical Substances; ASIA-PAC, Asia-Pacific Substances Lists; CAS RN, Chemical Abstracts Service Registry Number; DSL, Domestic Substances List; ECL, Korean Existing Chemicals List; EINECS, European Inventory of Existing Commercial Chemical Substances; ENCS, Japanese Existing and New Chemical Substances; NCI, National Chemical Inventories; NZloC, New Zealand Inventory of Chemicals; PICCS, Philippine Inventory of Chemicals and Chemical Substances; SMILES, simplified molecular input line entry specification; SWISS, Swiss Giftliste 1 and Inventory of Notified New Substances; TSCA, Toxic Substances Control Act Chemical Substance Inventory.

Source: NCI (2008)

Physical and Chemical Properties

Table 2 contains experimental and modelled physical and chemical properties of methyl chloride that are relevant to its environmental fate. Acceptable experimental data for a parameter are preferred over those obtained through modelling; however, the latter provide support for the measured values.

Table 2. Physical and chemical properties of methyl chloride

Property	Type	Value[1]	Temperature (°C)	Reference
Melting point (°C)	Experimental	−97.7		Holbrook 2003
Boiling point (°C)	Experimental	−23.73		Holbrook 2003
Density (kg/m^3)	Experimental	2.305 (2.3045 g/L; gas)	0	Holbrook 2003
Vapour pressure (Pa)	Experimental	4.89×10^5 (3669.75 mmHg)	20	Holbrook 2003
		5.73×10^5 (4300 mmHg)	25	Daubert and Danner 1985
	Modelled	5.4×10^5 (4030 mmHg; mean of Antoine and Grain methods)	25	MPBPWIN 2000
Henry's Law constant (Pa·m^3/mol)	Experimental	396 (3.91×10^{-3} atm·m^3/mol)	10.3	Gossett 1987
		592 (5.84×10^{-3} atm·m^3/mol)	17.5	
		894 (8.82×10^{-3} atm·m^3/mol)	24.8	
	Modelled	830 (8.20×10^{-3} atm·m^3/mol; bond estimate)	25	HENRYWIN 2000
		900 (8.88×10^{-3} atm·m^3/mol; group estimate)		
		1066 (1.052×10^{-2} atm·m^3/mol; VP/WSol estimate)		
Log K_{ow} (dimensionless)	Experimental	0.91	25	Hansch et al. 1995
	Modelled	1.09	25	KOWWIN 2000
Log K_{oc} (dimensionless)	Modelled	1.2 (corrected value)	25	PCKOCWIN 2000

Property	Type	Value[1]	Temperature (°C)	Reference
Water solubility (mg/L)	Experimental	4800 (0.48 g/100 g)	25	Holbrook 2003
		5320	25	Horvath 1982
Other solubilities (g/L)	Experimental (alcohol)	Soluble		O'Neil et al. 2006
	Experimental (chloroform)	Miscible		
	Experimental (glacial acetic acid)	Miscible		

Abbreviations: K_{oc}, organic carbon–water partition coefficient; K_{ow}, octanol–water partition coefficient; VP, vapour pressure; WSol, water solubility.

[1] Values in parentheses represent the original values as reported by the authors or as estimated by the models.

Methyl chloride is a gas at standard temperature and pressure and has a high water solubility, very high vapour pressure, high Henry's Law constant, and low or very low octanol–water (log K_{ow}) and organic carbon–water (log K_{oc}) partition coefficients.

Sources

There are significant natural and anthropogenic sources of methyl chloride released to the environment. Recent efforts by the Reactive Chlorine Emissions Inventory of the Global Emissions Inventory Activity to quantify the global flux of methyl chloride have resulted in an estimate of the contribution of natural sources to total emissions of about 50% (Keene et al. 1999; RCEI 2007). This estimate is significantly different from earlier estimates, which placed the percentage emitted from natural sources at 90–99% (ATSDR 1998; OECD 2003). There remain large bounds of uncertainty in all the different global budgets of sources and sinks; nevertheless, a very large proportion of methyl chloride in the troposphere is from one of several natural sources.

The largest sources of methyl chloride emissions to the atmosphere from natural processes are biomass burning from wildfires, the open ocean, tropical plants and wood-rotting fungi. Globally, the most important anthropogenic sources of methyl chloride emissions include biomass burning for land clearing and other activities, such as heating and cooking, coal combustion for power and process heat, waste incineration and industrial processes (Keene et al. 1999; McCulloch et al. 1999; Keppler et al. 2005).

The worldwide industrial demand for methyl chloride in 2007 was 1.98 million tonnes. Demand in Canada was 2.2 million kilograms in 2007 and 1.0 million kilograms in 2006 (CIMT 2009). Nearly all methyl chloride imported into Canada is imported as an essentially pure chemical. In response to a notice issued under section 71 of CEPA 1999, Canadian companies reported that methyl chloride was present as an impurity in other

chlorinated solvents, vinyl chloride and quaternary ammonium chlorides. No company reported the manufacture of methyl chloride in Canada in 2006 for sale or use as a commercial product (Environment Canada 2008).

In Canada, the largest known point source of methyl chloride released to the environment is the LANXESS butyl rubber plant in Sarnia, Ontario, where methyl chloride is used as a solvent. Methyl chloride is also generated as a product of combustion of both biomass and fossil fuels, especially coal, in which chloride is present, and facilities where large quantities of these fuels are consumed may be significant point sources of methyl chloride.

In 2006, 15.25 million tonnes of solid wood waste and 21.51 million tonnes of spent pulping liquor were burned for energy production, principally in the forest products sector. The coal-fired power generating sector and the iron and steel sector are large consumers of coal in Canada. In 2006, the coal-fired power generating sector burned 50.77 million tonnes of coal, and 4.33 million tonnes of coal were converted to metallurgical coke and manufactured gases. The total demand for coal by other industries was 1.95 million tonnes in the same year (Statistics Canada 2008).

The relative importance of different anthropogenic sources of methyl chloride cannot be estimated on a facility or regional basis, but estimates of the quantity of methyl chloride emitted by industrial sectors can be made based on representative combustion conditions using emission factors developed by the US EPA (1995). The results are presented below in the Releases to the Environment section.

In addition to the above-noted industrial sources, incineration of municipal solid waste, especially of plastic wastes containing chloride, such as polyvinyl chloride, results in the release of methyl chloride to the atmosphere. Although it is stated in several reports that incineration of silicone rubber is a source of methyl chloride, toxicology staff of the Agency for Toxic Substances and Disease Registry (ATSDR), the apparent origin of this assertion, were unable to offer any evidence in support of that statement (2009 email from ATSDR to Existing Substances Division, Health Canada; unreferenced). Both municipal solid waste and hazardous waste landfills may be sources of methyl chloride emissions to groundwater and air (Sabel and Clark 1984). The total emission of methyl chloride in uncaptured landfill gas from all Canadian landfills was estimated to be less than 250 kg per year (2008 email from Environmental Protection Operations, Environment Canada, to Existing Substances Division, Health Canada; unreferenced; Environment Canada 1999).

A significant residential source of methyl chloride emissions to ambient air is combustion of wood in stoves and fireplaces. Wood-burning stoves and fireplaces also contribute to elevated concentrations of methyl chloride in indoor air. Tobacco smoke is both a source of direct exposure to methyl chloride as well as a source of the chemical released to air.

Uses

A total of 1 049 000 kg of methyl chloride was imported for use in Canada in 2006 (CIMT 2009). The use and disposition of hundreds of thousands of kilograms of methyl chloride in Canada are unknown.

The most important industrial uses of methyl chloride are as a chemical intermediate in manufacturing processes in which methyl chloride is consumed. Methyl chloride is used to produce the higher chlorinated methanes—methylene chloride, chloroform and carbon tetrachloride—generally in the same facility in which methyl chloride is produced. No methyl chloride or higher chlorinated methane is manufactured in Canada for commercial purposes. Globally, the largest market for methyl chloride, after production of higher chlorinated methanes, is in the production of methyl chlorosilanes, intermediates in the production of silicones. In 2007, methyl chlorosilane production accounted for about 89% of US demand (Glauser and Funada 2008). No company responding to the section 71 notice reported using methyl chloride to produce methyl chlorosilanes in Canada.

Globally, other important industrial uses of methyl chloride are the manufacture of methylcellulose ethers and quaternary ammonium chlorides, use as a methylating agent in the synthesis of pesticides, pharmaceuticals, quaternary ammonium compounds, organotin stabilizers and a variety of other chemicals, and use as a solvent in the production of butyl rubber (Dow Chemical 2007; Glauser and Funada 2008).

In Canada, the largest use of methyl chloride is as a solvent at the LANXESS butyl rubber facility in Sarnia, Ontario, which in 2006 consumed approximately 625 tonnes (Environment Canada 2008). Increased production capacity at that facility is thought to be largely responsible for an increase in the demand for methyl chloride in Canada from 1.0 million kilograms in 2006 to 2.2 million kilograms in 2007 (LANXESS 2007; CIMT 2009).

In Canada, the second largest reported use of methyl chloride in 2006 was in the manufacture of quaternary ammonium chlorides by one company that used 35 tonnes (Environment Canada 2008). Quaternary ammonium chloride compounds made with methyl chloride are usually either trimethyl alkyl ammonium chlorides or dimethyl dialkyl ammonium chlorides. They are present in a number of consumer products in Canada. They function as surface-active agents, particularly in some fabric softeners and anti-static treatments, but may also be used in personal care products, car wax and cleaner, hard surface cleaners and other consumer products. These compounds may also be found in industrial surfactants and emulsifiers (Porter 1991; Hargreaves 2003). Dimethyl dialkyl ammonium chlorides made with methyl chloride may also function as anti-microbial agents and fungicides. One company responding to the *Canada Gazette* notice for methyl chloride indicated that solutions of quaternary ammonium compounds sold for industrial use contained up to 0.03% methyl chloride (Environment Canada 2008).

No company reported use of methyl chloride to manufacture methylcellulose ethers in Canada, but methylcellulose ethers and derivatives are used in Canada. Methylcellulose ethers and derivatives, including methylcellulose, hydroxypropyl methylcellulose and hydroxybutyl methylcellulose, are used primarily in building products, such as drywall compound, plaster, stucco, mortars, grouts, wallpaper glues and paste. Methylcellulose and hydroxypropyl methylcellulose are also widely used as thickening agents in prepared foods and beverages and pharmaceuticals (Glauser and Funada 2008).

No company reported use of methyl chloride as a blowing agent to make polymeric foam in response to the section 71 notice, and a representative of the Canadian Plastics Industry Association stated that methyl chloride is not used as a foam-blowing agent for polystyrene in Canada (2008 email from Canadian Plastics Industry Association to Existing Substances Division, Health Canada; unreferenced). It is not known if polystyrene produced elsewhere with methyl chloride and imported into Canada is a source of methyl chloride migrating from the foam into occupied spaces.

No company reported use of methyl chloride as a chemical intermediate in the synthesis of pesticides, pharmaceuticals, organotin stabilizers or other chemicals, apart from quaternary ammonium chlorides.

The use of methyl chloride as a heat transfer fluid in domestic refrigerators was discontinued about 30 or 40 years ago (ATSDR 1998), but the use of R 40 in certain refrigerators was stated as a current application by a European manufacturer of methyl chloride (LII Europe 2002). It is unclear whether some minor applications of methyl chloride as a refrigerant or as a thermometric fluid in Canada remain. Methyl chloride was used in the past to manufacture the anti-knock fuel additive tetramethyl lead in Canada. No company reported using methyl chloride to manufacture tetramethyl lead in response to the section 71 notice (Environment Canada 2008). Methyl chloride is no longer used as a topical anaesthetic.

Methyl chloride is not used as a formulant or an active ingredient in any registered pest control products in Canada. Trace amounts of methyl chloride may be present as manufacturing impurities in some pest control products containing quaternary ammonium chloride active ingredients (2009 email from Pest Management Regulatory Agency to Existing Substances Division, Health Canada; unreferenced).

Releases to the Environment

It is estimated that the global annual release of methyl chloride to the atmosphere from natural and anthropogenic sources is 1.886 million tonnes (Keene et al. 1999).

Industrial releases of methyl chloride in 2006 in Canada reported to the National Pollutant Release Inventory (NPRI) were 255 tonnes, all but 30 kg of which were released to the atmosphere. The 30 kg was reported to have been released to water. The largest known industrial point source of methyl chloride release to the atmosphere in

Canada is the LANXESS butyl rubber plant in Sarnia, Ontario, which reported the release of 199 tonnes in 2006 and 244 tonnes in 2007 (NPRI 2009). The criteria for reporting release of methyl chloride to the NPRI are such that facilities manufacturing, processing or otherwise using fewer than 10 tonnes annually are not required to report, and these amounts are therefore not represented in the NPRI.

Responses to the section 71 notice pursuant to CEPA 1999 indicated that in 2006, between 100 and 1000 tonnes of methyl chloride were emitted to the atmosphere from a butyl rubber manufacturing facility and a small number of pulp and paper mills and cement plants. Data on the production and emission of methyl chloride in Canada are incomplete. The estimates of methyl chloride releases to the environment arising from combustion are presented for major industry sectors and the residential sector in Table 3. The estimates, with the exception of emissions arising from kraft pulping, which are based on process information together with solid wood waste consumption, are based on fuel consumption data that are publicly available and industrial emissions factors in US EPA (1995). Estimated emissions from chemical manufacturing in which methyl chloride is used are not included in Table 3 because there are insufficient data on which to base estimates.

Table 3. Estimated emissions of methyl chloride from combustion in Canada in 2006

Sector	**Estimated release of methyl chloride (kg)**
Pulp, paper and other forestry[1,2]	146 000
Coke and manufactured gases[1,3]	14 000
Coal-fired electrical utilities[1,3]	13 500
Other industrial coal combustion[1,3]	500
Mining, oil and gas[1,3]	<100
Residential heating[4]	47 700

[1] Statistics Canada (2008).
[2] 2009 email from Forestry, Agriculture and Aquaculture Division, Environment Canada, to Existing Substances Division, Health Canada; unreferenced.
[3] US EPA (1995): assumes by-product recovery for coke oven batteries and controlled coal combustion.
[4] 2009 email from Energy and Transportation Directorate, Environment Canada, to Existing Substances Division, Health Canada; unreferenced.

An estimate of the quantity of methyl chloride released from residential wood stoves and fireplaces in 2006 was based on the quantity of wood burned for residential space heating, which was about 7.5 million tonnes, and a database developed by Environment Canada of the types of wood-burning appliances and types of wood burned in Canada. This information, together with emission factors, resulted in an estimate of about 47.7 tonnes of methyl chloride emitted annually from residential space heating appliances (2009 email from Energy and Transportation Directorate, Environment Canada, to Existing Substances Division, Health Canada; unreferenced).

Using an estimate of the number of cigarettes smoked annually in Canada and experimental data on the quantity of methyl chloride released by smoking a cigarette, it was estimated that between 6.5 and 8.5 tonnes of methyl chloride are released annually by cigarette smoking in Canada (Häsänen et al. 1990; Novak et al. 2008; PSC 2008).

Environmental Fate

Based on its physical and chemical properties (Table 2), the results of Level III fugacity modelling (Table 4) suggest that methyl chloride will reside predominantly in air and/or water, depending on the compartment of release. The available information indicates that releases of methyl chloride in Canada are primarily to air (see Releases to the Environment section above).

Table 4. Results of the Level III fugacity modelling for methyl chloride (EQC 2003)

Substance released to:	Fraction of substance partitioning to each medium (%)			
	Air	Water	Soil	Sediment
Air (100%)	100	0	0	0
Water (100%)	19.8	80.1	0	0.1
Soil (100%)	98	0	2	0

Persistence and Bioaccumulation Potential

Environmental Persistence

Table 5a presents the empirical degradation data for methyl chloride. Based on consideration of releases and partitioning behaviour, air and water are the primary media of interest for this substance.

Substantial emissions of methyl chloride to the atmosphere occur from both natural and anthropogenic sources (see Sources and Releases to the Environment sections above), and the substance is considered to play an important role in the chlorine-catalysed destruction of stratospheric ozone (Saito and Yokouchi 2008). Upward diffusion and reaction with atmospheric hydroxyl radicals are the dominant loss mechanisms for methyl chloride in the lower atmosphere, although washout by rain may also contribute to overall losses (ATSDR 1998; HSDB 1983 –). Experimentally determined rate constants for the vapour-phase reaction of methyl chloride with photochemically produced hydroxyl radicals range from 4.36×10^{-14} cm^3/molecule per second (estimated half-life 245 days; Atkinson 1989) to 5.3×10^{-14} cm^3/molecule per second (estimated half-life 310 days; Brown et al. 1990). ATSDR (1998) reported atmospheric half-lives of 182.5–1095 days, with variability attributed to differences in the assumptions made on levels of hydroxyl free radical concentrations in the upper atmosphere. The estimated tropospheric half-life resulting from upward diffusion of methyl chloride is 80 days, whereas that of photodissociation of the substance in the upper atmosphere is 803 days (Robbins 1976).

Table 5a. Empirical data for degradation of methyl chloride

Medium	Fate process	Degradation value	Degradation endpoint, units	Reference
Air	Photodegradation	4.36×10^{-14}	Rate constant, cm^3/molecule per second	Atkinson 1989
		245	Half-life, days	
		5.3×10^{-14}	Rate constant, cm^3/molecule per second	Brown et al. 1990
		310	Half-life, days	
		182.5–1095	Half-life, days	ATSDR 1998
	Photodissociation	803	Half-life, days	Robbins 1976
Water	~~Volatilization~~	~~0.019 (25°C)~~	~~Half-life, days~~	~~Dilling 1977~~
	Hydrolysis	32 120 (0°C)	Half-life, days	Zafiriou 1975
		5110 (10°C)		Zafiriou 1975
		1679 (15°C)		Elliott and Rowland 1995
		~730; 912.5 (20°C)		Heppolette and Robertson 1959; Zafiriou 1975
		255.5–401.5; 339.45 (25°C)		Elliott and Rowland 1995; Mabey and Mill 1978
	Biodegradation	0–1[2]	Biodegradation, % in 28 days	MITI 1992
		19	Half-life, days	US EPA 1986

[1] Where more than one reference is given, the order of the references corresponds to the order of the values provided.

[2] Biodegradation was 1% at a test concentration of 3.79 mg/L and 0% at 19.2 mg/L.

Based on very high vapour pressure and high Henry's Law constant, methyl chloride will volatilize rapidly, and volatilization is therefore expected to be the most significant loss process for the substance in water. Dilling (1977) measured an average evaporation half-life of 0.019 day (27.6 minutes) from a dilute (approximately 1 mg/L) aqueous solution at 25°C and under still air (<0.32 km/hour) conditions, confirming that rapid volatilization of the substance occurs at the water surface. Hydrolysis and biodegradation may also occur, but at slower rates.

Hydrolysis half-lives of 256 days (25°C) to 32 120 days (0°C) have been estimated for methyl chloride based on measured rate constant data. These half-lives are too long to be of environmental significance in surface waters, considering the rapid volatilization of the substance from surface waters (Mabey and Mill 1978). However, hydrolysis may play a more significant role in groundwater, where volatilization does not occur and biodegradation rates are thought to be highly variable (ATSDR 1998).

Although only 1% or less ultimate biodegradation of methyl chloride was observed over 28 days in standard ready biodegradation testing (MITI 1992), biodegradation of the

substance has been reported under both aerobic and anaerobic conditions in laboratory testing with isolated bacterial strains (IPCS 2000). US EPA (1986) estimated a biodegradation half-life of approximately 19 days for methyl chloride in natural waters, based on an estimated microbial degradation rate constant for methyl chloride in natural aquatic medium of 3×10^{-9} mL/cell per hour (Jaber et al. 1984) and assuming the concentration of microorganisms in natural water that are capable of degrading methyl chloride to be 5×10^{5} cells/mL (Banerjee et al. 1984; Oduntan and Odeyemi 1984). Therefore, biodegradation is likely to be less significant than volatilization as a loss process for the substance in water.

Volatilization is likely to be the dominant loss process for methyl chloride in soil, particularly close to the surface. Based on the very low log K_{oc}, methyl chloride will not adsorb appreciably to organic materials, and it is therefore expected to be mobile in soil. Methyl chloride may leach downward in soil, possibly contacting groundwater, or diffuse upward to the surface, where volatilization will occur (ATSDR 1998). Although biodegradation of methyl chloride has been reported in isolated strains of bacteria and some fungi under both aerobic and anaerobic conditions in a laboratory setting, these laboratory conditions are unlikely to occur commonly in the environment, and therefore it is not known whether these same species will degrade methyl chloride in the environment. However, biodegradation cannot be ruled out based on the available information (ATSDR 1998).

Although experimental data on the degradation of methyl chloride are available, a quantitative structure–activity relationship (QSAR)-based weight of evidence approach (Environment Canada 2007) was also applied using the degradation models shown in Table 5b.

Table 5b. Modelled data for degradation of methyl chloride

Fate process	Model and model basis	Model output	Expected half-life (days)
Air			
Atmospheric oxidation	AOPWIN 2000	$t_{½}$ = 207 days	>2
Ozone reaction	AOPWIN 2000	n/a[1]	n/a
Water			
Hydrolysis	HYDROWIN 2000	$t_{½}$ = 8 197 900 days (pH 7) $t_{½}$ = 819 662 days (pH 8)	n/a
Biodegradation (aerobic)	BIOWIN 2000 Submodel 3: Expert survey (ultimate biodegradation)	2.9	≤182[2]
Biodegradation (aerobic)	BIOWIN 2000 Submodel 4: Expert survey (primary biodegradation)	3.7	≤182[2]
Biodegradation (aerobic)	BIOWIN 2000 Submodel 5: MITI linear probability	0.56	≤182[2]
Biodegradation (aerobic)	BIOWIN 2000 Submodel 6: MITI non-linear probability	0.61	≤182[2]
Biodegradation (aerobic)	TOPKAT 2004 Probability	0.0	>182[2]
Biodegradation (aerobic)	Mekenyan et al. 2005; CPOPs 2008 % BOD	10.0	>182[2]

Abbreviations: BOD, biological oxygen demand; MITI, Ministry of International Trade & Industry, Japan; n/a, not applicable; $t_{½}$, half-life.

[1] Model does not provide an estimate for this type of structure.

[2] Expected half-lives for BIOWIN, TOPKAT and CPOPs models are determined based on EPIsuite (2000-2008).

The model-estimated atmospheric half-life of 207 days (see Table 5b) is comparable to the empirical half-lives of 245 days and 310 days reported by Atkinson (1989) and Brown et al. (1990), respectively. AOPWIN (2000) predicts that methyl chloride will not react appreciably with other photo-oxidative species in the atmosphere, such as ozone; however, some degradation through direct photolysis is expected. With empirical and modelled atmospheric half-lives of much greater than 2 days, methyl chloride is considered to be persistent in air.

In water, the predicted hydrolysis half-life is much longer than 182 days (see Table 5b), indicating that this chemical is likely to be slowly hydrolysed. This concurs with empirical hydrolysis half-lives of up to 32 120 days reported in the literature, confirming that hydrolysis is unlikely to be a significant loss mechanism for methyl chloride in surface waters.

BIOWIN (2000) predicts that methyl chloride will biodegrade rapidly in water, with both primary and ultimate biodegradation occurring in the range of days to weeks. Although empirical biodegradation data are limited, a half-life estimate of 19 days for aerobic biodegradation is available in the published literature, and this value agrees well with the BIOWIN predictions. Aerobic biodegradation of the substance has been reported under laboratory conditions (IPCS 2000), although this testing was conducted using isolated bacterial strains, and therefore the results may not be directly comparable with actual conditions in the environment.

The two other biodegradation models, TOPKAT (2004) and CPOPs (2008), predict that methyl chloride will not undergo mineralization in a 28-day timeframe. TOPKAT (2004), which simulates the Japanese Ministry of International Trade & Industry (MITI) 28-day biodegradation test, predicts that there is a 0% probability of mineralization over the duration of the test period, whereas CPOPs (2008) predicts 10% biodegradation based on the Organisation for Economic Co-operation and Development (OECD) 301 ready biodegradation test (% biological oxygen demand). These model results are in agreement with empirical data that reported only 1% or less ultimate biodegradation over a 28-day test period (MITI 1992), suggesting that methyl chloride will not biodegrade readily (Aronson et al. 2006).

The empirical and modelled data are conflicting, indicating that methyl chloride is susceptible to microbial degradation, but is likely not "readily biodegradable" (OECD 2003). Based on the weight of available evidence, and applying precaution in light of uncertainty regarding the time required for complete mineralization in the environment, it is concluded that methyl chloride's biodegradation half-life may be >182 days in water; therefore, the substance is considered to be persistent in water.

Using an extrapolation ratio of 1:1:4 for a water:soil:sediment biodegradation half-life (Boethling et al. 1995), the half-life in soil is also >182 days, and the half-life in sediments is >365 days. This indicates that methyl chloride is persistent in soil and sediment.

Based on empirical and modelled data (see Tables 5a and 5b), methyl chloride meets the persistence criteria in air, water, soil and sediment (half-life in air ≥2 days, half-lives in soil and water ≥182 days and half-life in sediment ≥365 days), as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential for Bioaccumulation

Experimental and modelled log K_{ow} values for methyl chloride suggest that this chemical has low potential to bioaccumulate (see Table 2 above).

Table 6. Modelled data for bioaccumulation of methyl chloride

Test organism	Endpoint	Value (L/kg wet weight)	Reference
Fish	BAF	1.62	Arnot and Gobas 2003 (Gobas

	BCF	1.62	BAF/BCF Middle Trophic Level)
		15.8	Dimitrov et al. 2005; CPOPs 2008
		3.162	BCFWIN 2000

Abbreviations: BAF, bioaccumulation factor; BCF, bioconcentration factor.

Based on the available modelled bioaccumulation data (Table 6), methyl chloride does not meet the bioaccumulation criteria (bioaccumulation factor [BAF] or bioconcentration factor [BCF] ≥ 5000) as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

Potential to Cause Ecological Harm

Ecological Effects Assessment

Aquatic Compartment

Limited empirical toxicity data are available for methyl chloride.

Acute 96-hour median lethal concentration (LC_{50}) values of 270 and 550 mg/L were reported for tidewater silverside (*Menidia beryllina*) and bluegill sunfish (*Lepomis macrochirus*), respectively (Dawson et al. 1975/77), whereas Springborn Smithers Laboratories (2002) measured 48-hour no-observed-effect concentration (NOEC) and median effective concentration (EC_{50}) values for *Daphnia magna* of 53 and 200 mg/L, respectively (Table 7a). Actual test concentrations could not be verified for either study, and it is therefore possible that the reported toxicity endpoint values underestimate the toxicity of methyl chloride, as the high volatility of the substance suggests that some portion of the original test concentration may have been lost through evaporation over the study duration in these static or static renewal toxicity tests. If this occurred, concentrations eliciting the observed effects would be lower than nominal values and therefore would under-represent the actual toxicity of the substance.

Table 7a. Empirical data for aquatic toxicity

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fish	Acute (96 h)	LC_{50}	270	Dawson et al. 1975/77
			550	
Daphnia	Acute (48 h)	EC_{50}	200	Springborn Smithers Laboratories 2002
		NOEC	53	

Abbreviations: EC_{50}, the concentration of a substance that is estimated to cause some toxic sublethal effect on 50% of the test organisms; LC_{50}, the concentration of a substance that is estimated to be lethal to 50% of the test organisms; NOEC, the highest concentration in a toxicity test not causing a statistically significant effect in comparison with the controls.

Table 7b contains predicted ecotoxicity values that were considered reliable and were used in the QSAR weight of evidence approach for aquatic toxicity (Environment Canada 2007).

Table 7b. Modelled data for aquatic toxicity

Test organism	Type of test	Endpoint	Value (mg/L)	References
Fish	Acute (96 h)	LC_{50}	248, 369	ECOSAR 2004
			259	Dimitrov et al. 2005; CPOPs 2008
			17.8[1]	AIES 2003–2005
			375	ASTER 1999
			475	TOPKAT 2004
	Chronic (14 days)	LC_{50}	247	ECOSAR 2004
Daphnia	Acute (48 h)	LC_{50}	122	ECOSAR 2004
		EC_{50}	57	TOPKAT 2004
	Chronic (16 days)	EC_{50}	12.5	ECOSAR 2004
Mysid	Acute (96 h)	LC_{50}	474	ECOSAR 2004
Alga	Acute (96 h)	EC_{50}	39	ECOSAR 2004

Abbreviations: EC_{50}, the concentration of a substance that is estimated to cause some toxic sublethal effect on 50% of the test organisms; LC_{50}, the concentration of a substance that is estimated to be lethal to 50% of the test organisms.

[1] Categorization pivotal iT value.

Although a range of aquatic toxicity predictions was obtained from the various QSAR models, many model estimates exceed 200 mg/L and are in good agreement with the empirical data. The empirical and modelled data indicate that methyl chloride exerts only moderate to low toxicity. It is therefore not highly hazardous to aquatic organisms (i.e., acute LC_{50}/EC_{50} values for methyl chloride are >1.0 mg/L and/or chronic values are > 0.1 mg/L).

Other Environmental Compartments

Very little information is available on the effects of methyl chloride on non-aquatic organisms. Christ (1996) reported effect levels of greater than 5000 mg/m^3 (2400 parts per million [ppm]) for photosynthesis and transpiration in seven species of terrestrial plants exposed for 3 hours to methyl chloride gas and visible symptoms in the concentration range of 5000–10 000 mg/m^3 (2400–4800 ppm). Few details are available for the study, including the nature of the observed visible symptoms. The seven species tested were tomato (*Lycopersicum esculentum* Miller), sunflower (*Helianthus annuus* L.), bush bean (*Phaseolus vulgaris* L.), nasturtium (*Tropaeolum majus* L.), sugar beet (*Beta vulgaris* L.), soybean (*Glycine maxima* (L.) Merill) and wheat (*Triticum aestivum* L.).

In addition, laboratory studies using rodents and other mammals have been conducted in order to evaluate the potential for impacts on human health, and relevant data from these studies are considered here in the context of terrestrial wildlife species. The results indicate that chronic inhalation exposure to methyl chloride may be associated with neurotoxicity, reproductive and developmental effects, and possible carcinogenicity in mammals (see Health Effects Assessment section). The study endpoint value considered most relevant to potential impacts in terrestrial wildlife is a lowest-observed-effect concentration (LOEC) of 103 mg/m^3 (50 ppm) reported for evidence of neurotoxic effects

(i.e., nerve axonal swelling and degeneration) in male and female mice exposed to gas-phase methyl chloride for 6 hours/day for up to 22 months (CIIT 1981).

Ecological Exposure Assessment

Methyl chloride is a gas under most environmental conditions, and most environmental monitoring has been conducted for the air compartment. Low levels have also occasionally been detected in other environmental media, including water, soil and biota. As the substance is produced naturally (see Sources section), it is expected that low background levels will always be present in the environment. Because of this, it may sometimes be difficult to determine the relative contribution and sources of anthropogenically produced methyl chloride present in a medium.

A selection of measured concentrations relevant to the Canadian environment is presented in Table 8. No recent Canadian monitoring data for media other than air were found in the published literature.

Table 8. Concentrations of methyl chloride in the environment

Medium	Location; year	Number of samples	Concentration (mg/L)[1]	Reference
Air	Canada; 2006–2007	6098	0.7–8.54 (mean 1.12; maximum 8.54) µg/m^3	NAPS 2008
Fresh water	Canada; 1979	30	0.005 (maximum)	Otson et al. 1982
	Niagara River and Lake Ontario; year not provided	NS	Detected[2]	Great Lakes Water Quality Board 1982
	Ontario, Great Lakes; 1982–1983	42	<0.0001	Otson 1987
	New Jersey, USA; year not provided	24/605[3]	0.222 (maximum)	Page 1981
	New Jersey, USA; 1979–1980	50	Not detected[4]	Granstrom et al. 1984
	USA; 1980–1982	895	<10 (median; 1.4% detectable)	Staples et al. 1985
Seawater	Eastern Pacific Ocean; year not provided	NS	0.000 011 5 (average)	Singh et al. 1983

Medium	Location; year	Number of samples	Concentration (mg/L)[1]	Reference
Groundwater	New Jersey, USA; year not provided	3/1058[3]	0.006 (maximum)	Page 1981
	Massachusetts, USA; year not provided	NS	0.044	Burmaster 1982
	New Jersey, USA; year not provided	<10/408[3]	Detected[2]	Greenburg et al. 1982
	Across USA; 1985–2001	3500	0.000035 (median) 0.021(maximum)	Zogorski et al. 2006
Effluent	USA; 1980–1982	1298	<10 (median; 3.5% detectable)	Staples et al. 1985
Effluent:	USA; year not provided	NS	(median)	Shackelford et al. 1983
Non-ferrous metals		1	0.0216	
Paint and ink		2	4.129, 4.194	
Printing and publishing		1	0.006	
Organics and plastics		1	0.1567	
Pharmaceuticals		1	2.5583	
Organic chemicals		3	0.049	
Raw wastewater:	USA; year not provided			US EPA 1981
Metal finishing		78/149[3]	0.600 (mean) 4.70 (maximum)	
Ore mining, dressing		1/33[3]	0.045	
Organic chemicals; resins; plastics		3	0.000 01 (mean)	
Treated wastewater:				
Organic chemicals; resins; plastics		3	0.000 01 (mean)	
Photographic supplies and equipment		6/20[3]	0.001–0.960 0.480 (mean)	
Textile mills		1/64[3]	0.020	
Municipal landfill leachate	Wisconsin, USA; year not provided	1/5[3]	0.170	Sabel and Clark 1984
	Minnesota, USA; year not provided	4/6[3]	Detected[2]	
Sediment	USA; 1980–1982	345	<0.005 mg/kg dry weight (median; 0.3% detectable)	Staples et al. 1985
Biota[5]	USA; 1980–1982	84	<0.050 mg/kg wet	Staples et al.

Medium	Location; year	Number of samples	Concentration (mg/L)[1]	Reference
			weight (median; 1% detectable)	1985

Abbreviation: NS, not specified.
[1] Units are in mg/L unless otherwise stated.
[2] Qualitative assessment only.
[3] Number of samples in which substance was detected and total number of samples; e.g., 24/605 = detected in 24 out of 605 samples.
[4] Detection limit not specified.
[5] Species not specified.

Methyl chloride is included on a list of substances that are routinely measured as part of Environment Canada's National Air Pollution Surveillance (NAPS) program, a program that monitors air quality and the levels of certain substances at monitoring stations located across Canada. Based on the most recent NAPS data for the period January 2006–December 2007, concentrations of methyl chloride at 57 monitoring stations across Canada (42 urban and semi-urban stations and 15 rural stations) had an overall range of 0.7–8.54 μg/m^3, with a mean value of 1.13 μg/m^3. Average air concentrations were relatively constant across the country, with means ranging from 1.05 to 1.98 μg/m^3. The highest levels were reported at a sampling station in Sarnia, Ontario, where the maximum concentration of 8.54 μg/m^3 was recorded; the mean concentration for this station over the 2006–2007 sampling period was much lower, however, at 1.98 μg/m^3 (NAPS 2008).

Results from older (1980s) studies indicate that surface water concentrations of methyl chloride are low, most commonly below analytical detection limits. The presence of the substance in groundwater samples confirms that methyl chloride is mobile within the soil compartment. Methyl chloride has been detected in a variety of industrial effluents and wastewaters, as well as in landfill leachate. The highest concentrations, up to 4 mg/L, have been associated with effluent from the paint and ink and metal finishing industrial sectors.

Staples et al. (1985) provided an extensive review of data contained within the US Environmental Protection Agency's (EPA) STORET database (US EPA 1982), a data storage system for priority pollutant concentrations in US waterways. Over the period 1980–1982, methyl chloride was detected in 0.3% and 1% of sediment and biota samples, respectively. Median concentrations were <0.005 mg/kg dry weight for sediment samples recorded in the database and <0.050 mg/kg wet weight for biota samples. Maximum concentrations for each sample type were not provided in the review paper.

Characterization of Ecological Risk

As indicated previously, methyl chloride meets the *Persistence and Bioaccumulation Regulations* (Canada 2000) criteria for persistence in air, water, sediment and soil. Methyl chloride does not however meet the bioaccumulation criteria as specified in the *Persistence and Bioaccumulation Regulations*.

Methyl chloride is considered to play a role in the chlorine-catalysed destruction of stratospheric ozone. The Montreal Protocol on Substances that Deplete the Ozone Layer (UNEP 2000) is an international treaty administered by the Ozone Secretariat of the United Nations Environment Programme, to which Canada is an adherent. Measures for the comprehensive management of ozone-depleting substances are in place in Canada.

The available toxicity data indicate that methyl chloride is not highly hazardous to aquatic organisms. As well, environmental monitoring data for surface waters and groundwater indicate that concentrations in these media are well below levels found to elicit effects in aquatic species (Tables 7a, 7b and 8). Similarly, the highest measured air concentrations in Canada (up to 8.54µg/m^3) are much lower than the lowest effect values of 103 mg/m^3 reported to cause adverse effects in laboratory studies with rodents and higher plants. Based on this information, it is considered unlikely that methyl chloride is causing harm to aquatic or terrestrial organisms.

Some uncertainties were identified in the characterization of potential ecological risk. There are uncertainties associated with the use of QSAR models to estimate the properties of persistence, and to a lesser extent of bioaccumulation and aquatic toxicity. However, overall, the model-predicted values are comparable with empirical data and so provide additional support for the final conclusions. Additional and more recent Canadian environmental monitoring data would be useful in providing a more definitive measure of the exposure potential, particularly in surface waters; however, when considered together with the physical and chemical properties of the substance (for which there is generally sufficient and reliable empirical information), the available data were considered sufficient.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Diet

Because of the physical-chemical properties of methyl chloride and the fact that nearly all releases of methyl chloride are to the atmosphere, inhalation is expected to be the dominant route of human exposure. Methyl chloride is ubiquitous in ambient and indoor air.

There are extensive databases of measured concentrations of methyl chloride in air both in Canada and elsewhere (OECD 2003; NAPS 2008). The global background concentration of methyl chloride, thought to arise from natural sources alone, was established in a series of measurements at non-industrial sites in both hemispheres over a period of 16 years. The mean was found to be 600 parts per trillion by volume (pptv), or 1.2 µg/m^3. The range for marine environments was 570–620 pptv. For terrestrial environments, the range was 550–950 pptv (Khalil and Rasmussen 1999). The concentration of methyl chloride is reported in the NAPS database from the 57

monitoring stations across Canada that measure volatile organic compounds. In Canada, during the period of January 2006 to December 2007, the average concentration of methyl chloride measured during 24-hour periods at 42 NAPS urban and semi-urban monitoring stations was 1.13 µg/m^3. The average concentration of methyl chloride measured during 4-hour periods at 15 NAPS rural monitoring stations was 1.10 µg/m^3 (NAPS 2008). The highest concentration of methyl chloride measured over a 24-hour period during 2006–2007 recorded in NAPS was at Sarnia, Ontario: 8.54 µg/m^3. Analysis of an air sample collected in 3 minutes by two members of the Aamjiwnaang First Nation in January 2008 in Sarnia showed a short-term concentration of methyl chloride of 130 µg/m^3 (Global Community Monitor 2008).

Two reports on the concentrations in air of volatile organic compounds, including methyl chloride, in Windsor, Ontario, and Regina, Saskatchewan, were recently completed by Health Canada in partnership with the University of Windsor and the Regina Qu'Appelle Regional Health Authority, respectively (Health Canada 2008a, 2008b). Air samples were taken during both winter and summer in homes and outside. A number of 24-hour personal samples were taken in Windsor by individuals wearing a sampling apparatus. The range of concentrations of methyl chloride measured during the summer in these studies is shown in Table 9.

Table 9. Concentration of methyl chloride in air in summer in Windsor, Ontario, in 2005–2006 and in Regina, Saskatchewan, in 2007

Type of sample	Concentration of methyl chloride (µg/m^3)		
	Minimum	Maximum	Mean
Windsor			
Personal backpack 24 hour	1.110	6.580	1.588
Indoor static 24 hour	0.002	3.380	1.516
Outdoor static 24 hour	0.746	1.985	1.360
Regina			
Indoor static 24 hour home of smokers	1.317	16.200	4.522
Indoor static 24 hour home of non-smokers	0.945	3.075	1.268
Outdoor static 24 hour	0.834	1.371	1.009

The mean concentrations of methyl chloride in air sampled by static probes taken indoors and outdoors are within the range established by Khalil and Rasmussen (1999) for the concentration of methyl chloride in terrestrial environments not near a known point source. The maximum concentration of methyl chloride measured in outdoor air in the two studies (1.985 µg/m^3 = 960 pptv) is at the upper end of that range.

The data from Regina show clearly that cigarette smoking in indoor spaces results in an increased concentration of methyl chloride in air when compared with the concentration of methyl chloride in the homes of non-smokers and in outdoor air. The elevated concentrations of methyl chloride inside the homes of some non-smokers when compared with the concentrations outside the homes indicate the presence of residential sources of methyl chloride unrelated to tobacco smoke.

A study of personal exposure to volatile organic compounds in Toronto was undertaken by the Ontario Ministry of the Environment. Measurements were taken in indoor and outdoor environments and for short periods during specific tasks. The highest measured concentration of methyl chloride was 18.9 µg/m^3, sampled over 2 hours at a barbecue, indicating that combustion probably contributed to the elevated concentration. The next highest was 17.7 µg/m^3, measured over 16 hours at a residence and in an automobile through two rush-hour commuting periods (Bell et al. 1991), comparable with the result from a static 24-hour sample in the home of a smoker in Regina (see Table 9). There is no information about cigarette smoking for the Toronto samples. A study designed to examine correlations of the occurrence of several volatile organic compounds with location or activity found no correlation of the occurrence of methyl chloride with vehicular traffic (Hinwood et al. 2006).

Methyl chloride has been detected in both surface water and drinking water at potable water treatment facilities in Canada and elsewhere (OECD 2003). It was not detected in 42 samples of water taken from Lake Ontario, the source of drinking water for Toronto, and was also not detected in 42 samples of treated water (Otson 1987). In 30 samples of drinking water from Canadian water treatment plants, methyl chloride was detected in 2 samples, with a maximum concentration of 5 µg/L (Otson et al. 1982). In current testing programs for organic chemicals in municipal drinking water in Canada, methyl chloride is an infrequent analyte. Reports for only two municipalities that analyse untreated or finished drinking water for methyl chloride were located; in both cases, methyl chloride was not detected (City of Victoria 2005; Ville de Montréal 2005).

A synthesis of several studies of groundwater contamination during the period 1985–2001 by the US Geological Survey was reported by Zogorski et al. (2006). The highest concentration of methyl chloride reported in thousands of water samples analysed for that study was 21 µg/L from one aquifer. All other test results, including those from public and domestic drinking water wells, showed that the concentration of methyl chloride was below 2 µg/L. The authors proposed that chloroform was a source of both methylene chloride and methyl chloride, formed in a process of biodegradation underground in anoxic conditions. Chloroform is frequently present in municipally supplied treated water. There are also microbial sources of methyl chloride, which may contribute to its presence in aquifers.

Chlorination of water is frequently cited as a source of methyl chloride in air, but experimental evidence to support this assertion under conditions where oxygen is present was not located. Hinwood et al. (2006) reported the concentrations of volatile organic chemicals in the air above a swimming pool. Chloroform was detected, but methyl chloride was not detected in the same samples. The World Health Organization does not publish a standard for the concentration of methyl chloride in drinking water, but does publish a standard for trihalomethanes, drinking water disinfection by-products that are well characterized (WHO 2006).

Methyl chloride has no approved food additive use in Canada. However, it is used as an intermediate in the manufacture of methylene chloride, a food additive approved for use

as an extraction solvent (Canada 1978a) and it is possible that methylene chloride could contain residues of methyl chloride. Methyl chloride is also used as an intermediate in the manufacture of the food additives methyl cellulose and hydroxypropyl methylcellulose (Canada 1978b). No or negligible residues of methyl chloride in foods are expected from use of these additives in food and beverages (Foods Directorate, Health Canada, unreferenced). Residuals of methyl chloride may be present in selected rubber formulations used in food packaging materials. Residual methyl chloride may be available for possible migration into food. Exposure was derived from in-house available data and a probable daily intake was estimated at 0.013 µg/kg-bw/day for adults (January 2009 email, Foods Directorate, Health Canada, unreferenced).

Upper-bounding estimates of daily exposure to methyl chloride for various age groups are shown in Appendix 1. These estimates range from 3.51 µg/kg-bw per day for adults 60 years of age and over to 10.10 µg/kg-bw per day for children aged 6 months to 4 years. The assumptions on which these estimates are based are listed in footnotes to the table in Appendix 1.

Confidence in the upper-bounding estimate of exposure to methyl chloride through environmental media and diet is moderate to high. There are adequate Canadian data on the concentration of methyl chloride in indoor and ambient air, and estimated exposure to the substance for all age groups is dominated by inhalation. It is probable that the choice of 21 µg/L for use as the concentration of methyl chloride in drinking water overestimates exposure from this route, but no Canadian data on water supplies other than municipally treated water were located, so use of US groundwater data is reasonable. Confidence is high that dietary exposure is negligible for all age groups.

Consumer Products

Methyl chloride is not intentionally used in the formulation of consumer products, although it may be present as a residual in other chlorinated solvents or in chemicals synthesized with methyl chloride.

It was recently reported that methyl chloride was detected in a liquid fabric softener at an unspecified concentration (Steinemann 2009). It is probable that the source of the methyl chloride was the quaternary ammonium chloride used in the fabric softener. Some industrial quaternary ammonium chloride compounds contain up to 0.03% methyl chloride (Environment Canada 2008). Liquid fabric softeners typically contain 3–7% of a cationic surfactant; therefore, a fabric softener may contain up to 20 ppm (mg/L) of methyl chloride (AISE 1996). Uncertainties regarding release and partitioning of methyl chloride in fabric softener during laundering are considered too great to permit meaningful modelling of exposure. The small amount of methyl chloride that may be released from laundering into residential settings will be accounted for in the estimate of exposure via indoor air.

Dimethyl dialkyl ammonium chlorides made with methyl chloride are used in a small proportion of all-purpose cleaners. Benzalkonium chlorides are typically used in all-

purpose cleaners. The potential exposure by inhalation arising from the use of liquid and spray cleaners containing 0.3% dimethyl dialkyl ammonium chloride in which residual methyl chloride is present was estimated using consumer exposure modelling software (ConsExpo 2006). Use of liquid cleaner was estimated to result in an additional inhalation exposure to methyl chloride of 0.014 µg/kg-bw per day for an adult woman. Use of spray cleaner was estimated to result in an additional inhalation exposure to methyl chloride of 0.010 µg/kg-bw per day for an adult woman.

The potential exposure by inhalation arising from the use of personal care products made with quaternary ammonium chlorides in which residual methyl chloride is present was estimated using consumer exposure modelling software (ConsExpo 2006). Use of body lotion containing 0.1% quaternary ammonium chloride was estimated to result in an additional inhalation exposure to methyl chloride of 0.001 µg/kg-bw per day for an adult woman. Use of rinse-off hair conditioner containing 3% quaternary ammonium chloride was estimated to entail an additional inhalation exposure to methyl chloride of 0.004 µg/kg-bw per day for an adult woman. These values should be compared with the estimated daily exposure to methyl chloride of 0.30 µg/kg-bw per day estimated for exposure to air not contaminated by a known source, in which the mean concentration of methyl chloride is 1.3 µg/m^3.

Methyl chloride may also be present in methylcellulose ethers and derivatives, such as hydroxypropyl methylcellulose and hydroxybutyl methylcellulose, which are commonly used in consumer products, personal care products and pharmaceuticals. It is expected that the concentration of methyl chloride in these products will be in the parts per billion range.

Cigarettes are the consumer product that is likely to result in the highest exposure to methyl chloride, but an estimate of exposure arising from smoking tobacco is not presented here. Data from recent air quality studies by Health Canada, the University of Windsor and the Regina Qu'Appelle Regional Health Authority presented above show that cigarette smoking contributes to an elevated concentration of methyl chloride in indoor air.

Confidence in the numerical results of estimates of exposure arising from consumer products is moderate to low in the absence of experimental data, but confidence is high that consumer products, with the exception of tobacco, do not contribute significantly to exposure to methyl chloride.

Health Effects Assessment

An overview of the toxicological database for methyl chloride is presented in Appendix 2.

Methyl chloride is considered to be a Category 3 substance ("causes concern for humans owing to possible carcinogenic effects") with the risk phrase R40 ("limited evidence for a carcinogenic effect") by the European Commission; and is "not classifiable as to its

carcinogenicity to humans" by the International Agency for Research on Cancer (IARC) (Group 3) and the US EPA (Group D) (IARC 1986, 1999; US EPA 2001; ESIS 2008).

The only data available on the carcinogenicity of methyl chloride in experimental animals are from an unpublished 2-year inhalation bioassay in mice and rats (CIIT 1981). No exposure-related tumours were observed in female mice or in rats of either sex exposed to up to 2064 mg/m^3; however, male mice had an increased incidence of renal tumours. There was a significant increase in the number of renal cortical adenomas and renal cortical adenocarcinomas in the high-concentration group (2064 mg/m^3), as well as a non-significant increase in cortical adenomas in the middle-concentration group (464 mg/m^3). A dose–response relationship could not be determined. There was also a statistically significant increase in the development of renal tubuloepithelial hyperplasia, hypertrophy and/or karyomegaly in the high-concentration males beginning at 12 months and increasing in severity throughout the study. IARC (1986, 1999) reported only on a published abstract based on this study (Pavkov et al. 1982) and concluded that "the incomplete reporting precluded evaluation of the findings." Although the US EPA (2001) evaluated the complete study, their conclusion was also that the animal data were inadequate for assessing carcinogenicity. The mode of induction of renal tumours in male mice has not been fully elucidated. However, the presence of hyperplastic lesions could indicate that tumour induction is a progression from regenerative proliferation following chronic high-concentration exposure, rather than initiation by a direct genotoxic event.

In humans, no association has been found between exposure to methyl chloride and cancer of any type. Several cohort studies looking at causes of death in relation to occupational exposure to methyl chloride found no excess mortality from any specific cause of death, including cancers (Ott et al. 1985; Holmes et al. 1986; Olsen et al. 1989; Dow Chemical 1992). IARC (1999), US EPA (2001) and IPCS (2000) concluded that due to small numbers of cases, mixed exposures and a lack of quantitative exposure levels, the available studies are insufficient for assessing cancer risk.

In *in vitro* genotoxicity assays, methyl chloride was mutagenic in bacterial cells, and induced mutations, unscheduled DNA (deoxyribonucleic acid) synthesis (UDS), sister chromatid exchanges and structural chromosome aberrations in mammalian cells. *In vivo*, inhalation exposure to methyl chloride at 2064 mg/m^3 for 1–4 days induced DNA damage (single-strand breaks and DNA–protein cross-links [DPC]) in male mouse kidney. The damage appeared to be rapidly repaired, as none was detected when animals were sacrificed after a longer recovery period (up to 48 hours) post-exposure. Strand breaks and DPC were not detected in female mouse kidney or in male or female mouse liver. Methyl chloride does not appear to methylate rat or mouse DNA and did not induce UDS in rat spermatocytes, tracheal epithelial cells or hepatocytes at exposure concentrations of up to 7210 mg/m^3 for up to 9 days. Methyl chloride was weakly positive for UDS in rat hepatocytes in one study with an exposure concentration of 30 900 mg/m^3 for 3 hours and induced sex-linked recessive mutations in *Drosophila melanogaster* at 412 000 mg/m^3 (1- to 2-hour exposure). Positive results were obtained in dominant lethal assays in rats at exposure concentrations of 2064 mg/m^3 and above; however, several studies have indicated that the pre- and post-implantation losses observed may be due to cytotoxicity

to sperm and mutations caused indirectly by epididymal inflammation, rather than a direct genotoxic effect. Thus, methyl chloride is genotoxic in *in vitro* systems in both bacteria and mammalian cells and could be considered a weak mutagen *in vivo* based on some evidence of DNA–protein cross-linking, but it seems unlikely that methyl chloride toxicity results from direct genotoxic activity (see Appendix 2 for details and references).

The central nervous system (CNS) is the primary target for non-neoplastic methyl chloride toxicity in both humans and experimental animals. In humans, symptoms described in case reports on accidental exposure to methyl chloride include dizziness, weakness, blurred vision, confusion, slurred speech, convulsions and tremors. Clinical signs of neurotoxicity were observed at exposure concentrations of 412 mg/m^3 and above, for durations of 1 hour to several days (ATSDR 1998; IPCS 2000; US EPA 2001). Under controlled exposure conditions, a small but "marginally significant" impairment of performance on behavioural tests was observed following exposure of volunteers to 412 but not 206 mg/m^3 for 3 hours (Putz-Anderson et al. 1981). One study of neurological effects in humans after chronic occupational exposure to methyl chloride found "subtle differences in finger tremors and time-sharing tasks" in the exposed group (mean exposure concentration of 70 mg/m^3). Although this was the lowest effect concentration in any of the human and laboratory animal studies, it was excluded from use as the critical study for this assessment based on several limitations (possible exposure to multiple substances, potential prior exposure to high methyl chloride concentrations and significant differences in the ages of exposed and control groups) (Repko et al. 1976). In humans, effects in other organs, including kidney and liver, appear to be secondary to CNS effects following methyl chloride exposure (ATSDR 1998; IPCS 2000; US EPA 2001).

The critical lowest-observed-effect concentration (LOEC) for inhalation exposure is 103 mg/m^3, based on axonal swelling and degeneration in the spinal nerves of male and female mice exposed to methyl chloride for 6 hours/day for up to 22 months (CIIT 1981). The effects were increased in each exposure group relative to controls (103, 464 and 2064 mg/m^3), and the severity and extent of the neurotoxic effects increased with increasing exposure concentration and duration. This was the critical effect and lowest-observed-adverse-effect concentration (LOAEC) used by IPCS (2000) and ATSDR (1998) for determining a guidance value and a chronic inhalation minimal risk level (MRL), respectively. However, for derivation of a reference concentration (RfC), the US EPA (2001) selected a no-observed-adverse-effect concentration (NOAEC) of 103 mg/m^3 based on a study by Landry et al. (1985) in which cerebellar lesions were observed in all mice exposed to methyl chloride continuously (22.5 hours/day) for 11 days at concentrations of 206 mg/m^3 and above.

In rats, the male reproductive system is also a target of methyl chloride toxicity. In a two-generation reproductive toxicity study (Hamm et al. 1985), male rats exposed by inhalation to 979 mg/m^3 and above were less fertile than controls. Based on this study, the Health Council of the Netherlands Committee for Compounds Toxic to Reproduction recommends classifying methyl chloride as a Category 2 substance ("should be regarded as if it impairs fertility") (HCN 2004). Additionally, effects on male rat reproductive

organs were observed in studies ranging in duration from 2 days to 2 years at concentrations of 1030 mg/m^3 and above (see Appendix 2 for details and references).

In two developmental toxicity studies in mice, increased fetal heart defects (reduction or absence of atrioventricular valves, chordae tendineae and papillary muscles) were observed, in the absence of maternal toxicity, when pregnant dams were exposed to methyl chloride at 1030 mg/m^3 or above on gestation days 6–18. There was no evidence of teratogenicity in F344 rats exposed to up to 3090 mg/m^3 on gestation days 7–19 (Wolkowski-Tyl et al. 1983a, 1983b).

The confidence in the toxicity database is moderate, as data for acute toxicity, repeated-dose toxicity, carcinogenicity, genetic toxicity and reproductive and developmental toxicity in experimental animals are available, although limited; and studies in humans include case reports of accidental exposures to high levels of methyl chloride, multiple exposures in occupational settings, and short-term low-level exposures in a controlled environment. As CNS toxicity is a critical endpoint in both humans and experimental animals, and there is some evidence that methyl chloride induces fetal toxicity in rodents (heart defects in mice at exposure concentrations of 1030 mg/m^3 and above during gestation), a developmental neurotoxicity study at or below the LOEC for neurological effects (103 mg/m^3) would be a valuable addition to the database.

Characterization of Risk to Human Health

IARC and the US EPA concluded that the available human and experimental animal data are inadequate to determine the carcinogenicity of methyl chloride in humans. However, based on the European Commission classification, a critical effect for characterization of risk to human health is carcinogenicity.

In the only available chronic inhalation study (CIIT 1981), tumours in male mouse kidney were significantly increased at the highest exposure concentration. Hyperplastic lesions were also significant only in high-concentration animals and became more severe from 12 to 24 months. No histopathological evidence of kidney lesions was observed in mice or rats in an unpublished 90-day study (CIIT 1979) at concentrations up to 3096 mg/m^3, although degeneration and necrosis along with regenerative proliferation were noted in several short-term studies at concentrations of 2064 mg/m^3 and up (Morgan et al. 1982; Landry et al. 1985). Epithelial proliferation and increased basophilia (regeneration) in mouse kidney were also described in the chronic study for all exposure groups (CIIT 1981). This evidence suggests that enhanced cell proliferation due to regeneration may progress into tumours under conditions of chronic high-level exposure to methyl chloride.

Tumours in male mouse kidney may not be relevant to humans due to species differences in metabolism of methyl chloride. In humans and rodents, methyl chloride is metabolized primarily by conjugation with glutathione via the enzyme glutathione transferase (GSTT1-1) and, alternatively, via a minor oxidative pathway mediated by the cytochrome P450 isozyme 2E1 (CYP2E1). In the male mouse kidney, high levels of CYP2E1 may result in elevated concentrations of the metabolite formaldehyde following methyl chloride exposure. CYP2E1 protein levels are lower in kidney from female mouse and

rats of both sexes than in male mouse kidney (Dekant et al. 1995; Speerschneider and Dekant 1995). CYP2E1 protein was not detected in human kidney (Amet et al. 1997; Cummings et al. 2000; Lash et al. 2008). Thus, the potential for the generation of this genotoxic metabolite is much greater in the kidney of male mice than in humans.

Methyl chloride is genotoxic in *in vitro* systems in both bacteria and mammalian cells and could be considered a weak mutagen *in vivo* based on some evidence of DNA–protein cross-linking and sex-linked recessive and dominant lethal mutations. However, positive results in *in vivo* genotoxicity studies were obtained only following exposure to high concentrations of methyl chloride (2064 mg/m^3 and above). In addition, DNA damage *in vivo* appears to be reversible, and several studies have indicated that the pre- and post-implantation losses observed in the rat dominant lethal assay occurred via non-genotoxic pathways. Thus, although a thorough mode of action analysis is beyond the scope of this screening assessment, it is unlikely that tumours observed in male mouse kidney following exposure to methyl chloride result from direct genotoxic activity.

The concentration of methyl chloride required to induce hyperplastic lesions and tumours in the male mouse kidney (2064 mg/m^3) is 20-fold higher than the concentration that caused neurotoxicity in mice; similarly, effects in other organs (i.e., male reproductive, liver) occurred in rodents at exposure levels 2–10 times greater than the critical effect level. Therefore, a margin of exposure (MOE) based on neurotoxicity would be protective of these other effects.

Comparison of the critical effect concentration in experimental animals (i.e., 103 mg/m^3) with the upper-bounding estimate of general population exposure via inhalation—the expected principal route of exposure—results in an MOE of approximately 6760. This is based on a time-weighted average (TWA) of indoor air and ambient air concentrations[1]. An MOE based on total daily intake for the most highly exposed age group (6 months to 4 years old; 10.10 µg/kg-bw per day), using the same critical effect concentration of 103 mg/m^3, a breathing rate of 0.04 m^3/day and a body weight of 0.03 kg for mice (Health Canada 1994), and converted from intermittent exposure (6 hours/day, 5 days/week) to continuous exposure[2], would be 2430. For other age groups, the MOE based on total daily intake ranges from 3110 to 6990.

Uncertainties in Evaluation of Risk to Human Health

The mechanism of tumour induction has not been fully elucidated, and the relevance of male mouse kidney tumour formation to human carcinogenicity is unknown. This screening assessment does not take into account potential variability within the Canadian population, nor does it consider differences between humans and experimental animals in

[1] The TWA air concentration was calculated as follows: [(16.2 µg/m^3 × 21 hours/day) + (8.54 µg/m^3 × 3 hours/day)] / 24 hours/day = 15.24 µg/m^3.

[2] The MOE for children aged 6 months to 4 years was calculated as follows: [(103 mg/m^3 × 0.04 m^3/day / 0.03 kg-bw) × (5/7 days/week) × (6/24 hours/day)] / 10.10 × 10^{-3} mg/kg-bw per day = 2430.

terms of sensitivity to the potential effects of methyl chloride. However, the primary target organ for non-neoplastic effects is the same in humans and experimental animals. The lowest exposure concentration at which effects are induced in humans has not been quantified in the reports examined. However, no effects were observed in several clinical studies, case studies and occupational epidemiological studies following exposure to methyl chloride at concentrations up to about 412 mg/m^3, other than minimal effects observed in one limited study with mean exposure levels of about 70 mg/m^3. Since the critical non-neoplastic effects in mice occurred at the lowest concentration tested in the chronic study, it is unknown whether long-term exposure to lower concentrations would cause effects.

There remain significant data gaps on the industrial production of methyl chloride from combustion of fossil fuels and biomass and the release of methyl chloride from these sources. Modelling of the dispersion of methyl chloride from point sources to estimate exposure of people in communities has not been conducted in the absence of these data. A study of indoor air quality (Health Canada 2008b) showed an elevated concentration of methyl chloride in the homes of smokers, but the additional burden of methyl chloride accruing to the smoker through mainstream smoke remains uncertain.

Conclusion

Based on the information presented in this screening assessment, it is concluded that methyl chloride is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Based on the available information on its potential to cause harm to human health, it is concluded that methyl chloride is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that methyl chloride does not meet the definition of "toxic" as set out in section 64 of CEPA 1999. Additionally, methyl chloride meets the criteria for persistence but does not meet the criteria for bioaccumulation potential as set out in the *Persistence and Bioaccumulation Regulations* (Canada 2000).

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Appendix 1: Upper-bounding estimates of daily intake of methyl chloride by the general population in Canada

Route of exposure	Estimated intake (µg/kg-bw per day) of methyl chloride by various age groups							
	0–6 months[1]			0.5–4 years[5]	5–11 years[6]	12–19 years[7]	20–59 years[8]	60+ years[9]
	Breast fed[2]	Formula fed[3]	Fed solid food[4]					
Ambient air[10]	0.30			0.64	0.50	0.28	0.24	0.21
Indoor air[11]	3.97			8.51	6.63	3.77	3.24	2.82
Drinking water[12]	na	2.24	0.84	0.95	0.75	0.42	0.44	0.47
Food and beverages[13]	na	na	0.001	0.003	0.006	0.011	0.013	0.013
Soil[14]	<0.001			<0.001	<0.001	<0.001	<0.001	<0.001
Total intake	4.27	6.51	5.11	10.10	7.89	4.48	3.93	3.51

Abbreviations: na, not applicable

1 Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to drink 0.8 L of water per day (formula fed) or 0.3 L/day (fed solid food) and to ingest 30 mg of soil per day (Health Canada 1998).

2 No data on the concentration of methyl chloride in human breast milk were located.

3 For exclusively formula-fed infants, intake of water is only that required to reconstitute formula. Methyl chloride has been detected in drinking water (see footnote 12). No data on concentrations of methyl chloride in baby formula were identified for Canada.

4 The dietary intake is based on consumption of 0.3 L of water and up to 1.18 kg of food daily. This intake pattern is presented as a hypothetical extreme case and does not reflect recommended infant feeding practice. Approximately 50% of infants are introduced to solid foods by 4 months of age and 90% by 6 months of age (NHW 1990).

5 Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day (Health Canada 1998).

6 Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day (Health Canada 1998).

7 Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

8 Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

9 Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day (Health Canada 1998).

10 Methyl chloride has been measured in ambient air in Canada, the United States and elsewhere. The highest concentration of methyl chloride measured in an outdoor air sample in the period 2006–2007 in the NAPS database (6098 samples; maximum: 8.54 µg/m^3), measured in Sarnia, Ontario, was used to estimate exposure to methyl chloride via ambient air (NAPS 2008). Other data considered included the results of air sampling of indoor and ambient air using static sampling stations in the Windsor and Regina studies and the Toronto study (Bell et al. 1991; Health Canada 2008a, 2008b). Canadians are assumed to spend 3 h/day outside (Health Canada 1998).

11 Methyl chloride has been measured in indoor air in Canada and elsewhere. The highest concentration of methyl chloride measured in a 24-h static air sample (1067 samples; maximum: 16.20 µg/m^3) in the home of a smoker in Regina, Saskatchewan, was used to estimate exposure to methyl chloride via indoor air (Health Canada 2008b). Other data considered included the results of air sampling in the Toronto and Windsor studies (Bell et al. 1991; Health Canada 2008a). Canadians are assumed to spend 21 h/day inside (Health Canada 1998).

12 Methyl chloride has been detected in samples of municipally treated drinking water in Canada (Otson et al. 1982). Results of extensive testing of groundwater in the United States were reported by the US

Geological Survey (Zogorski et al. 2006). The highest reported concentration of methyl chloride in that summary report (21 µg/L) was used to estimate exposure. The data set considered included other US Geological Survey reports (Squillace et al. 1999; Grady and Casey 2001; Moran et al. 2002) comprising more than 14 500 measurements and 43 detections of methyl chloride. In one sample, the concentration of methyl chloride was found to be 79.3 µg/L. This datum was not used because it indicates that the groundwater was probably contaminated from a specific source.

[13] No data were identified for the concentration of methyl chloride in foods in Canada or elsewhere. The probable daily intake of methyl chloride from food packaging for an adult was estimated to be 0.013 µg/kg-bw per day (2009 email from Foods Directorate, Health Canada, to Existing Substances Division, Health Canada; unreferenced). The daily intake of methyl chloride from food packaging for other age groups was estimated based on body weight relative to adult body weight. Amounts of foods consumed on a daily basis by each age group are described by Health Canada (1998).

[14] The median concentration of methyl chloride in sediments in the US EPA STORET database reported by Staples et al. (1985) was <5 µg/kg dry weight. Methyl chloride has been detected in soil and sediment at waste sites in the United States (ATSDR 1998). Methyl chloride is not expected to be persistent in soil or present in soil that is not associated with waste sites.

Appendix 2: Summary of health effects information for methyl chloride

Endpoint	Lowest effect levels[1]/Results
Effects on laboratory animals and *in vitro*	
Acute toxicity	**Lowest inhalation LC_{50}** (male B6C3F1 mouse) = 4540 mg/m^3 (2200 ppm) (Chellman et al. 1986c) [Additional inhalation studies: White et al. 1982; others cited in IPCS 2000; OECD 2003] **Lowest oral LD_{50}** (rat) = 1800 mg/kg-bw (OECD 2003, citing Registry of Toxic Effects of Chemical Substances) (strain not stated) [No other oral studies identified.] No dermal studies identified.
Short-term repeated-dose toxicity	**Lowest inhalation LOEC** (mouse) = 206 mg/m^3 (100 ppm) based on degenerative changes in the cerebellum of female C57BL/6 mice exposed continuously (22.5 h/day) for 11 days [NOEC = 103 mg/m^3]. In the same study, similar lesions were observed following intermittent exposure (5.5 h/day) to 825 mg/m^3 (400 ppm) [NOEC = 310 mg/m^3]. Clinical signs of neurotoxicity were observed at 310 mg/m^3 (150 ppm) for continuous exposure and 1650 mg/m^3 (800 ppm) for intermittent exposure. The authors concluded that although the degree of cerebellar lesions was related to exposure concentration and duration, the relationship between effect levels and exposure concentration × time is not proportional, with a steeper dose–response curve for continuous exposure (Landry et al. 1985). [Additional inhalation studies: Burek et al. 1981; McKenna et al. 1981a; Morgan et al. 1982; Jiang et al. 1985] No oral or dermal studies identified.
Subchronic toxicity	**Lowest inhalation LOEC** (rat, mouse) = 1545 mg/m^3 (750 ppm) based on decreased body weight in rats, increased relative liver weight in mice and cytoplasmic vacuolization of hepatocytes in both species, following exposure for 6 h/day, 5 days/week, for 13 weeks [NOEC = 775 mg/m^3] (CIIT 1979) [Additional inhalation studies: McKenna et al. 1981b] No oral or dermal studies identified.
Chronic toxicity/ carcinogenicity	**Inhalation carcinogenicity bioassay in mice and rats:** B6C3F1 mice and F344 rats were exposed by inhalation to 0, 103, 464 or 2064 mg/m^3 (0, 50, 225 or 1000 ppm) 6 h/day, 5 days/week, for up to 2 years. No exposure-related tumours were observed in rats of either sex or in female mice; however, kidney tumours were increased in male mice. There was a significant increase in the number of renal cortical adenomas (12/120) and renal cortical adenocarcinomas (5/120) at 2064 mg/m^3 (0/120 in control and low-concentration animals). Cortical adenomas in the 464 mg/m^3 group (2/117) were non-significant but judged by the investigators to be exposure related. No concentration dependence could be established. Papillary cystadenomas (2/120), papillary cystadenocarcinomas (1/120) and tubular cystadenomas (2/120) were also observed in the high-concentration male mouse kidney (0 in controls, low and middle concentration). A large and statistically significant increase in the development of renal tubuloepithelial hyperplasia, hypertrophy and/or karyomegaly was observed in high-concentration males starting at 12 months and progressing in severity throughout the study (CIIT 1981; Pavkov et al. 1982). **Lowest inhalation non-neoplastic LOEC** (mouse) = 103 mg/m^3 (50 ppm) based on nervous system toxicity in both sexes (axonal swelling and degeneration in spinal nerves) exposed for up to 2 years (lowest concentration tested) (CIIT 1981). This was the LOAEC selected for this study by IPCS (2000) and ATSDR (1998); however, the

Endpoint	Lowest effect levels[1]/Results
	US EPA (2001) and OECD (2003) selected a NOAEC of 464 mg/m^3 (225 ppm), based on effects on the nervous system, kidney, liver and testes at 2060 mg/m^3 (1000 ppm). [No additional inhalation studies identified.] No oral or dermal studies identified.
Developmental toxicity	**Lowest inhalation LOEC for teratogenicity** (mouse) = 1030 mg/m^3 (500 ppm) based on an increase in fetal heart defects in the absence of maternal toxicity. The NOAEC was 515 mg/m^3 for absence of maternal and fetal toxicity and teratogenicity (Wolkowski-Tyl et al. 1983a, 1983b). C57BL/6 mice carrying B6C3F1 fetuses were exposed to 0, 206, 1030 or 3090 mg/m^3 (0, 100, 500 or 1500 ppm) on gestation days 6–18. Severe maternal toxicity (clinical signs of neurotoxicity) resulted in early sacrifice of dams treated at 3090 mg/m^3. An increase in fetal heart defects with no general fetal or maternal toxicity was observed at 1030 mg/m^3. There were no signs of fetal or maternal toxicity or teratogenicity at 206 mg/m^3 [NOAEC]. Increased ossification was observed at 206 and 1030 mg/m^3 (Wolkowski-Tyl 1983a). In a follow-up study by the same group, C57BL/6 mice carrying B6C3F1 fetuses were exposed to 0, 515, 1030 or 1545 mg/m^3 (0, 250, 500 or 750 ppm) on gestation days 6–18. At 1030 and 1545 mg/m^3, there was an increase in fetal heart defects with no other signs of embryo-fetal toxicity. At 515 mg/m^3, there were no signs of maternal or fetal toxicity or teratogenicity [NOAEC]. Maternal toxicity was observed only at 1545 mg/m^3 (decreased body weight and body weight gain, clinical signs of neurotoxicity) (Wolkowski-Tyl 1983b). Heart defects were not observed when C57BL/6 mice carrying B6C3F1 fetuses were exposed to 0, 515, 620 or 2064 mg/m^3 (0, 250, 300 or 1000 ppm) for 12–24 h on gestation day 11.5–12.5 (John-Greene et al. 1985). There was no evidence of teratogenicity in F344 rats exposed to 0, 206, 1030 or 3090 mg/m^3 (0, 100, 500 or 1500 ppm) on gestation days 7–19. Maternal and fetal toxicity were observed at 3090 mg/m^3, but not at the two lower concentrations (Wolkowski-Tyl et al. 1983a).
Reproductive toxicity	**Lowest inhalation LOEC for reproductive toxicity** (rat) = 979 mg/m^3 (475 ppm) based on decreased fertility in F_0 males in a two-generation study (Hamm et al. 1985) Male and female F344 rats were treated for 10 weeks (6 h/day, 5 days/week) and during a 2-week mating period (6 h/day, 7 days/week) at 0, 310, 979 or 3096 mg/m^3 (0, 150, 475 or 1500 ppm). Treated males were also mated with unexposed females after a recovery period of 2, 12 or 28 weeks. The F_1 pups were first exposed at weaning (postnatal day 28), then for 10 weeks plus 2 weeks of mating, as described for the F_0 generation, at 0, 310 or 979 mg/m^3. No litters were produced when the high-exposure (3096 mg/m^3) F_0 males were mated with exposed or unexposed females; significantly fewer litters were born to unexposed and exposed females mated to F_0 males exposed to 979 mg/m^3. The number of fertile males was significantly decreased at 979 mg/m^3. After a 10-week recovery period, the fertility of the males initially exposed to 979 mg/m^3 had returned to control values. There was a partial recovery of fertility in the 3096 mg/m^3 males after 10 weeks, but no further improvement was observed after an additional 18 weeks of recovery time. A non-significant decrease in the number of fertile males and number of litters was observed in the F_1 males exposed to 979 mg/m^3. [Additional studies: Male rats exposed to methyl chloride concentrations of ≥1030 mg/m^3 in studies ranging in duration from 2 days to 2 years had decreased testes and epididymal weights, testes degeneration, decreased testosterone, disrupted

Endpoint	Lowest effect levels[1]/Results
	spermatogenesis, decreased sperm numbers and motility, increased sperm abnormalities and epididymal sperm granulomas (Chapin et al. 1984; Working et al. 1985b; Chellman et al. 1986b, 1987).]
Genotoxicity and related endpoints: *in vivo*	**DNA damage: Single-strand breaks** **Positive:** In male mouse kidney [B6C3F1 mouse – inhalation; 2064 mg/m^3 (1000 ppm) for 8 h or 6 h/day for 4 days, sacrifice within 6 h (Jäger et al. 1988; Ristau et al. 1990)] **Negative:** In male mouse kidney [B6C3F1 mouse – inhalation; 2064 mg/m^3 (1000 ppm), 8-h exposure, sacrifice 48 h later (Ristau et al. 1990)] **DNA damage: DNA cross-links** **Positive:** In male mouse kidney [B6C3F1 mouse – inhalation; 2064 mg/m^3 (1000 ppm) for 8 h or 6 h/day for 4 days, immediate sacrifice (Ristau et al. 1989, 1990)] **Negative:** In male mouse kidney [B6C3F1 mouse – inhalation; 2064 mg/m^3 (1000 ppm), 6 h/day for 4 days, sacrifice ≥5 h later (Ristau et al. 1990)] **Negative:** In female mouse kidney; male and female mouse liver [B6C3F1 mouse – inhalation; 2064 mg/m^3 (1000 ppm), 8-h exposure, immediate sacrifice (Ristau et al. 1989)] **DNA damage: Unscheduled DNA synthesis** **Negative:** In rat spermatocytes, hepatocytes and tracheal epithelial cells [F344 male rat – inhalation; 6180–7210 mg/m^3 (3000–3500 ppm), 6 h/day, 1–9 days (Working and Butterworth 1984; Working et al. 1986)] **Weak positive:** In rat hepatocytes [F344 male rat – inhalation; 30 900 mg/m^3 (15 000 ppm), 3 h (Working et al. 1986)] **DNA binding** **Positive:** In rat liver (covalent) [F344 rat – oral; single dose of 9 µmol or 1.3 mg/kg-bw[2] (Xu et al. 1993)] **DNA methylation** **Negative:** In rat lung, liver, kidney, testes, brain, muscle, intestine [F344 rat – inhalation; 1030 or 3090 mg/m^3 (500 or 1500 ppm), 6 h (Kornbrust et al. 1982)] **Negative**: In rat and mouse kidney and liver [F344 rat, B6C3F1 mouse – inhalation; 2064 mg/m^3 (1000 ppm), 4 h (Peter et al. 1985)] **Dominant lethal assay** **Positive:** Increased pre-implantation loss, decreased total and live implants, and decreased fertility throughout the 8-week study and after an additional 8-week recovery; increased post-implantation loss only in week 1 [F344 rat – inhalation; 2064 or 6190 mg/m^3 (1000 or 3000 ppm); 6 h/day, 5 days, mated 8 weeks (Working et al. 1985a)] **Positive:** Increased post-implantation losses in weeks 1 and 2; decreased fertility and increased pre-implantation losses in weeks 2 and 3 [F344 rat – inhalation; 6190 mg/m^3 (3000 ppm); 6 h/day, 5 days, mated for 3 weeks (Chellman et al. 1986a)] [Additional studies: SRI International 1984; Working and Bus 1986; Working and Chellman 1989] **Sex-linked recessive mutations** **Positive:** *Drosophila melanogaster* [inhalation; 50–120 min at 412 000 mg/m^3 (200 000 ppm) or 373 000, 375 000 or 786 000 ppm-h (University of Wisconsin 1982)]

Endpoint	Lowest effect levels[1]/Results
Genotoxicity and related endpoints: *in vitro*	**Mutagenicity** **Negative:** *Salmonella typhimurium* TA98 and TA1537 with and without metabolic activation [duPont Inc. 1977; NTP 1991; JETOC 1997] **Positive:** *S. typhimurium* TA100 and TA1535 with and without metabolic activation [Andrews et al. 1976; duPont Inc. 1977; Simmon et al. 1977; Longstaff et al. 1984; JETOC 1997] **Positive:** *S. typhimurium* TM677 without metabolic activation (Fostel et al. 1985) **Positive:** *Escherichia coli* WP2 *uvr*A with and without metabolic activation (JETOC 1997) **Positive:** Human lymphoblasts (TK6 locus) without metabolic activation (Fostel et al. 1985) **DNA damage** **Negative:** Strand breaks in human lymphoblasts (Fostel et al. 1985) **Negative:** UDS in rat primary tracheal epithelial cells (Working et al. 1986) **Negative/weak positive:** UDS in human primary hepatocytes (Butterworth et al. 1989) **Positive:** UDS in rat primary spermatocytes and hepatocytes (Working and Butterworth 1984; Working et al. 1986; Butterworth et al. 1989) **Positive:** Induction of adaptive response to alkylation damage in *E. coli* B F26 (Vaughan et al. 1993) **Positive:** Enhanced transformation by adenovirus, Syrian hamster embryo cells (Hatch et al. 1983) **Positive:** Transformation of BHK21 cells (Longstaff et al. 1984) **Sister chromatid exchange** **Positive:** Human lymphoblasts without metabolic activation (Fostel et al. 1985) **Chromosome aberrations** **Positive:** Chinese hamster lung cells without metabolic activation (Asakura et al. 2008)
Effects on humans	
Neurotoxicity	Symptoms described in case reports of human exposure to methyl chloride include dizziness, ataxia, weakness, apathy, drowsiness, double and blurred vision, personality changes, loss of memory, confusion, hallucinations, slurred speech, headache, muscle spasms, convulsions and tremors. The exposure conditions were generally not quantified, but estimates ranged from 412 to $>10^6$ mg/m^3 for durations of 1 h to several weeks. In general, symptoms developed within a few hours of exposure, but recovery was highly variable: some effects were resolved within days of exposure cessation; others persisted for months or even years (reviewed in ATSDR 1998; IPCS 2000; US EPA 2001; OECD 2003). Repko et al. (1976) found "subtle differences in finger tremors and time-sharing tasks" in 122 subjects occupationally exposed to methyl chloride for 1 month up to 25 years compared with 49 unexposed controls. However, the levels of methyl chloride were measured only during 1 week (range from 1.8 to 70 ppm with a mean of 34 ppm [70 mg/m^3]), and the effect of possible prior exposure to higher concentrations is unknown. Also, subjects may have been co-exposed to other substances, and the control group was considerably younger than the exposed group. The US EPA (2001) considered this study inadequate for drawing conclusions. A small but "marginally significant" impairment of performance on behavioural tests was observed following exposure of volunteers to 200 ppm (412 mg/m^3) for 3 h (Putz-Anderson et al. 1981). A review of case history studies by Repko (1981) describes evidence that methyl chloride exposure results in degeneration of areas of the cerebral cortex and spinal cord

Endpoint	Lowest effect levels[1]/Results
	and frontal and parietal atrophy.
Chronic exposure/ carcinogenicity	In humans, no association has been found between exposure to methyl chloride and cancer of any type. Several cohort studies looking at causes of death in relation to occupational exposure to methyl chloride found no excess mortality from any specific cause of death, including cancers (Ott et al. 1985; Holmes et al. 1986; Olsen et al. 1989; Dow Chemical 1992). IARC (1999) and US EPA (2001) concluded that these studies were insufficient for assessing cancer risk due to the small numbers of deaths, mixture of exposures and lack of quantitative exposure levels. In a cohort study of 24 sailors who had survived accidental high-level exposure to methyl chloride 32 years previously, excess mortality and a slightly elevated risk for all cancers and for lung cancers were observed (Rafnsson and Gudmundsson 1997). However, IPCS (2000) and US EPA (2001) determined that the small number of cancers in the exposed group was insufficient for assessing cancer risk in humans.
Metabolism and toxicokinetics	Methyl chloride is readily absorbed during inhalation exposure. Humans and rodents have similar blood:air partition coefficients. Metabolism occurs primarily via a glutathione-mediated pathway and to a lesser extent via oxidation by the cytochrome P450 pathway (CYP2E1). Glutathione depletion results in a shift towards the alternative oxidative pathway, leading to increased formaldehyde production. Methyl chloride is eliminated via conjugated metabolites and exhaled carbon dioxide and incorporated into macromolecules via the single-carbon pool. There appears to be large interindividual variation in blood and breath levels of methyl chloride and a subpopulation with levels 2–6 times greater than in other subjects (rapid/slow metabolizers). This is thought to be due to polymorphisms in GSTT1-1 expression. Expression of CYP2E1 is tissue, sex and species specific, which may account for the varying sensitivities to methyl chloride exposure. For example, CYP2E1 levels are high in male mouse kidney, but not detected in human kidney or fetal liver. [Details and references in ATSDR 1998; IPCS 2000; US EPA 2001; OECD 2003]

[1] LC_{50}, median lethal concentration; LD_{50}, median lethal dose; LOAEC, lowest-observed-adverse-effect concentration; LOEC, lowest-observed-effect concentration; NOAEC, no-observed-adverse-effect concentration; NOEC, no-observed-effect concentration.

[2] 9 µmol = 9×10^{-6} mol × 50 490 mg/mol / 0.35 kg-bw = 1.3 mg/kg-bw (rat body weight from Health Canada 1994).