Screening Assessment for the Challenge

Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)oxy]- (M4Q)

Chemical Abstracts Service Registry Number
3555-47-3

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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 on Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)oxy]-, Chemical Abstracts Service Registry Number[1] 3555-47-3. This substance is referred to by its derived acronym, M4Q, in the assessment. M4Q was identified as a high priority for screening assessment and included in the Challenge initiative under the Chemicals Management Plan because it was found to meet the ecological categorization criteria for persistence, bioaccumulation potential and inherent toxicity to non-human organisms and was believed to be in commerce in Canada.

The substance, M4Q, was not considered to be a high priority for assessment of potential risks to human health, based upon application of the simple exposure and hazard tools developed by Health Canada for categorization of substances on the *Domestic Substances List*.

M4Q is an organic substance that is formed in low concentrations as an impurity during the production of certain siloxane products and intermediates. The substance does not occur naturally in the environment. M4Q is reported to be present at low levels as a reaction by-product or impurity in silicon-based adhesives, sealants, processing intermediates and anti-adhesive agents. The substance may also occur at low levels as an impurity in fillers, finishing agents, lubricants and lubricant additives, antifoaming agents, viscosity adjustors in consumer products such as paint and coating additives. M4Q is also present as an impurity in cosmetics.

Responses to notices published under section 71 of CEPA 1999 indicated that quantities of M4Q imported into Canada were in the range of 1001 to 100 000 kg for 2005 and 1000 to 10 000 kg for 2006. In all instances of import, the substance was reported to be present as an impurity in an end-use product. M4Q is formed as a reaction by-product; therefore, no manufacturing activities are associated with this substance.

Based on certain assumptions and reported use patterns in Canada, most M4Q is expected to be present in products directed to landfill following industrial or consumer/commercial use. Release to wastewater during industrial applications may also occur, with proportionally smaller losses through volatilization from consumer and commercial products. Information indicates that during processing operations where M4Q is formed, the substance becomes bound within the silicone matrix of the product, and that this limits but does not completely eliminate the potential for release into the environment.

The physical and chemical properties of M4Q indicate that, when released into the environment, the substance can be expected to distribute primarily into air, although it may also distribute into sediment when released into water.

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No empirical degradation data was found for M4Q and modelled estimates for M4Q, as well as empirical and modelled data for other chemically-similar volatile methylsiloxanes (VMS), were used to evaluate the potential for environmental persistence. The atmospheric half-life of 5.9 days predicted for M4Q is comparable with values derived for other VMS. Modelling predicts that M4Q will have significant atmospheric transport potential but is not likely to be deposited to water or soil in remote regions.

Modelled estimates predict that M4Q will biodegrade slowly in the environment which is consistent with data available for other VMS. However, the preponderance of data for other VMS such as the linear VMS, trisiloxane, octamethyl- (MDM), and the cyclic VMS, D4 and D5, indicates that these substances hydrolyze readily in water and soil. No empirical degradation data was found for VMS in sediment and the analysis of the potential for persistence was based on modelled and calculated biodegradation half-lives which indicate slow removal rates and therefore the potential to remain for long periods in this environmental medium. However, the other VMS examined in the assessment have demonstrated low potential for microbial biodegradation and, given the evidence for active abiotic degradation of these substances in both soil and water, it seems likely that an analysis of persistence in sediment based only on biodegradation data would underestimate the potential for removal in this medium.

No experimental bioaccumulation factor (BAF) or bioconcentration factor (BCF) data were found for M4Q. Based on the chemical properties of the substance, as well as BCF data for acceptable analogue substances, it is likely that M4Q will have some capacity for uptake into aquatic organisms via the surrounding water medium. In addition, BAF estimates calculated for M4Q determined that the substance may have significant potential to accumulate in organisms through dietary exposures. While M4Q may have the potential to accumulate in individual organisms, an empirical biomagnification factor (BMF) of less than 1 indicates that it is unlikely to transfer from one trophic level to the next highest trophic level in the foodweb studied.

M4Q has demonstrated low hazard potential in aquatic species, with no adverse effects observed following prolonged exposures at concentrations up to the limit of water solubility. Modelled estimates also predict no effects in fish, *Daphnia*, mysid shrimp and algae. Adverse effects were reported in one sediment toxicity study. No information was found on the potential for effects in terrestrial species; however, results obtained for a mechanistically-similar compound suggest that M4Q is not likely to be hazardous to terrestrial invertebrates or plants.

Monitoring data indicate that exposure levels of M4Q in the environment are very low. The substance was below detection limits in bottom sediments and biota samples, including those collected near potential M4Q sources of release. M4Q has been detected at low concentrations in a small number of suspended particulate matter samples, as well as in some wastewater treatment plant influents and effluents, pre-treatment industrial process waters and landfill leachates. However, the concentrations and frequency of occurrence are lower in effluents relative to influents collected at the same time and from the same treatment plant, indicating that wastewater treatment is effective at reducing the amount of M4Q available to enter receiving waters. The results of quantitative risk quotient analyses conducted for surface waters and sediment determined that the highest predicted concentrations of M4Q in the Canadian environment are much less than experimentally-determined no-effect levels.

The low presence of M4Q in products, as well as limitations to its direct release from these products and evidence for effective removal at wastewater treatment plants, indicate that M4Q will have low exposure potential in the environment. This low exposure, together with the observed lack of toxicity in laboratory testing conducted at concentrations up to the maximum water solubility or saturation limit of the substance, indicates that there is low risk of harm to organisms or to the broader integrity of the environment from M4Q. It is therefore concluded that M4Q does not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA 1999 as it is not entering the environment in a quantity or concentration or under conditions that have or may have immediate or long-term harmful effects on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends.

In terms of human health, exposure of the general population to M4Q is expected to occur mainly through use of paints, coatings, and cosmetics.

Limited empirical health effects data was available for M4Q. Health effects data for analogues indicate potential effects mainly on the liver in experimental animals following repeated-dose exposure. The margins between upper-bound estimates of exposure from environmental media (predominantly air) and from use of consumer products containing M4Q (alkyd coating) and cosmetics containing M4Q, and critical effect levels in experimental animals are considered adequate to address uncertainties in the health effects and exposure databases.

On the basis of the adequacy of the margins between upper-bound estimates of exposure to M4Q and critical effect levels in experimental animals, it is concluded that M4Q is a substance that does not meet criteria under paragraph 64(*c*) of CEPA 1999 as it 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.

Therefore, based on the information available, it is concluded that M4Q 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 in Canada; 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), that 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 Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)oxy]- was identified as a high priority for assessment of ecological risk as it was determined during categorization to meet criteria for persistence, bioaccumulation potential and inherent toxicity to aquatic organisms and is believed to be in commerce in Canada. The Challenge for this substance was published in the *Canada Gazette* on December 26, 2009 (Canada 2009a, 2009b). 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 pertaining to the chemical properties, bioaccumulation potential, persistence, hazard, uses and exposure potential of the substance were received.

Although Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)oxy]- was determined to be a high priority for assessment with respect to the environment, it did not meet the criteria for GPE or IPE and high hazard to human health based on classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

Screening assessments focus on information critical to determining whether a substance meets the criteria 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.[2] The use of the term "conservative" throughout this assessment refers to the protective approach taken.

This screening assessment includes consideration of information on chemical properties, fate, hazards, uses and exposure, including additional information submitted by stakeholders. Relevant data were identified up to September 2014. Key studies were critically evaluated and used, along with modelled results, to reach conclusions. When available and relevant, information presented in risk and hazard assessments from other jurisdictions was considered. The screening assessment does not represent an exhaustive or critical review of all available data. Rather, it presents the most critical studies and lines of evidence pertinent to the conclusion.

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 ecological and human health portions of this assessment have undergone external written peer review and consultation. The original draft of this screening assessment was released in January 2011 and was subject to a 60-day public comment period. Following receipt of substantial new information of relevance to this evaluation, extensive revisions were made to the ecological portion of this screening assessment and an updated draft was published in March 2014 for a second 60-day public comment period. No further comments were received on the updated draft during the second 60-day public comment period.

Approaches used in the screening assessments conducted under the Challenge have been reviewed by an independent Challenge Advisory Panel. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment Canada.

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

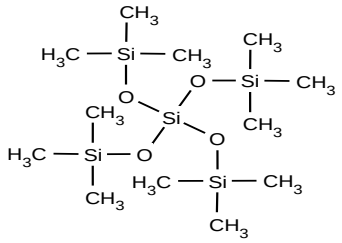
[2] A determination of whether one or more of the criteria of section 64 are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and the use of consumer products. A conclusion under CEPA 1999 on the substances in the Chemicals Management Plan (CMP) Challenge Batches 1-12 is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Controlled Products Regulations*, which is part of regulatory framework for the Workplace Hazardous Materials Information System [WHMIS] for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA 1999 does not preclude actions being taken under other sections of CEPA or other Acts.

Substance Identity

Substance Name

For the purposes of this document, Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)oxy]- will be referred to as M4Q, derived following the nomenclature rules for polydimethylsiloxanes presented in Fendinger et al. (1997).

Table 1. Substance identity for M4Q

Chemical Abstracts Service Registry Number (CAS RN)	**3555-47-3**
DSL name	**Trisiloxane,1,1,1,5,5,5-hexamethyl-3,3,-bis[(trimethylsilyl)oxy]-**
National Chemical Inventories (NCI) names[a]	*Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)oxy]-* (TSCA, AICS, PICCS, ASIA-PAC, NZIoC); *1,1,5,5,5-Hexamethyl-3,3-bis[(trimethylsilyl)oxy]trisiloxane*, (EINECS); *1,1,1,5,5,5-Hexamethyl-3,3-bis[(trimethylsilyl)oxy]trisiloxane* (ECL); *Tetra(trimethysiloxy)silane* (PICCS); *Silane, tetra(trimethylsiloxy)-* (PICCS)
Other names	*Silanol, trimethyl-, tetraester with silicic acid (H_4SiO_4); Silicic acid (H_4SiO_4), tetrakis(trimethylsilyl) ester; Tetrakis(trimethylsiloxy)silane; Tetrakis(trimethylsilyl) silicate; Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis(trimethylsiloxy)-*
Chemical group (DSL Stream)	Discrete organics
Major chemical class or use	Organosilicones
Major chemical sub-class	Branched volatile methyl siloxanes (branched VMS)
Chemical formula	$C_{12}H_{36}O_4Si_5$
Chemical structure	
SMILES[b]	[Si](O[Si](O[Si](C)(C)C)(O[Si](C)(C)C)O[Si](C)(C)C)(C)(C)C
Molecular mass	384.85 g/mol

[a] National Chemical Inventories (NCI). 2009: AICS (Australian Inventory of Chemical Substances); ASIA-PAC (Asia-Pacific Substances Lists); ECL (Korean Existing Chemicals List); EINECS (European Inventory of Existing Commercial Chemical Substances); NZIoC (New Zealand Inventory of Chemicals); PICCS (Philippine Inventory of Chemicals and Chemical Substances); and TSCA (Toxic Substances Control Act Chemical Substance Inventory).

[b] Simplified Molecular Input Line Entry System

Physical and Chemical Properties

Table 2 contains experimental and modelled physical and chemical properties of M4Q that are relevant to its environmental fate.

Table 2. Physical and chemical properties for M4Q

Property	Type	Value[a]	Temperature (°C)	Reference
Melting point (ºC)	Experimental	-60*	n/a	Acros Organics BVBA 2000
Melting point (ºC)	Modelled	-26.25	n/a	MPBPVPWIN 2008
Boiling point (ºC)	Experimental	221.71* (494.86 K)	n/a	Flaningam 1986
Boiling point (ºC)	Modelled	217.2	n/a	MPBPVPWIN 2008
Density (kg/m^3)	Experimental	868	n/a	Acros Organics BVBA 2000
Vapour pressure (Pa)	Experimental	8.96* (0.0672 mm Hg)[b]	25	Flaningam 1986
Vapour pressure (Pa)	Modelled	20.2 (0.151 mm Hg)	25	MPBPVPWIN 2008
Vapour pressure (Pa)	Calculated	8.98	n/a	Schenker et al. 2005
Henry's Law constant ($Pa \cdot m^3/mol$)	Estimated	4.61×10^{7}[c]	25	Kozerski 2012
Henry's Law constant ($Pa \cdot m^3/mol$)	Modelled	7.99×10^{4} (7.89×10^{-1} $atm \cdot m^3/mol$; Bond method)	25	HENRYWIN 2008
Henry's Law constant ($Pa \cdot m^3/mol$)	Modelled	1.17×10^{8} (1.16×10^{3} $atm \cdot m^3/mol$; VP/Wsol method)[d]	25	HENRYWIN 2008
Henry's Law constant ($Pa \cdot m^3/mol$)	Modelled	2.30×10^{7}* (2.27×10^{2} $atm \cdot m^3/mol$;	25	HENRYWIN 2008

Property	Type	Value[a]	Temperature (°C)	Reference
		VP/Wsol method)[e]		
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)	Calculated	9.84[f]	25	Kozerski 2012
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)	Modelled	9.6*	25	KOWWIN 2008
Log K_{ow} (Octanol-water partition coefficient) (dimensionless)	Calculated	9.48	25	Schenker et al. 2005
Log K_{oa} (Octanol-air partition coefficient) (dimensionless)	Calculated	5.17[g]	25	Xu and Kropscott 2006
Log K_{oa} (Octanol-air partition coefficient) (dimensionless)	Calculated	5.57[f]	25	Kozerski 2012
Log K_{oa} (Octanol-air partition coefficient) (dimensionless)	Modelled	5.5 (corrected value)	25	KOAWIN 2008; Schenker et al. 2005
Log K_{oc} (Organic carbon-water partition coefficient) (dimensionless)	Calculated	5.58[h]	25	Kozerski 2012
Log K_{oc} (Organic carbon-water partition coefficient) (dimensionless)	Calculated	5.29[f]	25	Nguyen et al. 200
Log K_{oc} (Organic carbon-water partition coefficient) (dimensionless)	Modelled	5.2* (MCI estimate) 8.3 (Log K_{ow} estimate)	25	KOCWIN 2008

Property	Type	Value[a]	Temperature (°C)	Reference
Water solubility (mg/L)	Experimental	0.00015*	23	Varaprath et al. 1996
Water solubility (mg/L)	Modelled	0.000066	25	WSKOWWIN 2008
Water solubility (mg/L)	Calculated	0.0001497	n/a	Schenker et al. 2005

Abbreviations: n/a, not applicable.
[a] Values in parentheses represent the original ones as reported by the authors or as estimated by the models.
[b] Extrapolated value in PhysProp (2006).
[c] Calculated from log K_{aw} of 4.27, which was derived from the equation: log K_{ow} = log K_{oa} + log K_{aw}. The log K_{ow} and log K_{oa} values used in the equation were 9.84 and 5.57, respectively, from Kozerski (2012).
[d] Input values used for VP/WSol estimate were 20.2 Pa for vapour pressure (MPBPVPWIN 2008) and water solubility value of 0.000066 mg/L (WSKOWWIN 2008).
[e] Input values used for VP/WSol estimate were 8.96 Pa for vapour pressure (Flaningam 1986) and water solubility value of 0.00015 mg/L (Varaprath et al. 1996).
[f] Estimated using the linear solvation energy relationship (LSER) model of Abraham et al. (1994).
[g] Value was derived based on an empirically-determined relationship between log K_{oa} and normal boiling point for several cyclic and linear permethylsiloxanes and directly measured values of K_{oa}. Using the boiling point of 222°C for M4Q, a log K_{oa} value of 5.17 was calculated (Xu and Kropscott 2006).
[h] Value was calculated by using a polyparameter model that included measured data for the cyclic permethylsiloxanes D4 and D5 in the training set.
*Indicates selected value for modelling

M4Q is a one of a group of organosilicone compounds (i.e., substances containing an alternating silicon-oxygen backbone) termed volatile methyl siloxanes (VMS) (Chandra 1997). VMS are oligomeric alkylsiloxanes with low molecular weight (less than 600 g/mol) and significant vapour pressure under ambient environmental conditions (Allen et al. 1997; Hobson et al. 1997). The group is also highly hydrophobic and has low aqueous solubility. M4Q is a branched VMS, indicating that the structural components of the siloxane molecule are arranged in a branched fashion around the silicon-oxygen backbone (Table 1).

Chemical property values selected for use in modelling the fate and behaviour of M4Q in the environment were checked for internal consistency using harmonization methods described in Schenker et al. (2005). Values used in the harmonization procedure were: 8.96 Pa (empirical vapour pressure), 0.00015 mg/L (empirical water solubility), log K_{aw} of 4.1 (derived from HENRYWIN VP/Wsol Henry's Law constant of 2.3×10^{7} Pa·m^3/mol), log K_{oa} of 5.5 (KOAWIN estimate of 8.1 corrected using empirical and estimated log K_{oa} values for the closely related analogue substance, Trisiloxane, octamethyl- (MDM; CAS RN 107-51-7)) and log K_{ow} of 9.6 (KOWWIN). The harmonization procedure determined that the least (0%) adjustment, and therefore greatest internal consistency, occurred for property values of: 8.98 Pa (vapour pressure), 0.0001497 mg/L (water solubility), log K_{aw} of 3.97, log K_{oa} of 5.51 and log K_{ow} of 9.48. The close agreement between harmonized values and those determined empirically and through modelling suggests that the selected property values are consistent with what would be empirically expected according to equilibrium theory.

Sources

There are no known natural sources of M4Q.

Responses to a survey notice published under section 71 of CEPA 1999 indicated that, for the 2005 calendar year, M4Q was not manufactured in Canada at or above the reporting threshold of 100 kg. However, two Canadian companies reported importing M4Q into Canada in a product or a mixture, with both companies reporting imports in the 1001 to 100 000 kg/year range (Environment Canada 2007).

A subsequent section 71 survey conducted for the 2006 calendar year indicated that M4Q was not manufactured in Canada in a quantity at or above the 100 kg reporting threshold. Total reported imports for that year were in the range of 1000 to 10 000 kg (Environment Canada 2010a). For all reported import activity, the substance was described as an impurity in end-use products.

M4Q was reported to be present in consumer applications in Norway, Denmark and Sweden in 2010 (the most recent reporting year); however, no quantities were provided (SPIN 2013). M4Q is not currently listed as a high production volume chemical (HPVC) or low production volume chemical (LPVC) in the European Union (ESIS c1995–2009) and is not included in the U.S. EPA High Production Volume (HPV) Challenge Program (HPVIS 2012).

Uses

Information provided in the year 2005 section 71 survey indicated that M4Q may be present in a range of products that are associated with the following business activities in Canada: residential and non-residential building construction; highway, street and bridge construction; use by foundation, structure and building exterior contractors; in the manufacture of rubber products, industrial machinery, converted paper products, resin, synthetic rubber, artificial synthetic fibres and filaments; pharmaceuticals and medicines, paints, coatings, adhesives, soap, cleaning compounds, toilet preparations, computers and peripheral equipment, semiconductor and other electronic components, household appliances, and aerospace products and parts, and in basic chemical and other chemical product and preparation manufacturing. Other business activities were also reported for mill production of fibre, yarn, and thread; textile and fabric finishing and fabric coating; textile furnishings and other textile products; as well as pulp, paper, and paperboard. Additional business activities reported include shoe stores and automotive parts, accessories, and tire stores (Environment Canada 2007).

M4Q is not deliberately manufactured and arises as an impurity formed in low concentrations during the production of certain siloxane products and intermediates (Dow Corning Corporation 2012). Most of the produced M4Q will be present in intermediates, elastomers, and rubber products, while a smaller portion will be present in processing aids including siloxane antifoam (Dow Corning Corporation 2012).

M4Q is reported to be present at low levels (equal to or less than 3% weight/weight [w/w]) as a reaction by-product or impurity in a wide range of silicon-based adhesives, sealants, processing intermediates and anti-adhesive agents (Environment Canada 2010a). The substance may also occur at low levels (equal to or less than 1.5% w/w) as an impurity in fillers, finishing agents, lubricants and lubricant additives, antifoaming agents, viscosity adjustors in consumer products such as paint and coating additives, and in cosmetics.

M4Q was reported under the section 71 survey as an impurity in cosmetic ingredients (Environment Canada 2010a). Based on notifications submitted under the Cosmetic Regulation to Health Canada, M4Q is present as an impurity in certain cosmetic products (face cream, eye shadow, face cleanser, body lotion and tanning lotion) (April 2013 email from Consumer Product Safety Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada; unreferenced). .

M4Q is present as an impurity in antifoam formulations, siloxane-based materials, and dimethyl siloxane-based materials used in food packaging material applications. Specifically it has been identified to be present in printing inks used on the exterior surfaces of paper/plastic milk cartons and in a defoamer used in the manufacture of paperboards that are intended for use in the manufacture of food packaging articles (2014 personal communication from Food Directorate, Health Canada; unreferenced).

This substance is not listed as an approved food additive in the Lists of Permitted Food Additives which have been incorporated by reference in Marketing Authorizations under the authority of the *Food and Drugs Act* (Canada 2014).

M4Q is not listed in the Drug Products Database, the Therapeutic Product Directorate's internal Non-Medicinal Ingredient Database, the Natural Health Products Ingredients Database or the Licensed Natural Health Products Database as a medicinal or non-medicinal ingredient present in pharmaceuticals, natural health products or veterinary drugs in Canada (NHIPD 2014; LNHPD 2014; DPD 2014; 2010 personal communication, Therapeutic Products Directorate, Health Canada; unreferenced: 2010 personal communication from Veterinary Drugs Directorate, Health Canada; unreferenced). M4Q is present in two pest control products (2013 personal communication from Pest Management Regulatory Agency, Health Canada; unreferenced).

Releases to the Environment

M4Q is not deliberately manufactured or imported but rather arises as an impurity formed in low concentrations during production of certain siloxane products (see Sources section). As M4Q may be present in a variety of silicon-related products, releases to the Canadian environment could occur during processing activities, including transportation and storage of materials, as well as during service life and at disposal of finished products. Based on this, both non-dispersive and dispersive releases of M4Q to the environment are possible. Results from the section 71 notice conducted for the year 2006 (Environment Canada 2010a) were used to estimate potential releases of M4Q to the Canadian environment.

In the majority of products and applications where it is present, M4Q is expected to be bound within the silicone matrix of the product (Environment Canada 2010a; Dow Corning Corporation 2012). This containment within products will limit but may not completely eliminate the potential for release of M4Q during product use. Some applications, such as industrial antifoam or lubricant, may result in some portion of the M4Q being released into wastewaters (Dow Corning Corporation 2012).

A method has been developed by Environment Canada to estimate losses of a substance during different stages of its life cycle, including its fate within a finished product or article (Environment Canada 2008). This method, referred to as Mass Flow, consists of a life cycle analysis and a spreadsheet tool (Mass Flow Tool or MFT) that integrates information on the manufacturing, importation and use patterns available for the substance. Starting with an identified mass of the substance, each life cycle stage is subsequently evaluated until no mass remains. Relevant factors are considered, uncertainties recognized and assumptions may be made during each stage, depending on information available. The estimated losses represent the complete mass balance of the substance over the life cycle and include releases to wastewater and other receiving compartments (land, air), chemical transformation, transfer to recycling activities and transfer to waste disposal sites (landfill, incineration). However, unless specific information on the rate or potential for release of the substance from landfills and incinerators is available, the method does not quantitatively account for releases to the environment during or after disposal.

In general, releases of a substance to the environment depend upon various losses from its manufacture, industrial use, and/or consumer/commercial use. These losses can be grouped into seven types: (1) discharge to wastewater; (2) emission to air; (3) loss to land; (4) chemical transformation; (5) disposal to landfill; (6) loss to incineration; and (7) disposal through recycling (i.e., recycling is deemed a loss and not considered further). They are estimated using regulatory survey data, industry data and data published by different organizations. The discharge to wastewater refers to raw wastewater prior to any treatment, whether it is on-site industrial wastewater treatment or off-site wastewater treatment. In a similar manner, loss via chemical transformation refers to changes in a substance's identity that may occur during manufacture, industrial use, and consumer/commercial use, but excludes those during waste management operations such as incineration and wastewater treatment. The loss to land includes unintentional transfer or leakage to soil or paved/unpaved surfaces during the substance’s use and service life (e.g., from the use of agricultural machinery or automobiles). The loss to land, however, does not include transfers subsequent to a substance’s use and service life (e.g., land application of biosolids and atmospheric deposition).

The losses estimated for M4Q over its life cycle (based on conservative assumptions) are presented in Table 3 (Environment Canada 2010b). As M4Q was not manufactured in Canada above reporting thresholds, estimated losses are based on import quantities reported in 2006.

Table 3. Estimated losses of M4Q during its life cycle

Type of loss	Proportion (%)	Pertinent life cycle stages
Wastewater (prior to wastewater treatment)	32.2	Industrial use
Air emission	0.7	Consumer/commercial use
Land	0.0	-
Chemical transformation	0.0	-
Landfill	64.1	Industrial and consumer/commercial use
Incineration	2.0	Consumer/commercial use
Recycling	0.0	-
Export	1.1	Consumer/commercial use

Most M4Q (64.1%) is expected to be present in products that are ultimately disposed of in landfills or incinerated following industrial or consumer/commercial use. Releases to wastewater (32.2%) from industrial use of products containing it may also occur. A small proportion (0.7%) is predicted to be emitted to air during consumer and commercial use of products, while an estimated 1.1% is present in exported end-use products.

Measured Environmental Concentrations

Data concerning the measured presence of M4Q in the environment are presented in Appendix II. No data were obtained for M4Q in air, water or soil. However, recent Canadian monitoring data are available for sediment, process effluents and wastewaters (i.e., wastewater treatment plant influents and effluents, landfill leachate, and industrial waters), and biota.

M4Q was not detected (detection limits 0.6 to 20 ng/g dw) in 93 sediment grab samples collected in 2011 from various locations in the Great Lakes region (Backus et al. 2012). A grab sample is one in which all test material in the sample is collected at the same time; therefore, a grab sample represents conditions specific to the location and time at which the sample was taken. Sampling locations for the study were selected to include sites situated near to known or potential point sources of M4Q, as well as sites away from potential point or non-point sources.

M4Q was present in three of 126 sediment samples collected in 2012 from locations in Newfoundland (n = 1), Nova Scotia (n = 3), New Brunswick (n = 2), Quebec (n = 78), Ontario (n = 39) and British Columbia (n = 3) (Pelletier et al. 2012). The monitoring program included sampling of both bottom sediments and particulate matter in the water column. M4Q was not detected in any of the bottom sediment samples, but was measured at concentrations of 3, 3.2 and 5 ng/g dw in three of 21 particulate matter samples collected from the Detroit River in Ontario.

Alaee (2012) analyzed influent and effluent grab samples collected in 2011 from 15 wastewater treatment plants (WWTPs) in Ontario, Quebec and British Columbia. M4Q was present in eight of 16 influent samples at concentrations of 5 to 238 ng/L, and in one of 15 effluent samples at a concentration of 5 ng/L.

Preliminary data from Alaee (2014) determined concentrations of 16 to 136 ng/L in four of 16 WWTP influent samples and 31 ng/L in one of 16 WWTP effluent samples collected in 2012 from WWTPs in Ontario, Quebec and British Columbia.

Preliminary measurements conducted by Khera (2014) found a concentration of 279 ng/L M4Q in one of 17 influent samples collected in 2012 from WWTPs across Canada. The substance was below the detection limit of 25 ng/L in all of 18 effluent samples collected from the plants. Concentrations of 147, 1507 and 10004 ng/L were measured in three of 16 influent samples collected from Ontario WWTPs in the first part of 2013, while two effluent samples from the plants contained 77 and 113 ng/L (n = 16 samples, detection limit 25 ng/L). The reason for the high M4Q concentration of 10004 ng/L in one of the influent samples is not clear. In light of the very low concentrations measured in wastewater samples from this and other monitoring programs (i.e. overall range in influents is 5 to 1507 ng/L in 19 of 110 samples, while overall range in effluents is 5 to 113 ng/L in 4 of 110 samples; see Appendix Table II-1), the measured concentration of 10004 ng/L is considered to be anomalously high. In July of 2013, the detection limit for both influent and effluent samples was increased to 53 ng/L. M4Q was found in two of 24 influent samples (at 46 and 56 ng/L) collected over the balance of 2013 but was not detected in 24 effluent samples (detection limit 53 ng/L). M4Q was measured at 59 and 137 ng/L in two of 21 WWTP influent samples collected in 2014 but was not found in 21 effluent samples (detection limit 53 ng/L).

M4Q was not detected (detection limit 0.5 to 1 ng/L) in nine grab water samples collected in 2011 from the on-site treatment plants of four industrial facilities in Ontario and Quebec (Alaee 2012). The substance was present at a concentration of 4 ng/L in one of four intermediate process water samples collected at a fifth facility but was not detected (detection limit 0.5 ng/L) in the final effluent from the facility. Concentrations of 4050 and 9990 ng/L were measured in two of three pre-treatment process waters at a sixth industrial facility, with effluent from the facility containing 567 ng/L. However the effluent from this facility is directed to a downstream publicly-owned WWTP and thus, the resulting concentrations of M4Q discharged into surface waters would be reduced.

In preliminary data from Alaee (2014), M4Q was present at concentrations of 30 and 3470 ng/L in two of three process waters collected in 2012 from an industrial facility in Ontario.

One grab sample of leachate collected in 2011 from a landfill in Quebec contained M4Q at the detection limit of 1 ng/L (Alaee 2012). M4Q was not detected (detection limit 0.5 ng/L) in leachate grab samples collected in the same year from two landfills in Ontario.

Preliminary data from landfills in Ontario, Quebec and British Columbia measured M4Q at concentrations of 1.8 to 6.2 ng/L in four of 15 leachate samples collected in 2012 (Alaee 2014).

M4Q was not detected (detection limit 0.026 ng/g ww) in blood samples collected from snapping turtles (*Chelydra s. serpentina*; n = 32), cormorants (*Phalacrocorax auritus*; n = 22) and harbour seals (*Phoca vitulina*; n = 15) at reference and contaminated sites in the Great Lakes region of Canada (Wang et al. 2012). Contaminated sampling locations were those situated close to urban

and industrial centres, while reference sites were located upstream and/or at a greater distance from potential sources of M4Q.

M4Q was not detected (detection limit 0.24 ng/g ww) in whole body homogenates of lake trout (*Salvelinus namaycush*; n = 60) and walleye (*Sander vitreus*; n = 17) collected from the Great Lakes, Kusawa Lake (Yukon), Lake Athabasca (Alberta) and Lake Winnipeg (Manitoba) (McGoldrick et al., 2014).

M4Q was not detected (detection limit 0.10 ng/g ww) in whole body samples of northern pike (*Esox lucius*; n = 7), walleye (*Sander vitreus*; n = 4), yellow perch (*Perca flavescens*; n = 2), round goby (*Neogobius melanostomus*; n = 4 pooled samples of 8 to 12 gobies) and mussels (*Elliptio complanata*; n = 7 pooled samples of 5 mussels each) collected in 2012 and 2013 from the St. Lawrence River (Pelletier 2013). The sampling locations were selected from within the immediate dispersion plume of effluent originating from the dense urban centre of Montréal, QC and are reflective of near-source exposure to urban contamination.

Environmental Fate

Level III fugacity modelling (EQC 2011) simulates the distribution of a substance in a hypothetical, evaluative environment known as the "unit world". The updated 2011 EQC model simulates the environmental distribution of a chemical at a regional scale (i.e., 100,000 km^2) and outputs the fraction of the total mass in each compartment from an emission into the unit world and the resulting concentration in each compartment.

The mass-fraction distribution of M4Q determined using the EQC model is given in Table 4, using individual steady-state emissions to air, water and soil. The Level III EQC model assumes non-equilibrium conditions between environmental compartments, but equilibrium within compartments. The results in Table 4 represent the net effect of chemical partitioning, inter-media transport, and loss by both advection (out of the modelled region) and degradation/transformation processes.

The results of Level III fugacity modelling suggest that M4Q can be expected to predominantly reside in air when the substance is released into this compartment or into soil. When released into water, M4Q is expected to primarily distribute into sediment with a small proportion remaining in the water column. Similarly, while M4Q released into soil is expected to primarily distribute into air, a small proportion is predicted to remain within the soil compartment. Input values used in the modelling are provided in Appendix I.

Table 4. Results of Level III fugacity modelling (EQC 2011), showing percent partitioning into each medium for three release scenarios

Substance released to:	Air	Water	Soil	Sediment
Air (100%)	100	0	0	0
Water (100%)	3	19	0	78
Soil (100%)	92	0	8	0

The moderate vapour pressure (8.96 Pa at 25°C; Table 2) indicates that M4Q is volatile and, if released into air, can be expected to remain within this compartment with little tendency to move into other environmental compartments. The EQC model predicts that approximately 67% of the amount emitted to air will be advected out of the unit world and undergo further atmospheric transport, while the remaining 33% will be reacted (degraded) in the atmosphere.

The very low water solubility of 0.00015 mg/L (25°C) and high calculated log K_{oc} values of 5.2 to 5.6 (Table 2) indicate that M4Q released into water will tend to adsorb to suspended solids and sediment. Thus, if water is a receiving medium, M4Q is expected to primarily reside within the sediment compartment, with a small proportion remaining in the water column. The EQC model predicts that under steady-state conditions of continuous release into water, approximately 19% will remain in the water (of the 19% in water about 4% will be adsorbed to suspended solids) and the remaining amount will distribute to sediment (78%) or escape from water surfaces into air (3%). While the calculated Henry's Law constant for this substance is high, volatilization from water surfaces is not predicted to be a dominant fate process according to the Level III model. However, in the environment, evaporation from the water surface could be enhanced under some environmental conditions such as those of increased surface turbulence and temperature. As well, other factors will influence the relative importance of sorption and volatilization in the partitioning of M4Q in water. These include the nature of the receiving water body, in particular the concentrations of suspended sediment and organic matter, as well as a longer predicted half-life in sediment as compared with water, resulting in a larger mass fraction being retained in the sediment compartment due to slower removal processes.

If released to soil, the moderate vapour pressure suggests there will be significant tendency (92%) for M4Q to volatilize from the soil surface into air. About 8% of the amount released to soil is expected to remain within the soil compartment (Table 4), with approximately 33% of this amount expected to exist in soil pore air and 67% adsorbed to solids. This adsorptivity, along with low water solubility (0.00015 mg/L; Table 2), suggests that M4Q will be relatively immobile in soil.

Long-range Transport Potential

The Transport and Persistence Level III Model (TaPL3) (TaPL3 2000) was used to estimate the Characteristic Travel Distance (CTD), defined as the maximum distance traveled in air by 63% of the substance. Beyer et al. (2000) have proposed that CTDs of greater than 2000 km represent high long-range atmospheric transport potential (LRATP), 700 to 2000 km represent moderate LRATP, and less than 700 km represent low LRATP. Based on a TaPL3 CTD estimate of 2959 km, the LRATP of M4Q is considered to be high. This means that M4Q is judged to be subject to atmospheric transport to remote regions such as the Arctic.

The OECD POPs Screening Model can also be used to help identify chemicals with high persistence and long-range transport potential (Scheringer et al. 2009). The OECD model is a global model that compartmentalizes the earth into air, water and soil. This model is "transport-oriented" rather than "target-oriented", as it simply identifies the CTD without indicating specifically where a substance may be transported to (Fenner et al. 2005). Klasmeier et al. (2006) have suggested that a threshold of 5098 km, based on the model's CTD estimate for PCB-180, can be used to identify substances with high long-range-transport potential. PCB-180 is empirically known to be found in remote regions. The CTD calculated for M4Q using the OECD model is 2963 km, indicating that M4Q has significant potential for transport in air, although this is below the boundary suggested for global pollutants by Klasmeier et al. (2006). The OECD POPs Screening Model also calculates the transfer efficiency (TE), which is the percentage of emission flux to air that is deposited to the surface (water and soil) in a remote region (TE % = D/E × 100, where E is the emission flux to air and D is the deposition flux to surface media in a target region). The TE for M4Q was calculated to be 5.2×10^{-3} %, which is below the boundary of 2.248 % (PCB-28) established based on the model's reference substances empirically known to be deposited from air to soil or water. The low TE means that although M4Q has the potential for long-range travel in the atmosphere, it is unlikely to be deposited to Earth's surface in any remote region, even cold environments.

Input values used to model the long-range transport potential of M4Q are provided in Appendix I.

In addition, the log K_{oa} of 5.17 and log K_{aw} of 4.27 (Xu and Kropscott 2006; Kozerski 2012) suggest that M4Q will have a low Arctic contamination potential (ACP) when examined using chemical partitioning space plots as described by Wania (2003, 2006). Chemicals such as these are often referred to as "fliers", in that they have LRATP, but do not necessarily end up in other environmental media due to their high vapour pressures.

Model estimates indicate that M4Q has significant atmospheric transport potential and may be capable of reaching areas far from its emission sources. However, despite the ability for long-range travel in the atmosphere, the substance lacks the potential to be deposited to water or soil in remote regions and is considered to have low Arctic contamination potential. It is expected that airborne M4Q will eventually be degraded by hydroxyl radicals in the air.

Persistence and Bioaccumulation Potential

Environmental Persistence

Relevant Media

Based on the results of Level III fugacity modelling, air and sediment are considered to be primary media of relevance for M4Q, depending upon the compartment of release. The substance is expected to be present to a lesser extent in water and soil when released directly into these media (see Table 4).

Data Sources and Modelling of Persistence

No experimental degradation data were found for M4Q and Quantitative Structure-Activity Relationships (QSARs) were used to evaluate the potential for degradation in the environment. The results are summarized in Table 5 below. Given the ecological importance of the water compartment and the fact that M4Q can be expected to be released to this compartment, biodegradation in water was primarily examined. In the absence of suitable biodegradation models for soil and sediment, the results obtained for water were extrapolated to obtain estimates for the biodegradation potential of M4Q in these media.

Empirical and modelled data derived for other volatile methyl siloxanes (VMS) also provided an important line of evidence, particularly with regard to abiotic degradation processes, and were ultimately used to conclude on the potential for persistence in water and soil.

Table 5. Modelled data for degradation of M4Q

Fate process	Model and model basis	Model result and prediction	Extrapolated half-life (days)
Atmospheric oxidation	AOPWIN 2008[a]	$t_{1/2}$ = 5.9 days	> 2
Ozone reaction	AOPWIN 2008[a]	n/a[b]	n/a
Hydrolysis	HYDROWIN 2008[a]	n/a[b]	n/a
Primary biodegradation (aerobic)	BIOWIN 2008[a] Sub-model 4: Expert Survey (qualitative results)	3.3[c] "biodegrades slowly"	< 182
Ultimate biodegradation (aerobic)	BIOWIN 2008[a] Sub-model 3: Expert Survey (qualitative results)	2.3[c] "biodegrades slowly"	> 182
Ultimate biodegradation (aerobic)	BIOWIN 2008[a] Sub-model 5: MITI linear probability	-0.4[d] "biodegrades very slowly"	> 182
Ultimate biodegradation (aerobic)	BIOWIN 2008[a] Sub-model 6: MITI non-linear probability	0.0[d] "biodegrades very slowly"	> 182
Ultimate biodegradation (aerobic)	CATABOL c2004-2008 % BOD (biological oxygen demand)	% BOD = 6.5 "biodegrades very slowly"	> 182

[a] EPI Suite (2000-2008).
[b] Model does not provide an estimate for this type of structure.
[c] Output is a numerical score from 0 to 5, corresponding to approximate degradation time frames as follows: 5.0, hours; 4.0, days; 3.0, weeks; 2.0, months; 1.0, longer.
[d] Output is a probability score.

The predicted atmospheric half-life of 5.9 days (AOPWIN 2008; Table 5) indicates that M4Q will oxidize in air. AOPWIN (2008) predicts a slightly longer atmospheric half-life of 8.9 days for the linear VMS, MDM (CAS RN 107-51-7) and half-lives of 5.96 to 8.9 days for the cyclic VMS, D4 (CAS RN 556-67-2), D5 (CAS RN 541-02-6) and D6 (CAS RN 540-97-6). By comparison, empirical atmospheric half-lives for MDM are 5.8 and 8.8 days (Environment Canada, Health Canada 2014), while those of the cyclic VMS range from 3.0 to 22.8 days (Environment Canada, Health Canada 2008a, 2008b, 2008c). No estimate is available for the

reaction half-life of M4Q with other photo-oxidative species in the atmosphere, such as ozone. However, as with other VMS, it is expected that reactions with hydroxyl radicals will be the most important degradation process for M4Q in the atmosphere.

HYDROWIN (2008) provides no estimate for the hydrolysis potential of M4Q, as organosilicones such as M4Q are not represented in the training set of the model and are therefore outside the model domain. Empirical data for other VMS indicate that hydrolysis is an important degradation pathway for these substances in the environment. Hydrolysis half-lives of 0.12 to 60.9 days were reported for MDM in the water temperature range of 10 to 35˚C and pH range of 7 to 9 (Mosey and Kozerski 2008). Half-lives for the cyclic VMS D4 and D5 under similar conditions were 0.008 to 23 days (Durham 2005) and 0.18 to 425 days (Durham 2006), respectively. Slowest hydrolysis rates for all three VMS occurred at a neutral pH of 6.9 to 7. The difference in rate between neutral pH and more acidic or basic pH was most marked for D5, where half-lives in the pH range of 4 to 9, excluding pH 7, were 0.18 to 15 days while those at pH 7 were 25 to 425 days (Durham 2006). Brooke et al. (2009) reviewed the D5 results and concluded that the kinetics of VMS hydrolysis can be described in terms of an acid (hydronium ion) catalyzed component and a base (hydroxonium ion) catalyzed component, with only a small contribution of uncatalyzed reaction to the overall reaction rate. The greater presence of these ions at lower and higher pH relative to neutral pH therefore accounts for the observed higher hydrolysis rates.

Degradation through surface-acid-catalyzed hydrolysis reactions has been demonstrated to contribute significantly to the removal of VMS in a soil environment, and it is expected that M4Q present in soil will also be subject to this degradation pathway. Degradation half-lives of 1.5 to 120 days were reported for MDM in soil at 21˚C and a relative humidity (RH) range of 32% to 100% (Xu and Doede 2010; Xu et al. 2012), while those of D4 were 3.54 to 5.25 days in soils of 32% and 93% RH, respectively (Xu and Chandra 1999). Volatilization from the soil surface is also a factor in the removal of VMS from soil. Hirner et al. (2003) described the interaction between degradation and volatilization of VMS in soil, with degradation predominating in soils having low moisture content. As soil moisture increases, volatilization is accelerated and becomes the dominant removal process. Based on the interaction between the two processes, the authors considered that VMS were unlikely to persist in any soil within a wide range of moisture conditions (Hirner et al. 2003).

BIOWIN Sub-model 4, a primary survey model, estimates that M4Q will undergo primary biodegradation in water with a half-life of less than 182 days; however, ultimate biodegradation (i.e., complete mineralization) will occur slowly. Results from all four ultimate degradation models (BIOWIN Sub-models 3, 5 and 6 and CATABOL c2004-2008; Table 5) suggest that the half-life for ultimate biodegradation of M4Q in water will likely exceed 182 days.

While organosilicone substances have limited representation in the training sets of the selected biodegradation models, the predicted slow ultimate biodegradation is considered reasonable in terms of what would be expected for biodegradation of a highly branched structure such as that of M4Q (see Table 1). As well, the results are consistent with empirical and modelled data obtained for other VMS which indicate that biodegradation for these substances is slow. For example, the linear VMS MDM showed little biodegradation in standard ready biodegradation

testing (OECD 2006), with a mean percent biodegradation of -3.7% at the end of the 28-day test period (Schaefer and Matthews 2009). Low potential for biodegradation was also observed in similar testing with the cyclic VMS D4, D5 and D6, with mean percent biodegradation results ranging from 0.14 to 4.47% for the three substances (Springborn Smithers Laboratories 2004, 2005a, 2005b). SEHSC (2011) reported a biodegradation half-life of 365 days for D4 in sediment. Considered together, the results indicate that biodegradation is unlikely to be an important removal process for VMS such as M4Q in the environment.

Summary of Persistence Potential

No empirical degradation data were found for M4Q and modelled estimates, as well as read-across data from other VMS, were used to analyze the potential for environmental persistence. A predicted half-life of 5.9 days was determined for the degradation of M4Q in air. The predicted half-life is comparable with those derived for other VMS, which range from 5.96 to 8.9 days, adding weight to the prediction. The results indicate that M4Q is not recalcitrant in air, although the longer residence time suggests that M4Q may have significant atmospheric transport potential and may be capable of reaching areas far from its emission sources. However, it has low Arctic contamination potential (see Environmental Fate section) as it is not likely to be deposited to water or soil in remote regions.

Modelled biodegradation half-life estimates predict that M4Q will biodegrade slowly in the environment, with ultimate biodegradation half-lives of greater than 182 days in water and soil and greater than 365 days in sediment. This predicted slow biodegradation is consistent with empirical and modelled data available for other VMS. However, the empirical evidence indicates that abiotic degradation processes such as hydrolysis are important removal mechanisms for linear and cyclic VMS in the environment and these processes are also expected to contribute to the removal of M4Q. The preponderance of data indicates that VMS will hydrolyze readily in water and soil, and based on this, M4Q is considered to not persist in these media. No empirical degradation data were found for VMS in sediment. Based on a modelled biodegradation half-life of greater than 182 days for the ultimate biodegradation of M4Q in water, and using a proportionality ratio of 1:4 for half-life in water: sediment as derived by Boethling et al. (1995), the biodegradation half-life of M4Q in sediment is estimated to be in the order of years. This half-life is consistent with the calculated value of 365 days reported for the cyclic VMS, D4, and indicates that M4Q has a high potential to remain resident in sediment for an extended period of time.

Potential for Bioaccumulation

Data Gathering

In order to provide the best possible weight of evidence for bioaccumulation potential of M4Q, empirical and modelled property data for M4Q as well as property data for the structurally and mechanistically similar substances L4, L5, MDM and PTS were considered. Their structures and relevant physical-chemical property data are given in Appendix V for comparison purposes.

The analogous structures described in Appendix V have greater than 83% structural comparability using the CHEMID (2010) software. Based on data in Appendix V, M4Q is considered to have less pelagic bioavailability than MDM or L4 but comparable bioavailability to PTS and L5. M4Q is slightly more water soluble than L5 (or perhaps comparable if measurement variability is considered) and slightly less soluble in water than PTS. However, the predicted K_{oc} for these three compounds is very comparable. M4Q has comparable molecular dimensions to PTS, suggesting that uptake in fish during laboratory BCF testing could be comparable, which cannot easily be said for L5 because it is somewhat larger than M4Q. The dimensions of L4 and MDM are smaller than M4Q and these compounds appear to be more bioavailable in water, which would suggest that uptake rates from water could be substantially different between these chemicals and M4Q. Therefore, for reasons explained further on in this section, it is reasonable to consider PTS as the primary analogue for bioconcentration. Data for MDM, L4 and L5 should provide lower and upper boundaries of bioconcentration for M4Q, respectively, if molecular size is considered in isolation. It is reasonable, however, to consider all four analogues for dietary uptake (i.e., BMF) for real world exposures. Factors addressing aqueous bioavailability via the gills may not apply to dietary uptake. Also, molecular dimensions of these chemicals vary only a small amount from M4Q and the gastrointestinal tract (GIT) is not subject to the same molecular resistance as gill surfaces (Arnot et al. 2010) (see below discussion).

Bioconcentration Factor (BCF)

No experimental BCF data were found for M4Q. However, experimental data are available for an acceptable analogue substance, PTS (Trisiloxane, 1,1,1,5,5,5-hexamethyl-3- phenyl-3-[(trimethylsilyl)oxy]-; CAS RN 2116-84-9). Blankenship et al. (2004) exposed bluegill sunfish, *Lepomis macrochirus*, to water concentrations of 0.0008 mg/L (0.001 nominal) and 0.0044 mg/L (0.006 nominal) PTS for 45 days, followed by a 60-day depuration period. Steady-state BCF values for the low-dose concentration were 404, 1508 and 1011 for edible, non-edible and whole fish fractions, respectively, while those for respective fractions in the high dose were 164, 566 and 384 (Table 6). The study also determined kinetic BCFs of 620, 3827 and 2292 for edible, non-edible and whole fish fractions, respectively. The kinetic rate constants from this study are reported in Table 8. The concentration of PTS depurated slowly in fish and the mean measured concentration of PTS in edible, non-edible, and whole fish by Day 60 depuration was 0.073, 0.678 and 0.407 mg/kg, respectively. Estimates of time to reach 50% clearance for edible, non-edible and whole fish tissue were 24, 50 and 43 days, respectively (Blankenship et al. 2004).

A bioconcentration study was conducted using L5 (Pentasiloxane, dodecamethyl-; CAS RN 141-63-9) (SEHSC 2006). Fathead minnow, *Pimephales promelas*, were exposed for 35 days to nominal concentrations of 7.0×10^{-5} and 7.0×10^{-6} mg/L in a flow-through test system, followed by a depuration period of 35 days. The water solubility of L5 is 7.0×10^{-5} mg/L. The high volatility and low water solubility of L5 required application of special procedures to minimize loss of the substance from the test system. These included use of a solvent, sealed mixing jars, and maximizing of diluter system flow rates in order to reduce evaporative losses. Despite these precautions, some loss of the test substance occurred and mean measured doses were 3.9×10^{-5} and 4.0×10^{-6} mg/L in the high and low dose concentrations, respectively. Steady-state BCFs of 1240 and 1430 were determined for the 3.9×10^{-5} and 4.0×10^{-6} mg/L concentrations, respectively,

while the respective kinetic BCF values calculated from uptake and depuration rates were 1240 and 1450 (Table 6). Greater than 90% of the test substance was removed from the fish tissue over the 35-day depuration period. The kinetic rate constants from these studies are reported in Table 8.

Table 6. Empirical data for bioaccumulation of PTS and L5

Substance	Test organism	Endpoint	Steady-State and Kinetic Values (L/kg)[a]	Reference
PTS	Bluegill sunfish, *Lepomis macrochirus*	BCF	404-1508 (0.0008 mg/L)[b] 164-566 (0.0044 mg/L)[b] 620-3827[c]	Blankenship et al. 2004*
L5	Fathead minnow, *Pimephales promelas*	BCF	1430[b], 1450[c] (4.0×10^{-6} mg/L) 1240[b], 1240[c] (3.9×10^{-5} mg/L)	SEHSC 2006

[a] Values in parentheses represent the test concentrations at which the BCFs were derived.
[b] Steady-state BCF values
[c] Kinetic BCF values
* A Robust Study Summary for this study is available upon request.

The BCF of M4Q was estimated using a kinetic mass-balance model based on Arnot and Gobas (2003a) which included normalized metabolic rate constants (as explained in the kinetic rate constants discussion below). The resulting BCF predicted for the middle trophic level fish using the Arnot-Gobas mass-balance model (v1.11) and the normalized k_M of 0.010 day^{-1} is 1260, which compares well with the analogue values in Table 6. The predicted BCF using the Arnot-Gobas mass balance model (v1.11) using a k_M of approximately 0.016 d^{-1} for a 10g fish with a 5% lipid content fish results is a BCF of 812, which is also very comparable to the steady-state BCFs reported in Table 6.

Arnot and Gobas (2006) critically evaluated available bioaccumulation data (BCF and BAF) for fish and other organisms and created an empirical database of quality BCF and BAF values (Arnot and Gobas 2003b). In Arnot and Gobas (2006), at a log K_{ow} of 9.6 for M4Q, the empirical distribution of "acceptable" fish BCF data shows that there are no recorded BCFs above approximately log K_{ow} 8.2.

The ranges of steady-state and kinetic BCFs for analogues of M4Q in Table 6 are in the range 164 to 3827 (even with the use of solubilizing agents). This is likely due to the uptake rate from water being mitigated to some extent by steric hindrance, thus permitting other elimination processes to mitigate the overall bioconcentration. Information regarding molecular size and cross-sectional diameters are useful to consider and are commonly used by international jurisdictions such as the European Union (ECHA 2012) as weight of evidence for bioaccumulation potential. Recent investigations relating fish BCF data and molecular size parameters (Dimitrov et al. 2002, 2005) suggest that the probability of a molecule crossing cell membranes as a result of passive diffusion declines significantly with increasing maximum diameter (D_{max}). The probability of passive diffusion decreases appreciably when the maximum diameter is greater than approximately 1.5 nm and much more so for molecules having a maximum diameter of greater than 1.7 nm. Sakuratani et al. (2008) have also investigated the effect of cross-sectional diameter on passive diffusion in a BCF test set of about 1200 new and existing chemicals. They observed that substances that do not have a very high bioconcentration

potential (BCF less than 5000) often have a D_{max} of greater than 2.0 nm and an effective diameter (D_{eff}) greater than 1.1 nm.

However, as Arnot et al. (2010) have noted, there are uncertainties associated with the thresholds proposed by Dimitrov et al. (2002, 2005) and Sakuratani et al. (2008) since the BCF studies used to derive them were not critically evaluated. Arnot et al. (2010) point out that molecular size influences solubility and diffusivity in water and organic phases (membranes), and larger molecules may have slower uptake rates. However, these same kinetic constraints apply to diffusive routes of chemical elimination (i.e., slow in = slow out). Thus, significant bioaccumulation potential may remain for substances that are subject to slow absorption processes, if they are slowly biotransformed or slowly eliminated by other processes. Therefore, when evaluating bioaccumulation potential, molecular size information is examined with care and considered together with other relevant lines of evidence.

Based on 3D analysis of the conformers calculated using the Baseline Bioaccumulation Model with Mitigating Factors (Dimitrov et al. 2005), the maximum diameter of PTS and L5 ranges from 1.7 nm to 1.2 nm and the effective diameter ranges from 1.1 nm to 1.1 nm. The maximum diameter of M4Q is 1.3 nm and the effective diameter is 1.2 nm. This suggests that M4Q, PTS and L5 have very similar molecular dimensions, albeit L5 is slightly larger. These compounds may experience some restricted uptake from steric effects at the gill surface (via effective diameter size) and this may help to explain the lower empirical BCFs.

Biomagnification Factor (BMF)

Dow Corning Corporation (2010d) reported an apparent steady-state BMF for M4Q of 0.045 and a lipid-normalized BMF of 0.16 for juvenile rainbow trout, *Oncorhynchus mykiss*, exposed to ^{14}C-radio-labelled M4Q on fish food (approximately 400 µg/kg) for a 42-day period, followed by a 28-day clearance period with clean food (Table 7). Kinetic BMFs based on uptake and depuration rates of 0.00252 g/g/d and 0.0245 d^{-1}, respectively, were 0.10 and 0.37 (for the lipid-adjusted value) and were estimated not including growth rate dilution of the fish over the study period.

A kinetic biomagnification factor (BMF) of 0.26 and a lipid-adjusted kinetic $BMF_{L/L}$ of 0.86 were reported for juvenile rainbow trout, *Oncorhynchus mykiss*, exposed to ^{14}C-radiolabelled MDM on fish food (approximately 500 µg/g) for a 35-day period, followed by a 28-day clearance period with clean food (Drottar 2010; Table 7). The steady-state BMF calculated based on MDM concentrations in fish tissue and feed was 0.11 and the corresponding lipid-normalized value was 0.38. The lipid-normalized BMF is considered to be a more relevant endpoint for assessing biomagnification potential (Arnot and Gobas 2006). Dietary assimilation efficiency in the exposed fish was calculated to be 32% and the elimination or clearance half-life was 18 days, based on a clearance rate constant of 0.0378/day (Drottar 2010).

BMF values describe the process in which the concentration of a chemical in an organism reaches a level that is higher than that in the organism's diet, due to dietary absorption (Gobas and Morrison 2000). A BMF exceeding 1 indicates that biomagnification is occurring. BMF data are considered as indicators of the potential for uptake and accumulation in biota via the diet.

The available biomagnification data suggest that the BMF of M4Q does not exceed 1 for the foodwebs examined.

Table 7. Empirical data for the biomagnification factor of MDM (L3) and M4Q

Substance	Test organism	Endpoint	Steady-State, Kinetic and Lipid Normalized Values (/kg)	Reference
MDM	Rainbow Trout *Oncorhynchus mykiss*	BMF	0.11-0.86	Drottar 2010*
M4Q	Rainbow Trout *Oncorhynchus mykiss*	BMF	0.045-0.37	Dow Corning Corporation 2010d*

* A Robust Study Summary for this study is available upon request.

In the bioaccumulation study for M4Q, Dow Corning Corporation (2010d) noted that comparison of the parent M4Q concentrations and total radioactivity in fish tissue demonstrated that they were essentially the same, indicating that the radioactivity present in the fish tissue was generally parent M4Q. Similar indications were observed with the digestive tract samples over time. Comparison of the parent M4Q concentrations and total radioactivity in digestive tract over time indicated that the radioactivity present in the digestive tract was unchanged M4Q. Comparison of the parent M4Q concentrations with the total radioactivity found in the liver indicated that the radioactivity present in the liver was also primarily parent M4Q (Dow Corning Corporation 2010d).

Similarly, in the MDM bioaccumulation study, comparison of the parent MDM concentrations and total radioactivity in fish tissue and digestive tract samples showed that the radioactivity present was associated with parent MDM (Drottar 2010). However, comparison of parent MDM concentrations and total radioactivity in liver extracts collected on Day 1 of depuration indicated the presence of one or more metabolites. Comparison of radioactivity to parent in the liver extract provided evidence that MDM can be metabolized in rainbow trout (Drottar 2010).

While this provides evidence for some degree of metabolism of M4Q and MDM by rainbow trout, the study results suggest that little biotransformation occurred. In addition, the presence of unknown metabolites does not establish that M4Q and MDM were completely metabolized nor is there any information on the rate of metabolism. The kinetic rate constants from these studies are also reported in Table 8.

Dietary assimilation efficiency (E_D) is also a key parameter for estimating the BAF using kinetic mass-balance models such as that of Arnot and Gobas (2003a, 2004) because it is used to calculate the dietary uptake rate constant (k_D) and is related to log K_{ow} of the substance in question (Kelly et al. 2004). As noted by Arnot (2010), some chemicals are subject to degradation in the gastrointestinal tract (GIT) and gut epithelial tissues and these processes can reduce the chemical transfer efficiency into the organism and thus the overall biomagnification. In theory, a substance that is highly metabolized in the GIT should have low dietary assimilation

efficiency and slowly metabolized substances a potentially higher assimilation and thus higher biomagnification.

The dietary assimilation efficiency of M4Q reported by Dow Corning Corporation (2010d) is only 8.4% which is well below that of 40 to 60% range reported for some polyhalogenated biphenyl compounds known to have BMF greater than 1 (Kelly et al. 2004). This further suggests some limitation to the uptake of M4Q from the GIT either from steric effects, bound residues in the food, or both. It should be noted that a BMF using the proposed equation in the OECD dietary portion of the draft revision to the 305 guideline (OECD 2011) cannot be calculated for M4Q because the growth rate is higher that the depuration rate constant leading to a negative growth corrected depuration rate constant (i.e., k_{2g}). This shows the effect of growth rate "swamping" the kinetics of the BMF test (see Table 8). Efforts are being made via the OECD to deal with growth rate influences in the 305 dietary test (OECD 2011).

A modified three trophic level version of the Arnot and Gobas (2003a) BAF model was applied in order to estimate the BMF at a log K_{ow} of 9.6 and assuming a dietary assimilation efficiency of 8.4% and a metabolic rate constant of 0.01 d^{-1} for a middle trophic level fish (based on body weight normalization of geomean k_M value from Table 8). The resulting BMF is 0.5, which is quite comparable to the upper range of kinetic BMF reported for M4Q in Table 7, and slightly lower than the upper kinetic BMF of 0.86 reported for MDM.

Kinetic Rate Constants

The Arnot-Gobas model was employed using metabolic rate constants initially normalized to the weight, temperature and lipid content of the fish in the BCF and BMF studies. This was performed using the approach outlined in Arnot et al. (2008a) when BCF or the depuration rate constant is known. The purpose of this is to fit the kinetic model to agree with the observed BCF data, thus providing reasonable estimations of rate constants. The empirically observed and calculated kinetic rate constants are summarized in a mass-balance format in Table 8 below.

Table 8. Kinetic rate constants calculated by Environment Canada for M4Q, PTS, L5 and MDM based on BCF and BMF studies

Substance	Study endpoint	Uptake rate constant day^{-1} (k_1)	Depuration rate constant day^{-1} (k_D)[a]	Gill elimination rate constant day^{-1} (k_2)	Metabolic rate constant day^{-1} (k_M)
M4Q	$BMF_{kinetic}$ (0.10)[a]	0.0025[a]	0.025[a]	0.0000	approximately 0.020[e]
PTS	$BCF_{kinetic}$ (2292)[a]	36.9[a]	0.0161[a]	0.0002[b]	approximately 0.011[c]
PTS	$BCF_{kinetic}$ (1096)[b]	1001.6[b]	n/a	0.0002[b]	0.056[b]
L5	$BCF_{kinetic}$ (1450)	n/a	n/a	n/a	n/a
L5*	$BCF_{kinetic}$ (1445)	1427.0[b]	n/a	0.002[b]	0.060[b]
MDM	BMF_{ss} (0.11)	0.01[a]	0.038[a]	0.00[d]	0.028[d]

Abbreviations: n/a, not available or calculation not needed.
[a] Reported in Blankenship et al. 2004, SEHSC 2006, Dow Corning Corporation 2010d and Drottar 2010.

[b] Calculated using mass-balance approach as outlined in Arnot et al. (2008a) when BCF is known. Rate constants corrected for log K_{ow}, body weight, temperature and lipid content of fish in Dow Corning Corporation study (2010d).
[c] $k_T = k_2 + k_G + k_M + k_E$
[d] Calculated using one compartment BAF model and correcting for log K_{ow}, body weight, temperature and lipid content of fish in Dow Corning Corporation 2010d and Drottar 2010.
[e] Calculated using mass-balance approach as outlined in Arnot et al. (2008a) when depuration rate is known. Rate constants corrected for log K_{ow}, body weight, temperature and lipid content of fish.
* Study details not available at the time of this analysis.

Table 8. Kinetic rate constants calculated by Environment Canada for M4Q, PTS, L5 and MDM based on BCF and BMF studies (continued)

Substance	Study endpoint	Growth rate constant day^{-1} (k_G)	Fecal egestion rate constant day^{-1} (k_E)	Total elimination rate constant day^{-1} (k_T)[e]	Reference
M4Q	$BMF_{kinetic}$ (0.10)[a]	0.037[a]	0.005[d]	0.062	Dow Corning Corp 2010d; Environment Canada (see text)
PTS	$BCF_{kinetic}$ (2292)[a]	0.002[b]	0.004[b]	0.021[b]	Blankenship et al. 2004
PTS	$BCF_{kinetic}$ (1096)[b]	0.002[b]	0.004[b]	0.062	Environment Canada (see text)
L5	$BCF_{kinetic}$ (1450)	n/a	n/a	n/a	SEHSC 2006
L5*	$BCF_{kinetic}$ (1445)	0.002[b]	0.004[b]	0.068	Environment Canada (see text)
MDM	BMF_{ss} (0.11)	0.040[a]	0.010[d]	0.078[d]	Drottar 2010

Abbreviations: n/a, not available or calculation not needed.
[a] Reported in Blankenship et al. 2004, SEHSC 2006, Dow Corning Corporation 2010d and Drottar 2010.
[b] Calculated using mass-balance approach as outlined in Arnot et al. (2008a) when BCF is known. Rate constants corrected for log K_{ow}, body weight, temperature and lipid content of fish in Dow Corning Corporation study (2010d).
[c] $k_T = k_2 + k_G + k_M + k_E$
[d] Calculated using one compartment BAF model and correcting for log K_{ow}, body weight, temperature and lipid content of fish in Dow Corning Corporation 2010d and Drottar 2010.
[e] Calculated using mass-balance approach as outlined in Arnot et al. (2008a) when depuration rate is known. Rate constants corrected for log K_{ow}, body weight, temperature and lipid content of fish.
* Study details not available at the time of this analysis.

The kinetic mass-balance approach fitted to the analogue BCF data predicts BCF values of 1096 and 1445 for PTS and L5, respectively (see Table 8), and these values agree well with those of 2292 (whole fish) and 1240 to 1450 derived empirically for PTS and L5 (Table 6).Thus, there is good confidence that the kinetic rate constants approximate those under laboratory conditions. The calculated total elimination rate constants are in very good agreement with each other (approximately 0.02 to 0.08 d^{-1}) whether derived based on BCF or BMF data. The metabolic rate constants are also in very good agreement and range from 0.01 to 0.06 d^{-1} suggesting a slow rate of biotransformation and supporting the BCF and BMF observations of little biotransformation of parent VMS compounds. For comparison, depuration rate constants of 0.035 and 0.040 d^{-1} were calculated for D4 and D5, respectively, in rainbow trout, *Oncorhynchus mykiss* (Woodburn et al., 2013).

The metabolic competency of an organism can be related to body weight and temperature (e.g., Hu and Layton 2001; Nichols et al. 2007). In order to provide a more representative metabolic rate constant, the geometric mean of the aqueous and dietary metabolic rate constants (i.e., 0.029 d^{-1}) for all compounds in Table 8 was determined. This rate constant was further normalized to

the weight of the middle trophic level fish in the modified Arnot-Gobas model (fish weight =184 g, lipid content = 6.8%, temperature = 10˚C) according to the procedures outlined in Arnot et al. (2008b). The resulting k_M when rounded is 0.010 d^{-1}. To provide some context within the broader class of VMS substances, this k_M value lies within the ranges of the values available for other low molecular weight VMS of 0.008 to 0.08 (median value 0.02) and 0.001 to 0.01 (median 0.004) for D4 and D5, respectively (Environment Canada, Health Canada 2008a, 2008b). The middle trophic level fish was used to represent overall model output as suggested by the model developer and is most representative of fish weight likely to be consumed by an avian or terrestrial piscivore; it also has a lipid content of 6.8%, which is considered representative of Canadian conditions. The calculated k_M value is consistent with the analysis for metabolites conducted at steady-state conditions in the bioaccumulation study from the Dow Corning Corporation (2010d) in which the radio-labelled material was present primarily as the parent M4Q, thus supporting the notion of "slow metabolic breakdown" of this substance.

The k_M, based on the data from Table 8, for M4Q for a 10 g fish at 15˚C was calculated to be 0.016 d^{-1} using the method of Arnot et al. (2008b). Examination of the k_M database from Arnot et al. (2008b) for a 10 g fish at 15˚C shows that chemicals with log K_{ow} approximately 7.8 to 9.0 have a lower k_M of approximately 0.001 to 0.003 day^{-1}, but can range to 0.01 day^{-1}. These substances (e.g., decachlorobiphenyl, nonachlorobiphenyl, heptachlorobiphenyl), all have BCFs in the 10^5 range noting that octachloronapthalene has a measured BCF of less than 1000 (Fox et al. 1994; Gobas et al. 1989; Oliver and Nimi 1988). The laboratory BCF data are much lower than the majority of these highly chlorinated substances. This suggests that a slightly faster rate of metabolism (0.016 d^{-1} at 10g), lower aquatic bioavailability, possible steric effects and other routes of elimination (e.g., fecal egestion and growth dilution) could be significant for mitigating the bioconcentration potential of M4Q compared with the halogenated organics.

Trophic Magnification Factor (TMF)

The TMF is a measure of the biomagnification potential of a substance within a studied foodweb under field conditions. It is estimated by correlating the normalized substance concentrations in biota at different trophic levels. A positive slope of the lipid-normalized concentration to trophic level regression line indicates that the substance concentration increases over several trophic levels and biomagnification is occurring (Weisbrod et al. 2009). Conversely, a TMF below 1 indicates trophic dilution, which is largely a function of metabolism.

No TMF values were available for M4Q or its analogues at the time of this analysis. Based on an empirical BMF range of 0.045 to 0.37 (Table 7), M4Q is expected to have low potential to biomagnify through foodwebs and is therefore likely to have a TMF of less than 1.

Bioaccumulation Factor (BAF)

Bioaccumulation factors are measured under field conditions as the ratio of the whole body burden of chemical taken up from all exposures to that of the ambient water concentrations. No such field data are available for any of the VMS considered in this bioaccumulation analysis. Measures of BAF are a preferred metric for assessing the bioaccumulation potential of substances because they incorporate all chemical exposures to an organism including the diet

which predominates for substances with log K_{ow} greater than approximately 4.0 (Arnot and Gobas 2003a).

At a log K_{ow} of 9.6, the predicted bioavailable fraction of M4Q in the water column (excluding loss from volatilization) according to mass-balance fish models is less than 1%, which suggests that uptake from water via the gills is not a relevant exposure for M4Q. However, if the log K_{oc} of approximately 5.2 is used, the majority fraction (approximately 90%) of M4Q will be in the dissolved phase in water. This analysis suggests that gill uptake from the water phase is of high relevance for this chemical.

In the absence of empirical data, estimates of BAF were generated using a three trophic level version of the mass-balance kinetic model from Arnot and Gobas (2003a) by correcting the default dietary assimilation efficiency of 19% according to the alpha value of 8.4% reported in the M4Q BMF study from Dow Corning Corporation (2010d). This has a direct impact on the default dietary uptake rate (k_D) assumed by the model. The BAF prediction for the middle trophic level fish using the normalized metabolic rate constant of 0.010 d^{-1} and E_D of 8.4% results in a BAF for the middle trophic level fish of approximately 288 000 which is considered to be consistent with the slow metabolism rate of M4Q and high log K_{ow}.

Possible overestimation of the middle trophic level fish BAF was considered, given the low dietary assimilation efficiency of M4Q. The predicted BMF used in the model for calculation of the BAF is in good agreement with observed BMF results for M4Q and MDM, but the BAF model assumes the "realized foodweb magnification factor"[3] or total trophic magnification factor is 14 which is likely over-estimated in the model. If this value is set to less than 1 to be comparable to a TMF for D5 (using upper bound TMF of 0.7) and thus representing a much lower total magnification in the model, the resulting BAF is approximately 14 800. These predictions have some degree of uncertainty because the log K_{ow} of M4Q at 9.6 is outside of the empirical log K_{ow} domain of the model, suggesting that substances at this log K_{ow} are simply not bioavailable to aquatic organisms or BAFs have not been measured for extremely hydrophobic substances. However, given a log K_{oc} orders of magnitude lower than the log K_{ow}, M4Q can still be considered in the model domain for bioavailability making predictions less uncertain. Although there is some uncertainty regarding the absolute value of BAF generated by the model, it is not likely that, with some exposure, the BAF is substantially less than the value calculated given the kinetic information, particularly slow metabolic rate, relatively high aquatic bioavailability as well as some dietary uptake.

Summary of Bioaccumulation Potential

There is very good consistency between lines of evidence to strongly infer that M4Q will be bioaccumulated from both water and the diet, but may not biomagnify between trophic levels and within foodwebs. M4Q has a very high log K_{ow} and slow rate of metabolism not easily compared to other chemicals that have been empirically observed to highly bioconcentrate or bioaccumulate from water. The intrinsic properties of M4Q indicate that there is potentially a

[3] The realized foodweb magnification factor is the model estimate of total magnification from the base of the foodweb to the diet of the middle trophic level fish. This is called 'beta" in the model and is different from a TMF which is the average magnification per trophic level.

significant bioavailable fraction of M4Q in natural waters and thus water remains a relevant exposure medium contributing to potential body burdens in biota. There is also very good consistency between the kinetic parameters calculated for all the VMS analysed in this assessment which suggests that elimination of M4Q for fish is likely not a result of significant metabolism. However, uptake efficiency of M4Q from water and diet is likely at a slower rate than smaller VMS and cyclic VMS which may limit the maximum potential body burden. Greater weight would be given to this line of evidence if metabolism of M4Q in biota was faster, because together the two factors of decreased uptake efficiency and rapid metabolism would likely result in much lower concentrations of M4Q in the tissues and organs. The estimate of BAF (approximately 14 800) is based on the intrinsic properties of M4Q and the model receptor and assumes a steady-state of exposure in the environment. Actual environmental exposure to M4Q may be limited because of low emission rates, but field measurements of BAFs near to emission sources are not currently available to preclude its relevance in this assessment. The BAF has important implications for exposures at individual trophic levels of foodwebs, but perhaps not between trophic levels or the entire foodweb suggested by factors such as the BMF and TMF.

Potential to Cause Ecological Harm

Ecological Effects Assessment

Data Sources

Both empirical and modelled toxicity data were considered for M4Q. Consideration was also given to information on the possible mode of action. In the absence of empirical and modelled terrestrial toxicity data for M4Q, empirical data for the cyclic VMS, D5, were used for comparative purposes in the examination of potential for terrestrial effects. As non-polar narcosis is the most likely mode of action for all organosilicone compounds (see below), and chemical structure is of lesser importance for this mode of action, examining terrestrial toxicity data for D5 in the context of potential M4Q terrestrial toxicity was considered meaningful.

Mode of action

No information was found on the mode of action of M4Q. However, a non-specific, non-polar narcosis mechanism of toxicity has been proposed for other organosilicone compounds, such as the linear VMS octamethlytrisiloxane (MDM; CAS RN 107-51-7; see Environment Canada, Health Canada 2014) and the cyclic VMS octamethylcyclotetrasiloxane (D4; CAS RN 556-67-2) (Hobson and Silberhorn 1995; Redman et al. 2012).

Empirical Studies – Aquatic/Sediment Compartment

Experimental ecological effects data for M4Q that were used to evaluate the potential for adverse effects in the Canadian aquatic environment are summarized in Table 9a.

Table 9a. Empirical aquatic toxicity data for M4Q

Test organism	Type of test	Endpoint	Value[a]	Reference
Rainbow trout, *Oncorhynchus mykiss*	Acute (96 hours)	NOEC[b]	0.000182 mg/L	Dow Corning Corporation 2010a*
Rainbow trout, *Oncorhynchus mykiss*	Acute (96 hours)	LOEC[c]	> 0.000182 mg/L	Dow Corning Corporation 2010a*
Rainbow trout, *Oncorhynchus mykiss*	Chronic (14 days)	NOEC	0.000159 mg/L	Dow Corning Corporation 2010c*
Rainbow trout, *Oncorhynchus mykiss*	Chronic (14 days)	LOEC	> 0.000159 mg/L	Dow Corning Corporation 2010c*
Water flea, *Daphnia magna*	Chronic (21 days)	Survival, growth, reproduction NOEC	0.000191 mg/L	Dow Corning Corporation 2010b*
Water flea, *Daphnia magna*	Chronic (21 days)	Survival, growth, reproduction LOEC	> 0.000191 mg/L	Dow Corning Corporation 2010b*
Chironomus riparius, *midge*	Chronic (28 days)	Emergence NOEC	56 mg/kg dw	Dow Corning Corporation 2013
Chironomus riparius, *midge*	Chronic (28 days)	Emergence LOEC	> 56 mg/kg dw	Dow Corning Corporation 2013
Chironomus riparius, *midge*	Chronic (28 days)	Development rate NOEC	10 mg/kg dw	Dow Corning Corporation 2013
Chironomus riparius, midge	Chronic (28 days)	Development rate LOEC	17 mg/kg dw	Dow Corning Corporation 2013

Abbreviations: dw, dry weight (of sediment)
[a] All values are reported as mean measured concentrations.
[b] NOEC – The no-observed-effect concentration is the highest concentration in a toxicity test not causing a statistically significant effect in comparison to the controls. In this study, the NOEC was equal to the highest concentration tested.
[c] LOEC – The lowest-observed-effect concentration is the lowest concentration in a toxicity test that caused a statistically significant effect in comparison to the controls.
* A Robust Study Summary for this study is available upon request.

No observable adverse effects were seen at test concentrations up to and slightly above the reported water solubility of 0.00015 mg/L in acute water column testing with rainbow trout, *Oncorhynchus mykiss*, and in chronic testing with *O. mykiss* and the water flea, *Daphnia magna* (Dow Corning Corporation 2010a, 2010b, 2010c). Analytical determinations were performed in all studies, and the results presented in Table 9a are expressed in terms of mean measured concentrations.

Mean percent emergence and development rate were examined in 28-day sediment toxicity testing with the freshwater midge, *Chironomus riparius*, and M4Q incorporated into natural sediment containing 3.1% organic carbon (OC) (Dow Corning Corporation 2013). Percent emergence in the treatments did not differ significantly from that in the controls, however development rates were statistically lower at a lowest mean measured test concentration of 17 mg/kg dw of sediment. The lowest-observed-effect concentration (LOEC) for the study was therefore 17 mg/kg dw and the no-observed-effect concentration (NOEC) was 10 mg/kg dw.

The saturation concentration of M4Q in sediment can be determined using the relationship:

$$C_s = C_w \times K_{oc} \times f_{oc}$$

where:
C_s = saturation concentration (mg/kg dw)

C_w = water solubility of M4Q (mg/L) = 0.00015 mg/L (Table 2)
K_{oc} = organic carbon-water partition coefficient of M4Q = 158,489 L/kg OC (log K_{oc} 5.2; Table 2)
f_{oc} = fraction of organic carbon (OC) in the sediment (unitless)

Saturation concentration reflects the theoretical thermodynamic saturation concentration of a compound in a given medium at equilibrium. It cannot be exceeded according to thermodynamic principles. In surface water, however, the presence of co-solvents or surfactants can create conditions that allow for an "apparent solubility" to be observed which is greater than the maximum solubility. In solid phases, such as sediments and soils, saturation concentration is a direct function of the amount of organic carbon present in the matrix if it is assumed that only hydrophobic interactions with organic matter occur. Sediment organic carbon content can vary from location to location and often average carbon contents are used for calculating saturation concentrations in sediments. The apparent solubility in water, and saturation concentrations in sediment or soil, can increase or decrease the bioavailability of a compound. The values calculated above therefore represent the theoretical saturation concentrations which, for the purposes of bioavailability, may be exceeded under some circumstances. For example, it is difficult to be certain that only hydrophobic interactions are responsible for defining the theoretical saturation concentration in solid phases. These circumstances cannot be easily predicted without specific information regarding the nature of release and the characteristics of the receiving environment.

The saturation concentration of M4Q in sediment having 3.1% OC is 0.71 mg/kg dw, therefore the endpoint values reported in the study exceeded the saturation concentration of M4Q in this sediment. This suggests that free M4Q was present in the test system and may have contributed to the observed effects through factors such as the physical clogging of respiratory surfaces.

Empirical studies – Terrestrial Compartment

No ecological effects studies were found for M4Q in terrestrial plants, soil-dwelling organisms (such as earthworms) or wildlife. A laboratory study using rodents has been conducted with M4Q in order to evaluate the potential for impacts to human health. Relevant data from this study are presented in the Human Health Effects section of this assessment.

Soil toxicity studies with the cyclic VMS D5 are described in the literature and, based on a probable similarity in mode of action, these results are considered relevant to M4Q. A median inhibition concentration (IC_{50}; concentration causing a 50% reduction in a biological measurement) of 767 mg/kg dw of soil was reported for significantly reduced young production in the springtail, *Folsomia candida*, exposed to D5 for 28 days, while the 56-d IC_{50} for the same endpoint in earthworm, *Eisenia fetida,* was greater than the highest test concentration of 4074 mg/kg dw (Environment Canada 2010c). In 14-d testing with D5 and four terrestrial plant species, the most sensitive species was barley, *Hordeum vulgare*, with an IC_{50} of 209 mg/kg dw of soil based on significantly reduced dry mass of roots. The same endpoint was greater than the highest test concentration of 3533 to 4306 mg/kg dw for the other three species tested, red clover (*Trifolium pretense*), durum wheat (*Triticum durum*) and radish (*Raphanus sativus*) (Environment Canada 2010c). By comparison, D5 levels measured in samples of biosolids-

amended soils collected from sites in southern Ontario and Quebec ranged from 0.006 to 0.221 mg/kg dw (Wang et al. 2010). Although soils amended with biosolids represent a maximum or worst-case scenario for D5 in this medium, the measured range is well below the lowest laboratory-derived effect level of 209 mg/kg dw. The proposed similarity in mode of action for D5 and M4Q suggests that terrestrial toxicity endpoint values will be similar between the two substances. As well, M4Q is expected to be present at lower levels in soils than D5, given the higher reported quantities of D5 in Canada relative to that of M4Q (Environment Canada, Health Canada 2008a). Based on this, it is likely that M4Q poses low hazard to terrestrial invertebrates and plants.

Modelled Results

While empirical aquatic toxicity data are available for M4Q, modelled estimates based on Structure-Activity Relationships (SAR) were also considered in evaluating the potential for adverse effects in organisms. The neutral organic SAR in ECOSAR was used to evaluate the potential for effects and, while few siloxanes are present in the training set of this model, the model domain is defined by mode of action, log K_{ow} and water solubility rather than chemical structure. For this reason, the results are considered meaningful for evaluating the potential for toxicity.

Modelled ecotoxicity values used in the analysis of aquatic hazard potential are provided in Table 9b. No reliable modelled estimates are available for terrestrial species.

Table 9b. Modelled data for aquatic toxicity

Test organism	Type of test	Endpoint	Value (mg/L)	Reference
Fish	Acute (96 hours)	LC_{50}[a]	5.9×10^{-5}[b] 4.6×10^{-5}[b]	ECOSAR 2008
Fish	Chronic (14 days)	LC_{50}	6.8×10^{-5}[b]	ECOSAR 2008
Fish	Chronic (30 days)	ChV	1.0×10^{-5}[b]	ECOSAR 2008
Daphnia	Acute (48 hours)	LC_{50}	1.0×10^{-4}[b]	ECOSAR 2008
Daphnia	Chronic (ns[c])	ChV	4.0×10^{-5}[b]	ECOSAR 2008
Mysid shrimp	Acute (96 hours)	LC_{50}	2.6×10^{-7}[b]	ECOSAR 2008
Algae	Acute (96 hours)	EC_{50}[d]	0.001[b]	ECOSAR 2008
Algae	Chronic (ns)	ChV	0.094[b]	ECOSAR 2008

Abbreviations: ChV, chronic value; ns, not specified.
[a] LC_{50} – The concentration of a substance that is estimated to be lethal to 50% of the test organisms.
[b] The log K_{ow} value of 9.6 for M4Q exceeds the maximum log K_{ow} limit defined by the model for this Structure-Activity Relationship (SAR); therefore, no effects at saturation are predicted.
[c] Not specified, i.e., the model does not provide an exposure duration for the estimated chronic value.

[d] EC_{50} – The concentration of a substance that is estimated to cause some effect on 50% of the test organisms.

Maximum log K_{ow} limits defined in ECOSAR were exceeded for all acute and chronic toxicity endpoints; therefore, the model predicts there will be no effects at the water solubility limit for M4Q of 0.00015 mg/L (Table 2).

In summary, no adverse effects were seen in laboratory testing with fish and *Daphnia* exposed to M4Q concentrations up to the limit of water solubility for periods of 96 hours to 21 days. Although considered to be out of the parametric property domain, modelling estimates obtained using the neutral organics SAR in ECOSAR (2008) are consistent with those observed experimentally, and predict no effects at saturation following acute exposure in fish, *Daphnia*, algae and mysid shrimp as well as chronic exposure in fish, *Daphnia* and algae. Therefore, based on the available empirical and modelled data, M4Q has low hazard potential to pelagic organisms at or below the water solubility limit of 0.00015 mg/L.

Significantly reduced development rates were observed in *Chironomus riparius* exposed to M4Q in a 3% OC natural sediment. However, the testing was conducted at concentrations well above the saturation concentration of M4Q in sediment having this OC, and the results may have been influenced by physical factors relating to the presence of undissolved M4Q in the test system.

No information was found on the potential for effects in sediment organisms or terrestrial species, such as terrestrial plants, soil-dwelling invertebrates, and wildlife. Based on results obtained for a mechanistically-similar compound, M4Q is not likely to be hazardous to terrestrial invertebrates or plants.

Derivation of the PNEC

Aquatic compartment

No adverse effects were observed in testing with water column species and a Critical Toxicity Value (CTV) for the aquatic compartment was derived using a no-effect rather than a lowest-effect level. The highest NOEC of 0.000191 mg/L, reported by Dow Corning Corporation (2010b) for 21-day toxicity testing with the water flea, *Daphnia magna*, was selected as the CTV. In addition to providing the highest measured test concentrations available, the 21 day study duration ensured that exposure to the test substance occurred over a sustained period of time. As this endpoint is already a chronic no-effect value, no Assessment Factor (AF) was applied and the Predicted No-Effect Concentration (PNEC) is therefore 0.000191 mg/L.

Sediment compartment

A lowest effect value of 17 mg/kg dw of sediment was obtained in testing with the sediment species, *Chironomus riparius*, and this value is selected as the CTV for sediment. An AF of 10 was applied to the CTV of 17 mg/kg dw in order to account for inter- and intraspecies variability in sensitivity to M4Q, resulting in a PNEC of 1.7 mg/kg dw.

Terrestrial compartment

No ecological effects data were found for M4Q in terrestrial plants, soil-dwelling organisms or wildlife species; therefore, a PNEC could not be derived for the terrestrial compartment.

Ecological Exposure Assessment

Information on the chemical properties of M4Q and business activities associated with its presence in products suggests that most of the substance will remain within products that are ultimately disposed of to landfill. However, release into wastewaters and receiving waters could also occur during some consumer and industrial applications. M4Q released into receiving waters is predicted to distribute primarily into sediment, although a proportion will also remain within the water column or volatilize into the atmosphere. Release of M4Q from consumer applications is expected to be diffuse and, for this reason, industrial sources are considered to provide the highest potential for more concentrated releases into the environment.

Recent monitoring data have reported low concentrations of M4Q in a small number of suspended particulate matter samples; however, the substance was below detection limits in bottom sediments (see Appendix II). Potential concentrations in surface waters near WWTP outfalls were estimated using a modelling approach which considered information relating to import, use and estimated release quantities of the substance, as well as characteristics of Canadian receiving environments.

The concentration of M4Q calculated to be present in receiving waters situated near the discharge point of a wastewater treatment plant was used as the Predicted Environmental Concentration (PEC) in evaluating risk in Canadian surface waters. This surface water PEC was calculated using the equation:

$$C_{water-ind} = \frac{1000 \times Q \times L \times (1-R)}{N \times F \times D}$$

where:

$C_{water-ind}$:	aquatic concentration resulting from industrial releases, mg/L
Q:	total substance quantity used annually at an industrial site, kg/yr
L:	loss to wastewater, fraction
R:	wastewater treatment plant removal rate, fraction
N:	number of annual release days, d/yr
F:	wastewater treatment plant effluent flow, m^3/d
D:	receiving water dilution factor, dimensionless

An exposure analysis was conducted for the aquatic compartment at five sites where products that could contain M4Q were used industrially in 2006 (Environment Canada 2010a). These sites were selected to represent realistic worst-case release scenarios across Canada based on the general assumption that the quantity of a substance released is proportional to the quantity consumed or produced. In the site-specific exposure analysis, each scenario included one facility, one wastewater treatment plant and one receiving water body. The PEC in the receiving water was estimated based on the concentration in the wastewater treatment effluent and a dilution

factor in the receiving water body limited to a maximum value of 10. The concentration in the wastewater treatment effluent was determined based on reported data and a removal rate of 95.2% assuming a level of secondary treatment at the WWTP and was derived using the computer model ASTreat (2006). The effluent flow of a local wastewater treatment plant is proportional to the population served and was in the range of 8000 to 200 000 m^3 per day for the sites considered.

The assumed number of days of release for industrial users (small- or medium-sized facilities) used in the estimation was 250 to 350 days/year, for a continuous release scenario. The PEC values obtained are considered to represent a steady-state level of exposure under a realistic worst-case release scenario in receiving waters near the point of discharge from a WWTP at an industrial site in Canada. Potential losses to pre-treatment wastewaters were estimated as 2.2% based on generic assumptions for four of the five sites and as 90% for a fifth site. These estimated losses were derived using information provided under section 71 of CEPA 1999 (see Sources section above).

Based on the above input values and assumptions, PECs for M4Q are estimated to be in the range of 0.00001 to 0.000026 mg/L. The highest receiving water PEC value of 26 ng/L (0.000026 mg/L) is in the range of the highest measured Canadian WWTP effluent concentration of 31 ng/L (0.000031 mg/L) reported by Alaee (2014) in one of 16 samples collected in 2012(see Appendix Table II-1). Khera (2014) reported higher concentrations of 77 and 113 ng/L in two of 16 effluent samples collected in 2013, although the substance was below detection limits in 63 effluent samples collected from 2012 to 2014 (detection limits were 25 and 53 ng/L). In light of the effect of dilution on these and all effluent samples, the PEC of 26 ng/L is considered to provide a conservative estimate of potential concentrations in Canadian surface waters.
An equilibrium partitioning relationship (EqP) was applied to the highest surface water PEC value of 0.000026 mg/L in order to derive an estimated PEC for the sediment compartment. Based on the principles of hydrophobic interactions,

$$PEC_{sediment} = PEC_{water} \times K_{oc\ sediment} \times f_{oc}$$

where:

$PEC_{sediment}$ = Predicted Exposure Concentration in sediment (mg/kg dw)
PEC_{water} = Predicted Exposure Concentration in water (mg/L) = 0.000026 mg/L
K_{oc} = organic carbon – water partitioning coefficient (L/kg OC) = 158 498 (see Table 2)
$F_{oc\ sediment}$ = fraction of organic carbon in sediment (unitless)

The fraction of organic carbon (OC) present in sediment ($F_{oc\ sediment}$) is expected to vary substantially between locations and an average value of 3% OC was used to represent Canadian sediments.

The resulting $PEC_{sediment}$ value is then 0.124 mg/kg dw of sediment.

Characterization of Ecological Risk

This screening assessment examines information critical to determining whether M4Q meets criteria under section 64 of CEPA 1999, including whether the substance has the potential to cause ecological harm in Canada. Lines of evidence considered in reaching a conclusion include those pertaining to import quantities, environmental release and distribution, potential for environmental persistence, bioaccumulation potential, toxicity and hazard potential, environmental monitoring results, and the results of quantitative risk quotient analyses based on empirical and modelled exposure and effects data.

M4Q is not deliberately manufactured and arises as a reaction by-product or impurity formed in low concentrations during the production of some siloxane products and intermediates. The level of M4Q present in individual products is in the range of equal to or less than 1.5 to equal to or less than 3% w/w. Information indicates that during processing operations where M4Q is formed, the substance becomes bound within the silicone matrix of the product, and that this limits but does not completely eliminate the potential for release into the environment. Import quantities of M4Q into Canada are relatively low, in the range of 1000 to 10 000 kg in 2006.

A life cycle analysis of M4Q in Canada determined that most of the substance (64%) is expected to remain within products that are ultimately disposed of to landfill, while some (32%) may enter pre-treatment wastewaters during industrial activities. Small proportions are also predicted to be incinerated in products (2%), exported out of Canada in products (1%) or released into air from products in use (less than 1%).

M4Q is volatile and it is expected to preferentially distribute into air whenever it is in contact with this environmental medium. This means that M4Q released into air will tend to remain within this compartment, while that released into soil will primarily volatilize and distribute into air. M4Q present in air is predicted to undergo abiotic degradation, primarily through reaction with photochemically-produced atmospheric hydroxyl radicals. The estimated half-life for this reaction is 5.9 days, indicating that the substance is not recalcitrant in air. The longer atmospheric residence time suggests that M4Q may be capable of moving in air currents to areas some distance from the site of release. Modelling conducted to evaluate this potential determined that M4Q does have significant long-range atmospheric transport potential. However, the modelling predicts that M4Q has low Arctic contamination potential, as it is unlikely to deposit from air to water and soil in remote regions.

The distribution of M4Q released into the aquatic environment is less well defined. The low water solubility and high sorption coefficient (log K_{oc}) suggest that M4Q will mostly leave the water phase and sorb to suspended solids with subsequent settling to bed sediment. Recent monitoring data have indeed measured the presence of low concentrations of M4Q in a small number of suspended particulate matter samples, although the substance has not been detected in bottom sediments. A lesser proportion of M4Q is predicted to remain dissolved within the water column and some limited volatilization is also expected to occur. However, environmental conditions such as temperature and surface turbulence can be expected to influence distribution of the substance between the air and water compartments and, for this reason, the ultimate partitioning behaviour of M4Q released into water will likely reflect interactions between

external factors and the chemical properties of moderate vapour pressure, low water solubility, and predicted strong sorption potential.

No empirical degradation data were found for M4Q and modelled biodegradation data, as well as analogue data for other VMS, were used to evaluate the potential for environmental persistence. Modelled estimates predict that M4Q will biodegrade slowly in the environment, which is consistent with empirical and modelled data available for the linear and cyclic VMS. However, the empirical evidence indicates that abiotic degradation processes such as hydrolysis are important removal mechanisms for other VMS in the environment and these processes are also expected to contribute to the removal of M4Q. The preponderance of data indicates that VMS will hydrolyze readily in water and soil and will therefore not persist to a high degree in these media. No empirical degradation data were found for VMS in sediment; therefore, evaluation of the potential for persistence was based on modelled and calculated biodegradation half-lives which indicate slow removal of VMS from this environmental medium. As noted, however, evidence for abiotic degradation in other media suggests that an analysis of potential for persistence in sediment that is based only on biodegradation data is likely to underestimate the potential for removal.

No empirical bioconcentration (BCF) data are available for M4Q. Based on the reported log K_{oc} range of 5.2 to 5.6, as well as data for acceptable analogue substances, it is likely that M4Q will have some capacity for uptake into aquatic organisms via the surrounding water medium. However, the low water solubility of this substance (150 ng/L at 23°C) suggests that it will not be present in significant quantities in the dissolved form that is most suitable for uptake across gill membranes and this reduced exposure potential may limit bioconcentration. Mass-balance kinetic modelling was used to estimate the potential for bioaccumulation, i.e., uptake from both the surrounding aquatic medium and via the diet. The resulting bioaccumulation factor (BAF) incorporates consideration of empirical information on the assimilation efficiency and metabolic potential of M4Q, and concludes that the substance will be bioaccumulated from both water and the diet. An empirical biomagnification factor (BMF) of less than 1 for M4Q indicates that the substance is unlikely to transfer from one trophic level to the next highest trophic level in the foodweb studied.

No link has been established between exposure to M4Q in the environment and adverse effects in organisms. No adverse effects were seen in fish and *Daphnia* exposed in a laboratory setting to M4Q concentrations up to the water solubility limit. Modelled estimates predict no effects in fish, *Daphnia*, mysid shrimp and algae at the limit of water solubility. Adverse effects were observed in laboratory testing with the sediment species, *Chironomus riparius*. However, the saturation concentration of M4Q was exceeded in the study, suggesting that the results may have been affected by physical factors resulting from the presence of undissolved M4Q in the test system, a situation that is not expected to occur in the environment. No information was found on the potential for effects in terrestrial species, such as terrestrial plants, soil-dwelling invertebrates and wildlife. Based on results obtained for a mechanistically-similar substance, M4Q is not likely to be hazardous to terrestrial invertebrates or plants. In addition, properties of moderate vapour pressure, low water solubility and high adsorptivity suggest that M4Q will have only limited distribution into soil even when released directly into this medium and limited mobility within the soil compartment.

The environmental presence of M4Q is closely associated with industrial activities and waste treatment processes. M4Q has been detected at low concentrations in some wastewater treatment plant (WWTP) influents and effluents, some pre-treatment industrial process waters, and landfill leachates. However, the concentrations and frequency of occurrence in WWTP effluents are lower than those in influents collected at the same time and from the same treatment plant, indicating that wastewater treatment processes are effective at reducing the quantity of M4Q available to enter surface receiving waters. Recent monitoring data have reported the presence of low concentrations of M4Q in a small number of suspended particulate matter samples; however, the substance has not been detected in bottom sediments and biota samples, including those collected near potential M4Q sources of release.

A quantitative estimation of potential for ecological harm was conducted by comparing Predicted Exposure Concentrations (PECs) in the Canadian aquatic environment with Predicted No-Effect Concentrations (PNECs) in a risk quotient analysis. For the pelagic compartment, a highest surface water PEC value of 0.000026 mg/L, determined using an industrial modelling scenario, was compared with a lowest PNEC of 0.000191 mg/L derived from the 21-day no-effect value for the water flea, *Daphnia magna*. The resulting risk quotient (PEC / PNEC) of 0.13 indicates that M4Q is unlikely to harm pelagic organisms. This risk quotient is considered to be conservative based on the conservative PNEC and PEC values used in the analysis, in particular, considering the absence of observed or modelled effects up to the solubility limit.

For the sediment compartment, a PEC of 0.124 mg/kg dw based on a 3% OC sediment was determined by applying the principles of Equilibrium Partitioning (EqP) to the highest predicted surface water concentration (PEC) of 0.000026 mg/L. By comparison, M4Q has not been detected in bottom sediments (detection limits 0.0006 to 0.020 mg/kg dw of sediment), although it was measured at concentrations of 0.003 to 0.005 mg/kg dw in three of 31 suspended particulate matter samples. Comparison of the PEC with a PNEC of 1.7 mg/kg dw, derived from the lowest effects level for chronic testing with the chironomid, *Chironomus riparius*, yields a risk quotient (PEC / PNEC) of 0.07. Therefore, based on the conservative assumptions used to derive both the surface water and sediment PEC values, it is unlikely that M4Q will harm sediment organisms in Canada.

The low presence of M4Q in products, as well as limitations to its direct release from these products and evidence for effective removal at WWTPs, indicate that M4Q will have low exposure potential in the environment. This low exposure is expected to mitigate opportunities for uptake of the substance into organisms. While M4Q may bioaccumulate to some degree within individual organisms, it is not expected to transfer between trophic levels, i.e., to biomagnify. There is also an observed absence of adverse effects in organisms exposed to concentrations of M4Q up to the limit of solubility for the substance. The low exposure and hazard potential indicate that there is low risk of harm to organisms or to the broader integrity of the environment from M4Q. It is therefore concluded that M4Q does not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA 1999 as it is not entering the environment in a quantity or concentration or under conditions that have or may have immediate or long-term harmful effects on the environment or its biological diversity, or that constitute or may constitute a danger to the environment on which life depends.

Uncertainties in Evaluation of Ecological Risk

The potential for M4Q to undergo abiotic degradation in the environment is not known and empirical data from suitable analogue substances were used as an important line of evidence in the analysis of environmental persistence. Based on consideration of all available data for M4Q and other VMS, it has been determined that M4Q may have long residence times in air and sediment, but does not persist to as high a degree in water and soil.

The bioaccumulation assessment is limited by the absence of empirical BAF and BCF data for M4Q, although an empirical BMF value for M4Q and empirical BCF and BMF data for suitable analogue substances are available. Based on consideration of data from all of these studies, as well as information on the chemical properties of M4Q, it has been determined that M4Q may have significant potential to accumulate in individual organisms exposed to the substance in the environment, but it is not likely that M4Q will transfer between trophic levels or along food webs.

Risk quotients were developed for both the pelagic and sediment compartments; however, both quotients contain uncertainties. For the pelagic compartment, a toxicity threshold value was not available and the PNEC was based on a no-effect rather than a lowest effect level. This means that the PNEC is unbounded, with water solubility providing the only limiting parameter. This uncertainty was addressed by not applying an Assessment Factor to the Critical Toxicity Value (CTV), given that the CTV was already a no-effect value. For the sediment compartment, the PNEC was derived from a study in which the critical toxicity endpoint value occurred at a test concentration that was well above the saturation concentration of M4Q calculated for the test sediment. This suggests that physical factors resulting from the presence of undissolved M4Q in the test system may have contributed to the observed effects, although the nature and extent of this contribution are unknown.

Model predictions have been used to provide information relating to the environmental distribution, persistence, bioaccumulation potential and toxicity of M4Q. However, there may be higher uncertainties associated with the use of modelling for this substance, as few siloxanes data have been included in the models. Programs such EPI Suite and EQC have recently begun to incorporate data for VMS, primarily cyclic VMS, into the training sets of the models and this should help to decrease uncertainties associated with applying these models to organosilicones such as M4Q. The most recent EPI and EQC versions were used to provide model output in this screening assessment and both incorporate consideration of siloxanes to some extent. Therefore, estimates derived from modelling were deemed sufficiently reliable for use in the evaluation of potential for ecological harm.

Potential to Cause Harm to Human Health

Exposure Assessment

Environmental Media and Food

As outlined in Appendix II, M4Q monitoring data is available in sediment and waste treatment products (i.e., sewage treatment plant influents and effluents, landfill leachate, and industrial waters). However since this data was primarily obtained from point sources it was not considered relevant to general population exposures. In addition, baseline data on concentrations of M4Q in environmental media or food in Canada or elsewhere were not identified. Therefore ChemCAN, a Canada-specific environmental exposure model, was used to estimate concentrations of M4Q in various environmental media (ChemCAN 2003). This model is a Level III fugacity model that is used to estimate average concentrations in various media to estimate general population exposures from the environment. ChemCAN differs from the point-source models used in the ecological assessment section of the document.

Based on information submitted in response to a notice published under section 71 of CEPA 1999, the total quantity of M4Q in commerce in Canada was reported to range from 1000 kg to 10 000 kg in 2006 (Environment Canada 2010a). The upper value of this range was used with the Mass Flow Tool (Environment Canada 2008) to predict environmental loss quantities. Annual release quantities were estimated to be 3220 kg to water from loss to wastewater, 270 kg to air from loss to air emissions and 6410 kg to soil from loss to landfill. Estimated environmental concentrations were calculated using these modelled annual release quantities (see Appendix III). It should be noted that these modelled quantities are considered to be overestimates of actual environmental releases (upper range of total quantity in commerce was used) as explained in the Releases to the Environment section.

As noted in the Uses section, M4Q has been identified in various food packaging applications. Exposure from the presence of M4Q in exterior packaging prints is not expected to be significant. Potential exposure from presence of M4Q in a defoamer, used in the manufacture of paperboards that are intended for use in the manufacture of food packaging articles, is expected to be negligible since the defoamer is not in direct contact with food (2010 personal communication from Food Directorate, Health Canada; unreferenced).

Conservative upper-bounding daily intakes of M4Q were derived for different age groups of the general population in Canada, based on the estimated environmental concentrations shown in Appendix III, resulting in total upper-bounding estimates of exposure from environmental media of 1 ng/kg-bw (nanogram per kilogram of body weight) per day and below.

Uncertainty in this exposure estimation is high as no empirical data on environmental concentrations of M4Q were identified and modelled environmental concentrations were used to estimate exposure. In addition, there is uncertainty due to assumptions used in the model.

Consumer Products and Cosmetics

As noted in the Uses section, M4Q was reported to be present as an impurity in a variety of silicone-based products (Environment Canada 2010a). It can be formed as an impurity in the production of three-dimensional organosilicate resins and is expected to be bound within the silicone matrix in the majority of the products/applications where it is present (Dow Corning 2012).

A review of the section 71 survey data indicated that M4Q may be present, as an impurity, in silicone-based paints, coatings, and four cosmetic ingredients (Environment Canada 2010a). Exposure of the general population from use of these products was estimated using ConsExpo 4.1 (ConsExpo 2007).

Information describing which paint products contain M4Q (outdoor paint vs. indoor paint, semi-gloss vs. latex etc.) was not available; however, the Canadian Paints and Coatings Association indicated that it could be present in trace amounts in all paint types (2010 personal communication from Canadian Paints and Coatings Association to Health Canada; unreferenced). Accordingly, exposure was estimated for four different generic types of paint and coatings (see Table 10 and Appendix IV) considered to be representative of typical paint scenarios used in household settings. Product concentrations were calculated using the maximum impurity concentration (1.5%) in ingredients and the maximum ingredients concentrations in end-use products (1.0%) (Environment Canada 2010a). Estimates of exposure are presented in Table 10.

Table 10. Estimates of exposure from use of different types of paints or coatings

Product	Mean event concentration (mg/m^3)	Dermal exposure (mg/kg-bw/event)
High solid paint	0.26	0.0076
Solvent-rich paint	0.14	0.0076
Waterborne paint	0.041	0.0076
Alkyd coating	1.1	0.00053

Based on notifications submitted under the *Cosmetic Regulations* to Health Canada, M4Q is present as an impurity in certain cosmetic products (face cream, eye shadow, face cleanser, body lotion and tanning lotion) (April 2013 email from Consumer Product Safety Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada; unreferenced) . M4Q concentration in cosmetics was derived based on the maximum impurity concentration (1%) in ingredients combined with the maximum ingredient concentrations obtained from submitted industry data in response to a notice submitted under section 71 of CEPA 1999 and notifications under the *Cosmetic Regulations* to Health Canada (Environment Canada 2010a). Dermal exposure was estimated to range from 4.6×10^{-5} to 0.0091 mg/kg-bw per day based on use of the 5 product types (assumption details are presented in Appendix V). Assuming an individual would use these products (face cream, eye shadow, face cleanser, body lotion or tanning lotion) on the same day results in an aggregate daily dermal exposure of 0.0079 to 0.012 mg/kg-bw per day. Although M4Q is a compound with moderate volatility (vapour pressure

0.0672 mmHg), there may be a potential for exposure via the inhalation route. Inhalation exposure was quantified but found to be low.

Other reported products/applications that may contain M4Q as an impurity are used predominantly for industrial or commercial applications (see Uses section, Environment Canada 2010a). Exposure to the general population may occur through use of adhesives (tapes) and textiles; however, based on low expected concentrations of M4Q in end-use products and the limited number of products, exposure is expected to be significantly less than exposure from use of cosmetics or paints.

Uncertainty in these exposure estimates is high due to the lack of specific product type data regarding the presence of M4Q in various paint and coating products. However, conservative assumptions were used in these calculations (maximum concentrations, 100% dermal and inhalation absorption). In addition, there may be low availability of the substance for exposure as it may be trapped in the silicon matrix of some products (Dow Corning 2012). Aggregating exposure to M4Q on a given day from its presence as an impurity in 5 cosmetic products is also considered conservative.

Health Effects Assessment

The available health effects information for M4Q is summarized in Appendix VI. Structure and identities of relevant analogues are presented in Appendix V. Data on M4Q analogues are summarized in Appendix VII.

No classifications or assessments of health effects of M4Q by national or international regulatory agencies were identified. The only empirical health effects data identified for M4Q were from a short-term study conducted in rats. In that study, animals were administered M4Q by gavage for 4 consecutive weeks, and no treatment-related effects on survival, body weight, food consumption, organ weights, gross pathological changes or behavioural changes were observed at 1500 mg/kg-bw per day, the only dose tested (Dow Corning Corporation 1990).

The outputs of predictive (Q)SAR models for M4Q were considered using four different models (DEREK 2008; TOPKAT 2004; CASETOX 2008; Model Applier 2008). For 3 of the 4 models (DEREK, CASETOX and Leadscope Model Applier), no predictions for the toxicity of M4Q could be generated. TOPKAT gave outputs that were inconclusive for all endpoints (unreliable prediction, based on user-defined model-specific criteria other than the models' applicability domain).

Since very limited health effects information was available for M4Q, information on analogue substances was also considered. Three suitable analogues were identified based on chemical similarity and availability of empirical hazard data: CAS RN 107-51-7 (octamethyltrisiloxane [MDM]), CAS RN 141-62-8 (decamethyltetrasiloxane [L4]) and CAS RN 141-63-9 (dodecamethylpentasiloxane [L5]) (see Appendix V for structures and similarity). The degree of structural similarity is quantified using the Tanimoto association coefficient in SciFinder; this coefficient was 73%, 85% and ≥ 99%, for similarity between M4Q and its three analogues MDM, L4 and L5, respectively; this was considered adequate. Additionally, one physical-

chemical property (i.e., water solubility) fell within comparable range for M4Q and its analogues.

A summary of the available health effects data for the three analogues is provided below (with more details presented in Appendix VII).

In *in vitro* assays, MDM and L5 were not mutagenic in *Salmonella typhimurium* reverse-mutation assays, with and without metabolic activation (Dow Corning Corporation 1979; Seifried et al. 2006; BioReliance 2008). MDM did not induce gene mutations in *Escherichia coli* and did not induce chromosomal aberrations in Chinese hamster ovary cells, with and without metabolic activation (BioReliance 2008, 2009). For MDM, positive results were reported in a mouse lymphoma cell-mutation assay in the absence of metabolic activation, but negative results were reported in presence of metabolic activation (Seifried et al. 2006).

Rats were exposed by gavage to MDM in an oral 28-day study. A significant increase in absolute and relative liver weight accompanied by hepatocellular hypertrophy and protoporphyrin accumulation with associated bile duct proliferation and chronic inflammation was observed in males at 250 mg/kg-bw per day and above (Harland Laboratories Ltd 2010). In a 28-day study conducted with L5, rats were dosed by oral gavage, and a significant increase in absolute and relative liver weight accompanied by liver lesions, such as periportal hepatocellular vacuolation, was observed in females at 25 mg/kg-bw per day and higher (Dow Corning Corporation 2009b). When L4 was administered by gavage to rats for the same dose term, the incidence and severity of perilobular fatty change was increased in female rats at 25 mg/kg-bw per day and higher. This increase in incidence and severity was still present after a 14-day recovery period for the females treated with 1000 mg/kg-bw per day, the highest dose tested, in comparison with the controls (Dow Corning Corporation 2009a). However, no treatment-related effects were observed in both male and female rats exposed in the diet to 500 mg L4/kg-bw per day, the only dose tested, in a 1-year study (Dow Corning Corporation 1966). The lowest lowest-observed-adverse-effect-level (LOAEL) for repeated-dose oral exposure to these analogues was 25 mg/kg-bw per day, based on adverse effect in the liver of female rats exposed to L4 and L5.

Dermal repeated-dose studies were identified for one of the analogues of M4Q. No treatment-related adverse effects were noted in male rats administered 1000 mg L4/kg-bw per day dermally, once daily for 28 days (Hobbs et al. 1972).

In a combined repeated-dose/reproductive/developmental toxicity screening test, increases in serum cholesterol and increases in absolute and relative liver weights were observed in both male and female rats exposed by inhalation to MDM for up to 28 to 29 days at 7740 mg/m^3 and above (Dow Corning Corporation 2007a). Hyaline droplet nephropathy was also observed in males exposed at this concentration, but appeared to be characteristic of kidney lesions induced by male-rat-specific alpha-2-urinary globulin. Because alpha-2-urinary globulin is only synthesized in the livers of sexually mature male rats, this mechanism of toxicity is not considered relevant to human health risk assessment. No treatment-related effects were observed in any of the reproductive or developmental parameters evaluated. No adverse reproductive or developmental effects were observed at 31 000 mg/m^3 the highest concentration tested (Dow Corning Corporation 2007). In another inhalation study, protoporphyrin accumulations along with

secondary effects of cholangitis/pericholangitis and bile duct proliferation were observed in male and female rats after exposure to 31 000 mg MDM/m^3 for 90 days (SEHSC 2011).

In the rabbit, MDM was not irritating to the skin following single exposure but was minimally to moderately irritating when applied following a repeated exposure (10 applications over a 14-day period) (Dow Corning Corporation 1994, 1999). MDM did not induce skin sensitization in a human patch test (Dow Corning Corporation 1998).

The confidence in the health effects database of M4Q is considered to be low, as very limited empirical data were identified for the substance. There is also uncertainty in the use of health effects information for analogues to characterize health effects data for M4Q.

Characterization of Risk to Human Health

There were no long-term studies available for M4Q or the three analogues identified (MDM, L4 and L5). Negative genotoxicity results for MDM and L5 indicate that M4Q is not likely to be genotoxic.

The predominant source of exposure to M4Q through environmental media for the general population is expected to be air. A comparison between the lowest inhalation LOAEC from a short-term study conducted with the analogue MDM (7740 mg/m^3, based on liver effects) with the estimated ambient air concentration of M4Q (1.8 ng/m^3, predominant source of environmental exposure for this substance) results in a margin of exposure of several orders of magnitude. This is considered adequate to address uncertainties in the health effects and exposure databases.

Estimates of exposure to M4Q for the general population of Canada from the use of consumer products such as paint, coating, and cosmetics that may contain M4Q as a reaction by-product were derived. Assuming 100% dermal absorption, comparison of the estimate of maximal aggregate dermal exposure from use of cosmetics (0.016 mg/kg-bw per day) with the only dose tested in the short-term oral study conducted with M4Q (no effects were observed at 1500 mg/kg bw per day)) results in a margin of exposure of approximately 93 750. This margin of exposure is considered adequate to address uncertainties in the health effects and exposure databases.

Consumer use of paint products is infrequent, and potential exposure to M4Q from use of these products is therefore considered to be short-term. Use of high solid, alkyd and waterborne paint is likely to result in the highest short-term dermal estimate among the paint scenarios, with an estimated dermal exposure of 0.0076 mg/kg-bw. Assuming 100% dermal absorption, comparison of the dermal exposure estimate with the dose of 1500 mg/kg-bw per day from the short-term study with M4Q results in a margin of exposure of approximately 200 000. These margins of exposure are considered adequate to address uncertainties in the health effects and exposure databases. Dermal absorption of M4Q is expected to be low based on its relatively large molecular weight and high log K_{ow}, therefore an assumption of 100% dermal absorption is considered conservative.

Characterization of exposure indicated that use of alkyd coating is likely to result in the highest level of inhalation exposure to consumer products containing M4Q, with an estimated mean event concentration of 1.05 mg/m^3. Comparison of this air concentration with the above-noted LOAEC of 7740 mg/m^3 results in a margin of exposure of approximately 7400. This margin of exposure is considered adequate to address uncertainties in the health effects and exposure databases.

Uncertainties in Evaluation of Risk to Human Health

Empirical health effects data for M4Q were very limited and there is uncertainty associated with the use of analogues to extrapolate to health effects for M4Q. No long-term studies have been identified for M4Q or its analogues. Uncertainty is also high due to lack of data available on presence of M4Q in the environment and specific product types. However, given the conservative assumptions used (upper range of in-commerce quantities to estimate environmental releases, maximal product concentrations, 100% inhalation and dermal absorption, aggregate exposure for 5 cosmetics, availability of M4Q from product matrix), there is confidence that these estimates of exposure are conservative.

Conclusion

Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from M4Q. It is concluded that M4Q does not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA 1999 as it 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 information presented in this screening assessment, it is concluded that M4Q does not meet the criteria under paragraph 64(*c*) of CEPA 1999 as it 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 concluded that M4Q does not meet any of the criteria set out in section 64 of CEPA 1999.

References

Abraham MH, Chadha HS, Whiting GS, Mitchell RC. 1994. Hydrogen bonding. 32. An analysis of water-octanol and water-alkane partitioning and the delta log P parameter of Seiler. J Pharmaceut Sci 83:1085-1100 [cited in Dow Corning Corporation 2012].

Acros Organics BVBA. 2000. Material safety data sheet. Tetrakis(trimethylsilyloxy)silane, 98%. Fairlawn (NJ): Acros Organics.

Alaee M. 2014. Unpublished CMP2 monitoring data submitted to Ecological Assessment Division of Environment Canada, Gatineau QC.

Alaee M. 2012. Linear and cyclic volatile methyl siloxanes in the leachate, influent, and effluent in various landfills, wastewater treatment plants, facilities from Canada. Unpublished report. Burlington (ON): Environment Canada, Water Science and Technology Directorate.

Allen RB, Kochs P, Chandra G. 1997. Industrial organosilicon materials, their environmental entry and predicted fate. In: Chandra G, editor. The handbook of environmental chemistry. Volume 3, Part H: Organosilicon materials. New York (NY): Springer-Verlag. p. 181–223.

[AOPWIN] Atmospheric Oxidation Program for Windows [Estimation Model]. 2008. Version 1.92a. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Arnot JA, Gobas FAPC. 2003a. A generic QSAR for assessing the bioaccumulation potential of organic chemicals in aquatic food webs. QSAR Comb Sci 22(3):337-345.

Arnot JA, Gobas FAPC. 2003b. Categorization of organic substances on the Domestic Substances List for bioaccumulation potential. Report to Environment Canada, Existing Substances Branch. June 2003. Gatineau (QC): Environment Canada.

Arnot JA, Gobas FAPC. 2004. A food web bioaccumulation model for organic chemicals in aquatic ecosystems. Environ Toxicol Chem 23:2343-2355.

Arnot JA, Gobas FAPC. 2006. A review of bioconcentration factor (BCF) and bioaccumulation factor (BAF) assessments for organic chemicals in aquatic organisms. Environ Rev 14:257-297.

Arnot JA, Mackay D, Bonnell M. 2008a. Estimating metabolic biotransformation rates in fish from laboratory data. Environ Toxicol Chem 27(2):341-351.

Arnot JA, Mackay D, Parkerton TF, Bonnell M. 2008b. A database of fish biotransformation rates for organic chemicals. Environ Toxicol Chem 27(11):2263-2270.

Arnot, JA. 2010. Estimating chemical absorption efficiency from dietary exposures and degradation rate constants in the gastro-intestinal tract. Draft Report. Prepared for Ecological Assessment Division, Environment Canada. March 2010. Gatineau (QC): Environment Canada.

Arnot JA, Arnot MI, Mackay D, Couillard Y, MacDonald D, Bonnell M, Doyle P. 2010. Molecular size cutoff criteria for screening bioaccumulation potential: fact or fiction? Integr Environ Assess Manag 6(2):210–224.

ASTreat Model [sewage treatment plant removal model]. 2006. Version 1.0. Cincinnati (US): Procter & Gamble Company. Available from Procter & Gamble Company, P.O. Box 538707, Cincinnati, OH 45253-8707, U.S.

Backus S, Moore S, Pelletier M. 2012. Unpublished CMP2 sediment monitoring data submitted to Ecological Assessment Division of Environment Canada, Gatineau QC.

Beyer A, Mackay D, Matthies M, Wania F, Webster E. 2000. Assessing long-range transport potential of persistent organic pollutants. Environ Sci Technol 34(4):699-703.

BioReliance. 2008. Bacterial reverse mutation assay with octamethyltrisiloxane. Study No. AC09FV.503. BTL.

BioReliance. 2009. L3 (Octamethyltrisiloxane; CAS No. 107-51-7): In vitro mammalian chromosome aberration test. Study Number AC19VU.331. BTL.

[BIOWIN] Biodegradation Probability Program for Windows [Estimation Model]. 2008. Version 4.10. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Blankenship MS, Kendall TZ, Krueger HO. 2004. Tris(trimethylsiloxy)phenylsilane: A flow-through bioconcentration test with the bluegill *(Lepomis macrochirus)*. Dow Corning Report Number: 2004-I0000-53746.

Boethling RS, Howard PH, Beauman JA, Larosche ME. 1995. Factors for intermedia extrapolations in biodegradability assessment. Chemosphere 30(4):741-752.

Brooke DN, Crookes MJ, Gray D, Robertson S. 2009. Environmental risk assessment: Decamethylcyclopentasiloxane. Bristol (UK): Environment Agency. Available from: http://www.environment-agency.gov.uk/

Canada. 1999. *Canadian Environmental Protection Act, 1999*. S.C., 1999, c. 33, Canada Gazette. Part III, vol. 22, no. 3. Available from: http://www.gazette.gc.ca/archives/p3/1999/g3-02203.pdf

Canada, Dept. of the Environment, Dept. of Health. 2006. *Canadian Environmental Protection Act, 1999*: *Notice of intent to develop and implement measures to assess and manage the risks posed by certain substances to the health of Canadians and their environment*. Canada Gazette Part I, vol. 140, no. 49, p. 4109-4117. Available from: http://www.gazette.gc.ca/archives/p1/2006/2006-12-09/pdf/g1-14049.pdf

Canada, Dept. of the Environment, Dept. of Health. 2009a. *Canadian Environmental Protection Act, 1999: Notice of twelfth release of technical information relevant to substances identified in the Challenge*. Canada Gazette Part I, vol. 143, no. 52, p. 3839-3843. Available from: http://www.gazette.gc.ca/rp-pr/p1/2009/2009-12-26/pdf/g1-14352.pdf#page=33

Canada, Dept. of the Environment. 2009b. *Canadian Environmental Protection Act, 1999: Notice with respect to Batch 12 Challenge substances.* Canada Gazette Part I, vol. 143, no. 52, p. 3813-3836. Available from: http://www.gazette.gc.ca/rp-pr/p1/2009/2009-12-26/pdf/g1-14352.pdf#page=7

Canada. 2014. *Food and Drug Regulations*,C.R.C., c.870 as amended September 15, 2010. Available from: http://laws.justice.gc.ca/eng/C.R.C.-c.870/index.html

CASETOX [Prediction module]. 2008. Version 2.0. Beachwood (OH): MultiCASE [cited 2010 August 6]. Available from: http://www.multicase.com/products/prod03.htm [restricted access].

[CATABOL] Probabilistic assessment of biodegradability and metabolic pathways [Computer Model]. c2004−2008. Version 5.10.2. Bourgas (BG): Bourgas Prof. Assen Zlatarov University, Laboratory of Mathematical Chemistry. Available from: http://oasis-lmc.org/?section=software&swid=1

Chandra G. 1997. Introduction. In: Chandra G, editor. The handbook of environmental chemistry, Volume 3, Part H: Organosilicon materials. New York (NY): Springer-Verlag. p. 181-223.

ChemCAN [Level III fugacity model of 24 regions of Canada]. 2003. Version 6.00. Peterborough (ON): Trent University, Canadian Centre for Environmental Modelling and Chemistry [cited Aug 2010]. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/CC600.html

[ChemID] ChemIDplus Advanced [website on the internet]. 2010. Bethesda, MD: United States National Library of Medicine. National Institutes of Health. Available from: http://chem.sis.nlm.nih.gov/chemidplus/

[ConsExpo] Consumer Exposure Model [Internet]. 2007. Version 4.1. Bilthoven (NL): Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment). Available from: http://www.rivm.nl/en/healthanddisease/productsafety/ConsExpo.jsp#tcm:13-42840

[CPOPs] Canadian POPs Model. 2008. Gatineau (QC): Environment Canada, Ecological Assessment Division; Bourgas (BG): Bourgas Prof. Assen Zlatarov University, Laboratory of Mathematical Chemistry. [Model developed based on Mekenyan et al. 2005]. Available from: Environment Canada, Ecological Assessment Division.

[DEREK] Deducting Estimation from Existing Knowledge [Prediction module on CD ROM]. 2008. Version 10.0.2. Cambridge (MA): Harvard University, LHASA Group [cited 2010 August 6]. Available from: http://lhasa.harvard.edu/?page=toxicology.htm [restricted access].

Dimitrov S, Dimitrova N,Walker J, Veith G, Mekenyan O. 2002. Predicting bioconcentration potential of highly hydrophobic chemicals. Effect of molecular size. Pure and Appl Chem 74(10): 1823-1830.

Dimitrov S, Dimitrova N, Parkerton T, Comber M, Bonnell M, Mekenyan O. 2005. Base-line model for identifying the bioaccumulation potential of chemicals. SAR QSAR Environ Res 16(6):531-554.

Dow Corning Corporation. 1965. Chronic (8-month) feeding studies with methyl siloxanes in rabbits with cover letter dated 04/20/94. TSCA OTS0556517, Document ID: 1965-I0065-1179-01.

Dow Corning Corporation. 1966. Chronic (one-year) feeding studies with methyl siloxanes in rats with cover letter dated 04/20/94. TSCA OTS0556547, Document ID: 1966-I0065-1179-02.

Dow Corning Corporation. 1979. Mutagenicity evaluation of Dow Corning 200 Fluid in the Ames bacterial assay, with cover letter dated 04/20/94. TSCA OTS0558128, Document ID: 86940001347.

Dow Corning Corporation. 1990. A 28-day subchronic oral gavage feasibility study of various low molecular weight silicone oligomers in rats with cover letter dated 04/20/94. TSCA OTS0590105, Document ID: 1990-I0000-35105.

Dow Corning Corporation. 1994. Skin contact irritation tests with Tx-1302 A, Tx-1302 B, Tx-1302 C, Tx-1302 D and Tx 1302 E in albino rabbits with cover letter dated 04/20/94. TSCA OTS0590160, Document ID: 1976-I0065-1410Y03.

Dow Corning Corporation. 1998. Repeat insult patch test of six Dow Corning materials in human subjects. Report No. 1998-I0000-45918.

Dow Corning Corporation. 1999. Skin irritation of Dow Corning 200® Fluid, 1 cSt in the rabbit. Report No. 1999-I0000-47455.

Dow Corning Corporation. 2004. An acute whole-body inhalation toxicity study of octamethyltrisiloxane in rats. Report No. 2004-I0000-54030.

Dow Corning Corporation. 2006. An acute oral toxicity study in rats with octamethyltrisiloxane. Report No. 2004-I0000-53879.

Dow Corning Corporation. 2007. Combined repeated dose toxicity study with the reproductive/developmental toxicity screening test for octamethyltrisiloxane (L3) in Sprague-Dawley rats via inhalation exposure. HES Report Number 2007-I0000-58159, 11 April 2008.

Dow Corning Corporation. 2009a. Decamethyltetrasiloxane (L4): 28-day oral (gavage) toxicity study in the Sprague-Dawley rat with decamethyltetrasiloxane. Information submitted to EPA under TSCA; TSCA Document No. 8EHQ-09-17631B, Dated 09/10/09.

Dow Corning Corporation. 2009b. 28-day oral (gavage) toxicity study in the Sprague-Dawley rat with dodecamethylpentasiloxane. Information submitted to EPA under TSCA; TSCA Document No. 8EHQ-09-17683A, Dated 10/14/09.

Dow Corning Corporation. 2010a. Tetrakis(trimethylsiloxy)silane (M4Q, CAS No. 3555-47-3): A 96-hour flow-through acute toxicity test with the rainbow trout (*Oncorhynchus mykiss*). Dow Corning Report Number: 2010-I0000-62574.

Dow Corning Corporation. 2010b. Tetrakis(trimethylsiloxy)silane (M4Q, CAS No. 3555-47-3): A flow-through life cycle toxicity test with the Cladoceran (*Daphnia magna*). Dow Corning Report Number: 2010-I0000-62609.

Dow Corning Corporation. 2010c. Tetrakis(trimethylsiloxy)silane (M4Q, CAS No. 3555-47-3): A 14-day prolonged flow-through test with the rainbow trout (*Oncorhynchus mykiss*). Dow Corning Report Number: 2010-I0000-63123.

Dow Corning Corporation. 2010d. 14C-Tetrakis(trimethylsiloxy)silane (14C-M4Q): Dietary bioaccumulation in the rainbow trout (*Oncorhynchus mykiss*) under flow-through test conditions. Dow Corning Report Number: 2010-I0000-62865.

Dow Corning Corporation. 2012. Tetrakis(trimethylsiloxy)silane (M4Q). Background information. CAS No. 3555-47-3. Revised. October 12, 2012. Submission to Environment Canada from Dow Corning Corporation.

Dow Corning Corporation. 2013. M4Q – Toxicity test with sediment-dwelling midges (*Chironomus riparius*) under static conditions, following OECD Guideline 218 Dow Corning Report Number: 2013-I0000-68982.

[DPD] Drug Products Database [database on the internet]. 2014. Canada: Health Canada [cited August 2014]. Available from: http://webprod.hc-sc.gc.ca/dpd-bdpp/index-eng.jsp

Drottar KR. 2010. ^{14}C-Octamethyltrisiloxane (^{14}C-L3): Dietary bioaccumulation in the rainbow trout (*Oncorhynchus mykiss*) under flow-through test conditions. Silicones Environmental, Health and Safety Council (SEHSC). HES Study Number 11245-102.

Durham J. 2005. Hydrolysis of octamethycyclotetrasiloxane (D4). Silicones Environmental, Health and Safety Council (SEHSC). HES Study Number 10000-102.

Durham J. 2006. Hydrolysis of decamethycyclopentasiloxane (D5). Silicones Environmental, Health and Safety Council (SEHSC). HES Study Number 10040-102.

[ECHA] European Chemicals Agency. 2012. Guidance on information requirements and chemical safety assessment. Chapter R.11: PBT assessment. November 2012. Version 2.1. Guidance for the implementation of REACH. Helsinki (FI): European Chemicals Agency.

[ECOSAR] Ecological Structural Activity Relationships [Internet]. 2008. Version 1.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Environment Canada. 2007. Data for selected substances collected under the *Canadian Environmental Protection Act, 1999*, Section 71: *Notice with respect to selected substances identified as priority for action*. Data compiled by: Environment Canada, Program Development and Engagement Division.

Environment Canada. 2008. Guidance for Conducting Ecological Assessments under CEPA 1999, Science Resource Technical Series, Technical Guidance Module: Mass Flow Tool. Working document. Gatineau (QC): Environment Canada, Ecological Assessment Division.

Environment Canada. 2010a. Data for Batch 12 substances collected under the *Canadian Environmental Protection Act, 1999*, Section 71: *Notice with respect to certain Batch 12 Challenge substances.* Data compiled by: Environment Canada, Program Development and Engagement Division.

Environment Canada. 2010b. Mass Flow Tool report. Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethylsilyl)]-, CAS RN 3555-47-3. Internal technical supporting document. Gatineau (QC): Environment Canada, Ecological Assessment Division.

Environment Canada. 2010c. Evaluation of the ecological effects of siloxane D5 in soil. Unpublished report. December 2010. Ottawa (ON): Environment Canada, Soil Toxicology Laboratory, Biological Assessment and Standardization Section.

Environment Canada, Health Canada. 2008a. Screening assessment for the Challenge. Decamethylcyclopentasiloxane (D5). Chemical Abstracts Service Registry Number 541-02-6. November 2008. Ottawa (ON): Environment Canada, Health Canada.

Environment Canada, Health Canada. 2008b. Screening assessment for the Challenge. Octamethylcyclotetrasiloxane (D4). Chemical Abstracts Service Registry Number 556-67-2. November 2008. Ottawa (ON): Environment Canada, Health Canada.

Environment Canada, Health Canada. 2008c. Screening assessment for the Challenge. Dodecamethylcyclohexasiloxane (D6). Chemical Abstracts Service Registry Number 540-97-6. November 2008. Ottawa (ON): Environment Canada, Health Canada.

Environment Canada, Health Canada. 2014. Screening assessment for the Challenge. Trisiloxane, octamethyl- (Octamethyltrisiloxane). Chemical Abstracts Service Registry Number 107-51-7. Ottawa (ON): Environment Canada, Health Canada.

[EPI Suite] Estimation Programs Interface Suite for Microsoft Windows [Estimation Model]. 2000-2008. Version 4.1. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuitedl.htm

[EQC] Equilibrium Criterion Model. 2011. Version 1.00. Released August 2011. Peterborough (ON): Trent University, Canadian Environmental Modelling Centre. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/NewEQCv100.html

[ESIS] European Chemical Substances Information System [database on the Internet]. c1995–2009. European Chemical Bureau (ECB) [cited 2012 Jan 17]. Available from: http://esis.jrc.ec.europa.eu/

Fendinger NJ, Lehmann RG, and Mihaich EM. 1997. Polydimethylsiloxane. In: Chandra G, editor. The handbook of environmental chemistry. Volume 3, Part H: Organosilicon materials. New York (NY): Springer-Verlag. p. 181-223.

Fenner K, Scheringer M, MacLeod M, Matthies M, McKone TE, Stroebe M, Beyer A, Bonnell M, Le Gall A, Klasmeier J, et al. 2005. Comparing estimates of persistence and long-range transport potential among multimedia models. Environ Sci Technol 39:1932-1942.

Flaningam OL. 1986. Vapor pressures of poly(dimethylsiloxane) oligomers. J Chem Eng Data 31:266-272.

Fox K, Zauke GP, Butte W. 1994. Kinetics of bioconcentration and clearance of 28 polychlorinated biphenyl congeners in zebrafish (*Brachydanio rerio*). Ecotox Environ Saf 28(1):99-109.

Gobas FAPC, Clark KE, Shiu WY, Mackay D. 1989. Bioconcentration of polybrominated benzenes and biphenyls and related superhydrophobic chemicals in fish: Role of bioavailability and elimination into the feces. Environ Toxicol Chem 8:231-245.

Gobas FACP, Morrison HA. 2000. Bioconcentration and biomagnification in the aquatic environment. In: Boethling RS, Mackay D, editors. Handbook of property estimation methods for chemicals, environmental and health sciences. Boca Raton (FL): CRC Press. pp. 189-231.

Harland Laboratories Ltd. 2010. 28-Day oral toxicity (gavage) study in the Sprague-Dawley rat with octamethyltrisiloxane (L3). Study number C53655.

Health Canada. 1995. Investigating human exposure to contaminants in the environment: A handbook for exposure calculations. Ottawa (ON): Health Canada.

[HENRYWIN] Henry's Law Constant Program for Microsoft Windows [Estimation Model]. 2008. Version 3.20. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Hirner AV, Flassbeck D, Gruemping R. 2003. Organosilicon compounds in the environment. In: Craig PJ, editor. Organometallic compounds in the environment. Chichester (GB): John Wiley & Sons, Ltd. pp. 305-351.

Hobbs EJ, Fancher OE, Calandra JC. 1972. Effect of selected organopolysiloxanes on male rats and rabbits reproductive organs. Toxicol Appl Pharmacol 21:45-54.

Hobson JF, Silberhorn EM. 1995. Octamethylcyclotetrasiloxane (OMCTS), a case study: Summary and aquatic risk assessment. Environ Toxicol Chem 14(10):1667-1673.

Hobson JF, Atkinson R, Carter WPL. 1997. Volatile methylsiloxanes. In: Chandra G. editor. The handbook of environmental chemistry, Volume 3, Part H: Organosilicon materials. New York (NY): Springer-Verlag. p. 137-180.

[HPVIS] High Production Volume Information System [database on the Internet]. 2012. United States Environmental Protection Agency [last updated 2009 Nov 23; cited 2010 Jun 24]. Available from: http://www.epa.gov/chemrtk/hpvis/index.html.

Hu TM, Layton WL. 2001. Allometric scaling of xenobiotic clearance: uncertainty versus universality. AAPS PharmSci [Internet] [cited 2010 Jun 21]. Vol. 3(4): Article 29. Available from: http://www.aapsj.org/view.asp?art=ps030429

[HYDROWIN] Hydrolysis Rates Program for Microsoft Windows [Estimation Model]. 2008. Version 2.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Industrial Bio-Test Laboratories, Inc. 1964. Report to Dow Corning Corporation irritation studies on seven samples (TX-46A, TX-46B, TX-46C, TX-46D, TX-46E, TX-47A, TX-47B) with cover letter dated 04/20/94. TSCA OTS0556505, Document ID:89940001051.

Industrial Bio-Test Laboratories, Inc. 1967. Report to Dow Corning Corporation range finding eye irritation test on TX-212B with Cover Letter Dated 04/20/94. TSCA OTS0556570, Document ID: 1967-I0065-1156-01.

Kelly BC, Gobas FAPC, McLachlan MS. 2004. Intestinal absorption and biomagnification of organic contaminants in fish, wildlife, and humans. Environ Toxicol Chem 23(10):2324-2336.

Khera N. 2014. Unpublished CMP2 wastewater monitoring data submitted to Ecological Assessment Division of Environment Canada, Gatineau QC.

Klasmeier J, Matthies M, MacLeod M, Fenner K, Scheringer M, Stroebe M, Le Gall AC, McKone TE, van de Meent D, Wania F. 2006. Application of multimedia models for screening assessment of long-range transport potential and overall persistence. Environ Sci Technol 40:53-60.

[KOAWIN] Octanol Air Partition Coefficient Program for Microsoft Windows [Estimation Model]. 2008. Version 1.10. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[KOCWIN] The Soil Adsorption Coefficient Program [Estimation Model]. 2008. Version 2.00. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[KOWWIN] Octanol-Water Partition Coefficient Program for Microsoft Windows [Estimation Model]. 2008. Version 1.68. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Kozerski G. 2012. Report in preparation [cited in Dow Corning Corporation 2012].

[LNHPD] Licensed Natural Health Products Database [database on the internet]. 2014. Canada: Health Canada [cited Aug 2014]. Available from: http://205.193.93.55/lnhpd-bdpsnh/start-debuter.do

Loretz LG, Api AM, Barraj LM, Burdick J, Dressler WE, Gettings SD, Han Hsu H, Pan YHL, Re TA, Renskers KJ, Rothenstein A, Scrafford CG, Sewall C. 2005. Exposure data for cosmetic products: lipstick, body lotion, and face cream. Food Chem Toxicol 43: 279-291.

Loretz LG, Api AM, Babcock L, Barraj LM, Burdick J, Cater KC, Jarrett G, Mann S, Pan YHL, Re TA, Renskers KJ, Scrafford CG. 2008. Exposure data for cosmetic products: Facial cleanser, hair conditioner, and eye shadow. Food Chem Toxicol 46: 1516-1524.

McGoldrick DJ, Letcher RJ, Barresi E, Keir MJ, Small J, Clark MG, Sverko E, Backus SM. 2014. Organophosphate flame retardants and organosiloxanes in predatory freshwater fish from locations across Canada. Environ Pollut 193:254-261.

Mekenyan G, Dimitrov SD, Pavlov TS, Veith GD. 2005. POPs: A QSAR system for creating PBT profiles of chemicals and their metabolites. SAR QSAR Environ Res 16(1-2):103−133.

[Model Applier] Leadscope FDA Model Applier [Prediction module on CD ROM]. 2008. Version 1.2.0-3. Columbus (OH): Leadscope, Inc. [cited 2010 August 6]. Available from: http://www.leadscope.com/model_appliers/ [restricted access].

Mosey JL, Kozerski GE. 2008. Hydrolysis of octamethyltrisiloxane (MDM). Silicones Environmental, Health and Safety Council (SEHSC). Dow Corning Study No. 10390-102 [cited in SEHSC 2010].

[MPBPVPWIN] Melting Point Boiling Point Program for Microsoft Windows [Estimation Model]. 2008. Version 1.43. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

[NCI] National Chemical Inventories [database on CD-ROM]. 2009. Issue 1. Columbus (OH): American Chemical Society. [cited 2010 Mar 15]. Available from: http://www.cas.org/products/cd/nci/index.html

Nguyen TH, Goss K-U, Ball WP. 2005. Polyparameter linear free energy relationships for estimating the equilibrium partition of organic compounds between water and the natural organic matter in soils and sediments. Environ Sci Technol 39(4):913-924.

[NHIPD] Natural Health Ingredients Products Database [database on the internet]. 2014. Ottawa (ON): Health Canada [cited Aug 2014]. Available from: http://webprod.hc-sc.gc.ca/nhpid-bdipsn/search-rechercheReq.do

Nichols JW, Fitzsimmons PN, Burkhard LP. 2007. In vitro – in vivo extrapolation of quantitative hepatic biotransformation data for fish. II. Modeled effects on chemical bioaccumulation. Environ Toxicol Chem 26:1304-1319.

[OECD] Organisation for Economic Co-operation and Development. 2006. Guidelines for the testing of chemicals. Test Guideline 310. Ready biodegradability – CO_2 in sealed vessels (Headspace test). Adopted 23 March 2006. Paris (FR): OECD, Environment Directorate.

[OECD] Organisation for Economic Co-operation and Development. 2011. Guidelines for the testing of chemicals. Bioaccumulation in fish: Aqueous and dietary exposure. Draft document V.10. Paris (FR): OECD, Environment Directorate.

Oliver BG, Niimi AF. 1988. Trophodynamic analysis of polychlorinated biphenyl congeners and other chlorinated hydrocarbons in the Lake Ontario ecosystem. Environ Sci Technol 22(4):388-397.

Pelletier M. 2013. Unpublished CMP2 monitoring data submitted to Ecological Assessment Division of Environment Canada, Gatineau QC.

Pelletier M, Moore S, Backus S. 2012. Unpublished CMP2 sediment monitoring data submitted to Ecological Assessment Division of Environment Canada, Gatineau QC.

[PhysProp] Interactive PhysProp Database [database on the Internet]. 2006. Syracuse (NY): Syracuse Research Corporation [cited 2010 Jun 18] Available from: http://www.syrres.com/esc/physdemo.htm

Redman AD, Mihaich E, Woodburn K, Paquin P, Powell D, McGrath JA, Di Toro DM. 2012. Tissue-based risk assessment of cyclic volatile methyl siloxanes. Environ Toxicol Chem 31(8):1911-1919.

Sakuratani Y, Noguchi Y, Kobayashi K, Yamada J, Nishihara T. 2008. Molecular size as a limiting characteristic for bioconcentration in fish. J Environ Biol. 29(1):89-92.

Schaefer EC, Matthews ME. 2009. Octamethyltrisiloxane (L3; CAS No. 107-51-7): Ready biodegradability – CO_2 in sealed vessels (headspace test). Silicones Environmental, Health and Safety Council (SEHSC). Wildlife International Ltd. Study No. – 570E-101 [cited in SEHSC 2010].

Schenker U, Macleod M, Scheringer M, Hungerbühler K. 2005. Improving data quality for environmental fate models: a least-squares adjustment procedure for harmonizing physicochemical properties of organic compounds. Environ Sci Technol 39:8434-8441.

Scheringer M, MacLeod M, Wegmann F. 2009. The OECD P_{OV} and LRTP Screening Tool [Internet]. Version 2.2. Zurich (CH): Swiss Federal Institute of Technology Zurich. Available from: http://www.oecd.org/document/24/0,3746,en_2649_34373_45373336_1_1_1_1,00.html#download

SciFinder. 2007. Columbus (OH): American Chemical Society. Available from: http://www.cas.org/products/scifindr/index.html [Restricted access].

[SEHSC] Silicones Environmental, Health and Safety Council. 2006. Linear volatile methyl siloxanes category. CAS Nos. 107-51-7, 141-62-8, 141-63-9, and 1000-05-1. June 9, 2006. Submission to Environment Canada under the Chemicals Management Plan Challenge initiative.

[SEHSC] Silicones Environmental, Health and Safety Council. 2010. Octamethyltrisiloxane (L3). Background information. CAS No. 107-51-7. June 23, 2010. Submission to Environment Canada under the Chemicals Management Plan Challenge initiative.

[SEHSC] Silicones Environmental, Health and Safety Council. 2011. Comments on the Draft Screening Assessment for Octamethyltrisiloxane (MDM; L3) Chemical Abstracts Service Registry Number (CAS RN): 107-51-7 Canada

Gazette, Part I, Vol. 145, No. 2 (January 8, 2011). Submission to Environment Canada under the Chemicals Management Plan Challenge initiative.

Seifried HE, Seifried RM, Clarke JJ, Junghans TB, San RHC. 2006. A compilation of two decades of mutagenicity test results with the Ames *Salmonella typhimurium* and L5178Y mouse lymphoma cell mutation assays. Chem Res Toxicol 19:627-624.

[SPIN] Substances in Preparations in Nordic Countries [database on the Internet]. 2013. Copenhagen (DK): Nordic Council of Ministers [cited 2012 Nov 2]. Available from: http://90.184.2.100/DotNetNuke/default.aspx

Springborn Smithers Laboratories. 2004. Cyclopentasiloxane, decamethyl-(D5) and cyclotrisiloxane, hexamethyl-(D3) – determination of the biodegradability of a test substance. Study No. 12023.6142. Silicones Environmental, Health and Safety Council (SEHSC).

Springborn Smithers Laboratories. 2005a. Determining the biodegradability of dodecamethylcyclohexasiloxane based on the draft OECD 310 Sealed Vessel CO_2 Evolution Biodegradation Test. Silicones Environmental, Health and Safety Council. Study No. 12023.6147.

Springborn Smithers Laboratories. 2005b. Determining the biodegradability of octamethylcyclotetrasiloxane based on the draft OECD 310 sealed vessel CO2 evolution biodegradation test. Study No. 12023.6146.

[TaPL3] Long Range Transport and Persistence Level III model [Internet]. 2000. Version 2.10. Peterborough (ON): Trent University, Canadian Environmental Modelling Centre. Available from: http://www.trentu.ca/academic/aminss/envmodel/models/TaPL3.html

Varaprath S, Frye CL, Hamelink J. 1996. Aqueous solubility of permethylsiloxanes (silicones). Environ Sci Technol 15(8):1263-1265.

Wang D, Steer H, Young T, Tait T, Williams Z, Pacepavicius G, Ng T, Smyth SA, Kinsman L, Sverko E, Svoboda L, Fazal S, Alaee M. 2010. Concentrations of cyclic volatile methyl siloxanes (cVMS) in various environmental media from Southern Ontario and Southern Quebec. Unpublished report. Burlington (ON): Environment Canada, Water Science and Technology Directorate.

Wang D, de Solla SR, Lebeuf M, Bisbicos T, Barrett GC, Alaee M. 2012. Determination of linear and cyclic volatile methylsiloxanes in blood of turtle, cormorant, and seal from Canada. Unpublished report. Burlington (ON): Environment Canada, Water Science and Technology Directorate.
Wania F. 2003. Assessing the potential of persistent organic chemicals for long-range transport and accumulation in polar regions. Environ Sci Technol 37:1344-1351.

Wania F. 2006. Potential of degradable organic chemicals for absolute and relative enrichment in the Arctic. Environ Sci Technol 40:569-577.

Weisbrod AV, Woodburn KB, Koelmans AA, Parkerton TF, McElroy AE, Borgå K. 2009. Evaluation of bioaccumulation using in vivo laboratory and field studies. Integr Environ Assess Manag 5(4): 598-623.

Woodburn K, Drottar K, Domoradzki J, Durham J, McNett D, Jezowski R. 2013. Determination of the dietary biomagnification of octamethylcyclotetrasiloxane and decamethylcyclopentasiloxane with the rainbow trout (*Oncorhynchus mykiss*). Chemosphere 93(5):779-788.

[WSKOWWIN] Water Solubility for Organic Compounds Program for Microsoft Windows [Estimation Model]. 2008. Version 1.42. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation. Available from: www.epa.gov/oppt/exposure/pubs/episuite.htm

Xu S, Chandra G. 1999. Fate of cyclic methylsiloxanes in soils. 2. Rates of degradation and volatilization. Environ Sci Technol 33: 4034-4039.

Xu S, Kropscott B. 2006. Non-regulated study: Method for determining air/1-octanol partition coefficients for trace level volatile methylsiloxanes. Dow Corning Report No. 2006-I0000-56478 [cited in Dow Corning Corporation 2012].

Xu S, Doede K. 2010. Degradation octamethyltrisiloxane (L3) (CAS No. 107-51-7) in soils. Final report to SEHSC. DCC HES Study No. 11297-102 [cited in SEHSC 2010, 2011].

Xu S, Doede K, Staples C. 2012. Degradation and volatilization of octamethyltrisiloxane (L3) in soils. Poster presented at the 33rd Annual North American Meeting of The Society of Environmental Toxicology and Chemistry (SETAC), held November 11–15 in Long Beach, CA.

Appendix I – Model Inputs Summary Table

Parameter	**Phys-Chem / Fate**	**Fate**	**Fate**	**Fate**	**PBT Profiling**	**Ecotoxicity**
Model	EPI suite	EQC (Type II chemical)	TaPL3 (Type II chemical)	OECD Pov – LRTP Tool	Canadian POPs (includes CATABOL, BCF Mitigating Factors, OASIS)	Artificial Intelligence Expert System (AEIPS, TOPKAT)
SMILES code	[Si](O[Si](O[Si](C)(C)C)(O[Si](C)(C)C)O[Si](C)(C)C)(C)(C)C	n/a	n/a	n/a	[Si](O[Si](O[Si](C)(C)C)(O[Si](C)(C)C)O[Si](C)(C)C)(C)(C)C	[Si](O[Si](O[Si](C)(C)C)(O[Si](C)(C)C)O[Si](C)(C)C)(C)(C)C
Molecular weight (g/mol)	n/a	384.85	384.85	384.85	n/a	n/a
Melting point (ºC)	-60	-60	-60	n/a	n/a	n/a
Boiling point (ºC)	221.71	n/a	n/a	n/a	n/a	n/a
Data temperature (ºC)	n/a	25	20	n/a	n/a	n/a
Vapour pressure (Pa)	8.96	8.96	8.96	n/a	n/a	n/a
Water solubility (mg/L)	0.00015	0.00015	0.00015	n/a	n/a	n/a
Henry's Law constant ($Pa \cdot m^3/mol$)	2.30×10^7	2.30×10^7	n/a	n/a	n/a	n/a
Log K_{aw} (Air-water partition coefficient; dimensionless)	n/a	4.27 [a]	n/a	4.27[a]	n/a	n/a
Log K_{ow} (Octanol-water partition coefficient; dimensionless)	9.6	9.6	9.6	9.6	n/a	n/a
Log K_{oc} (Organic carbon-water partition coefficient; dimensionless)	n/a	5.2	n/a	n/a	n/a	n/a
Soil-water partition coefficient (L/kg)	n/a	3170	n/a	n/a	n/a	n/a
Sediment-water partition coefficient (L/kg)	n/a	6340	n/a	n/a	n/a	n/a
Suspended particles-water partition coefficient (L/kg)	n/a	31700	n/a	n/a	n/a	n/a
Fish-water partition coefficient (L/kg)	n/a	1260	n/a	n/a	n/a	n/a
Half-life in air (days)	n/a	5.96	5.96	5.96	n/a	n/a

Parameter	**Phys-Chem / Fate**	**Fate**	**Fate**	**Fate**	**PBT Profiling**	**Ecotoxicity**
Model	EPI suite	EQC (Type II chemical)	TaPL3 (Type II chemical)	OECD Pov – LRTP Tool	Canadian POPs (includes CATABOL, BCF Mitigating Factors, OASIS)	Artificial Intelligence Expert System (AEIPS, TOPKAT)
Half-life in water (days)	n/a	37.5	37.5	37.5	n/a	n/a
Half-life in sediment (days)	n/a	365	365	n/a	n/a	n/a
Half-life in soil (days)	n/a	37.5	37.5	37.5	n/a	n/a
Half-life in suspended sediment (days)	n/a	n/a	37.5[b]	n/a	n/a	n/a
Half-life in fish (days)	n/a	n/a	37.5[b]	n/a	n/a	n/a
Half-life in aerosol (days)	n/a	n/a	1×10^{11}[b]	n/a	n/a	n/a

Abbreviations: n/a, not applicable.
[a] Kozerski (2012) in Dow Corning Corporation (2012).
[b] Modelling default value.

Appendix II - Environmental concentrations

Table II-1. Concentrations of M4Q in process effluents and wastewaters

Location; year	Concentration (ng/L)	No. of samples	Reference
Ontario, Quebec, British Columbia, Canada; 2011 WWTP influents	5–238 DL: 0.5	in 8 of 16	Alaee 2012
Ontario, Quebec, British Columbia, Canada; 2011 WWTP effluents	5 DL: 0.5–3	in 1 of 15	Alaee 2012
Ontario, Quebec, British Columbia, Canada; 2012 WWTP influents	16–136 DL: 1–251	in 4 of 16	Alaee 2014
Ontario, Quebec, British Columbia, Canada; 2012 WWTP effluents	31 DL: 1–251	in 1 of 16	Alaee 2014
Across Canada; 2012 WWTP influents	278.80 DL: 25	in 1 of 17	Khera 2014
Across Canada; 2012 WWTP effluents	BDL DL: 25	18	Khera 2014
Across Canada; 2013 WWTP influents	146.73 – 10003.74 DL: 25	in 3 of 16	Khera 2014
Across Canada; 2013 WWTP effluents	76.85 – 112.71 DL: 25	in 2 of 16	Khera 2014
Across Canada; 2013 WWTP influents	45.92 – 55.74 DL: 53	in 2 of 24	Khera 2014
Across Canada; 2013 WWTP effluents	BDL DL: 53	24	Khera 2014
Across Canada; 2014 WWTP influents	58.83 – 136.94 DL: 53	in 2 of 21	Khera 2014
Across Canada; 2014 WWTP effluents	BDL DL: 53	21	Khera 2014
Ontario, Quebec, Canada; 2011 Industrial process waters	4–9990 DL: 0.5–3	in 3 of 13	Alaee 2012
Ontario, Quebec, Canada; 2011 Industrial effluents	567 DL: 0.5–1	in 1 of 5	Alaee 2012
Ontario, Canada; 2012 Industrial process waters	30, 3470 DL: 1	in 2 of 3	Alaee 2014
Ontario or Quebec, Canada; 2011 Landfill leachate	1 DL: 0.5	in 1 of 3	Alaee 2012

Location; year	Concentration (ng/L)	No. of samples	Reference
Ontario, Quebec, British Columbia, Canada; 2012 Landfill leachate	1.8–6.2 DL: 1–251	in 4 of 15	Alaee 2014

Abbreviations: DL, detection limit; WWTP, wastewater treatment plant.

Table II-2. Concentrations of M4Q in sediment

Location; year	Concentration (ng/g dw)	No. of samples	Reference
Great Lakes region, Canada; 2011	BDL DL: 0.6–20	93	Backus et al. 2012
Newfoundland, Nova Scotia, New Brunswick, Quebec, Ontario, British Columbia; 2012	3–5 DL: 0.8–3	in 3 of 126	Pelletier et al. 2012

Abbreviations: BDL, below detection limit; DL, detection limit; dw, dry weight.

Table II-3. Concentrations of M4Q in biota

Location; year	Organism	Concentration (ng/g ww)	No. of samples	Reference
Ontario, Canada; 2008	Common snapping turtle (*Chelydra s. serpentine*)	BDL DL: 0.026	32	Wang 2012
Ontario, Canada; 2008	Double-crested cormorant *(Phalacrocorax auritus)*	BDL DL: 0.026	22	Wang 2012
Ontario, Canada; 2008	Northwest Atlantic harbour seal (*Phoca vitulina*)	BDL DL: 0.026	15	Wang 2012
Ontario, Manitoba, Alberta, Yukon, Canada; 2009-2010	Lake trout *(Salvelinus namaycush)*	BDL DL: 0.24	60	McGoldrick et al., 2014
Ontario, Manitoba, Alberta, Yukon, Canada; 2009-2010	Walleye *(Sander vitreus)*	BDL DL: 0.24	17	McGoldrick et al., 2014
Québec, Canada; 2012-2013	Northern pike *(Esox lucius)*	BDL DL: 0.10	7	Pelletier 2013

Location; year	Organism	Concentration (ng/g ww)	No. of samples	Reference
Québec, Canada; 2012-2013	Walleye *(Sander vitreus)*	BDL DL: 0.10	4	Pelletier 2013
Québec, Canada; 2012-2013	Yellow perch *(Perca flavescens)*	BDL DL: 0.10	2	Pelletier 2013
Québec, Canada; 2012-2013	Round goby *(Neogobius melanostomus)*	BDL DL: 0.10	4[a]	Pelletier 2013
Québec, Canada; 2012-2013	Eastern elliptio mussel *(Elliptio complanata)*	BDL DL: 0.10	7[b]	Pelletier 2013

Abbreviations: BDL, below detection limit; DL, detection limit; ww, wet weight.
[a] Four pooled samples of from 8–12 gobies.

[b] Seven pooled samples of 5 mussels each

Appendix III – Estimated Concentrations of M4Q in Environmental Media using ChemCAN Version 6.00 (ChemCAN 2003)

Medium	Estimated concentration[1,2]
Ambient air	1.8 ng/m^3
Surface water	0.84 ng/L
Soil	0.32 ng/g
Sediment	11 ng/g solids

[1]The concentrations were estimated for the area of southern Ontario.
[2]Default inflow concentrations of 2 ng/m^3 in air and 3 ng/L in water were specified by ChemCAN v6.00.

Appendix IV – Upper-bounding Estimates of Exposure to M4Q in Consumer Products and Cosmetics

Paint and coating products

Type of product	Assumptions[1]	Exposure estimates
High solid paint	Maximum M4Q fraction: 0.00015[2] **Inhalation[3]:** Exposure frequency: 1/year Applied amount: 1300 g Release area: 1.0×10^5 cm^2 Molecular weight matrix: 550 g/mol Mass transfer rate: 1920 m/min **Dermal: direct contact with product at constant rate:** Exposed area: 0.367 m^2 (area of hands and arms) Contact rate: 30 mg/min Release duration: 120 min Uptake fraction: 100%	Inhalation mean event concentration: 0.26 mg/m^3 Inhalation acute dose: 0.0053 mg/kg-bw Dermal acute dose: 0.0076 mg/kg-bw
Solvent-rich paint	Maximum M4Q fraction: 0.00015[2] **Inhalation[3]:** Exposure frequency: 1/year Applied amount: 1000 g Release area: 1.0×10^5 cm^2 Molecular weight matrix: 300 g/mol Mass transfer rate: 1920 m/min **Dermal: direct contact with product at constant rate:** Exposed area: 0.367 m^2 (area of hands and arms) Contact rate: 30 mg/min Release duration: 120 min Uptake fraction: 100%	Inhalation mean event concentration: 0.14 mg/m^3 Inhalation acute dose: 0.0030 mg/kg-bw Dermal acute dose: 0.0076 mg/kg-bw
Waterborne paint	Maximum M4Q fraction: 0.00015[2] **Inhalation[3]:** Exposure frequency: 2/year Applied amount: 3750 g Release area: 1.5×10^5 cm^2 Molecular weight matrix: 120 g/mol Mass transfer rate: 0.18 m/min **Dermal: direct contact with product at constant rate:** Exposed area: 0.367 m^2 (area of hands and arms) Contact rate: 30 mg/min	Inhalation mean event concentration: 0.0411 mg/m^3 Inhalation acute dose: 0.00086 mg/kg-bw Dermal acute dose: 0.0076 mg/kg-bw

Type of product	Assumptions[1]	Exposure estimates
	Release duration: 120 min Uptake fraction: 100%	
Alkyd coating (floor painting)	Maximum M4Q fraction: 0.00015[2] **Inhalation:** Exposure duration: 60 min Room volume of 34 m^2 Ventilation rate: 1.5/h Exposure frequency: 0.33/year Applied amount: 3000 g Release area: 15 m^2 Molecular weight matrix: 3000 g/mol Mass transfer rate: 1920 m/min Uptake fraction: 100% **Dermal: instant application:** Exposed area: 108 cm^2 (area of 1 palm) Product amount: 0.25 g Uptake fraction: 100%	Inhalation mean event concentration: 1.05 mg/m^3 Inhalation acute dose: 0.010 mg/kg-bw Dermal acute dose: 0.00053 mg/kg-bw

[1] For all calculations, an adult body weight of 70.9 kg and an inhalation rate of 16.2 m^3/day are assumed. Exposure was estimated for these product types using ConsExpo 4.1 (ConsExpo 2007).

[2] Maximum concentrations obtained from submitted industry data in response to a notice submitted under section 71 of CEPA 1999.

[3] The following assumptions were applied: inhalation model was based on "exposure to vapour by evaporation" with the following default parameters: exposure duration of 132 min, room volume of 20 m^3, ventilation rate of 0.6/h, application duration of 120 min and uptake fraction of 100%.

Cosmetic products

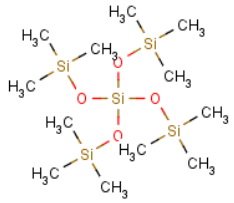
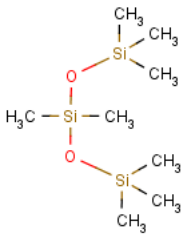
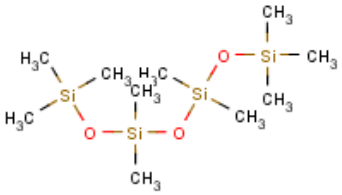
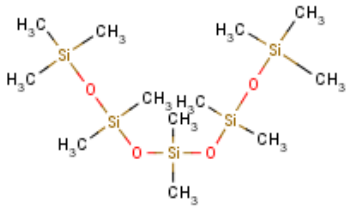
Type of product	Assumptions[1]	Exposure estimates
Face cream	Maximum M4Q fraction = 0.0003[2] Exposure frequency: 657×/year (Loretz et al 2005) Exposed area: 637 cm^2 (Health Canada 1995) Amount product applied: 1.2 g (Loretz et al 2005)	Dermal chronic dose: 0.0091 mg/kg/day
Eye shadow	Maximum M4Q fraction = 0.0003[2] Exposure frequency: 438×/year (Loretz et al. 2008) Exposed area: 24 cm^2 (ConsExpo 2007) Amount product applied: 0.009 g (Loretz et al 2008)	Dermal chronic dose: 4.6×10^{-5} mg/kg/day
Face cleanser	Maximum M4Q fraction = 0.0003[2] Exposure frequency: 730/year Exposed area: 637 cm^2 (Health Canada 1995) Retention factor: 10% (amount left on skin after wash off) Amount product applied: 2.5 g	Dermal chronic dose: 0.0021 mg/kg/day
Body lotion	Maximum M4Q fraction = 0.00003[2] Exposure frequency: 402×/year (Loretz et al 2005) Exposed area: 16 925 cm^2 (Health Canada 1995)	Dermal chronic dose: 0.0021 mg/kg/day

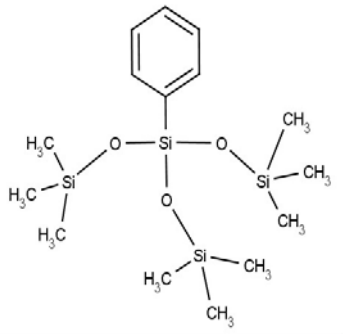
Type of product	**Assumptions**[1]	**Exposure estimates**
	Amount product applied: 4.4 g (Loretz et al 2005)	
Tanning lotion (body)	Maximum M4Q fraction = 0.0001[2] Exposure frequency: 60/year Exposed area: 17 562 cm^2 , whole body + face (Health Canada 1995) Amount product applied: 10 g	Dermal chronic dose: 0.0023 mg/kg/day

[1] For all calculations, an adult body weight of 70.9 kg and an inhalation rate of 16.2 m^3/day are assumed. Exposure was estimated for these product types using ConsExpo 4.1 (ConsExpo 2007).

[2] Maximum concentrations obtained from submitted industry data in response to a notice submitted under section 71 of CEPA 1999 and notifications under the *Cosmetic Regulations* to Health Canada.

Appendix V – Structures and Property Data for M4Q and Analogues Considered in the Screening Assessment*

Name / CAS RN / short name	Structure	Molecular formula / molecular weight (g/mol) / chemical properties	Analogue identification method (% similar)
Trisiloxane, 1,1,1,5,5,5-hexamethyl-3,3-bis[(trimethyl-silyl)oxy]- 3555-47-3 **M4Q**		**$C_{12}H_{36}O_4Si_5$** MW: 384.85 Low water solubility (0.15 µg/L)[a] Log K_{ow}: 9.6[a] Log K_{oc}: 5.2[a,b] D_{max}, D_{eff} (nm)[c]: 1.3, 1.2	n/a
Octamethyl-trisiloxane 107-51-7 **MDM**		**$C_8H_{24}O_2Si_3$** MW: 236.5 Low water solubility (34.0 µg/L)[d] Log K_{ow}: 6.6[d] Log K_{oc}: 4.3[d] D_{max}, D_{eff} (nm)[c]: 1.2, 0.9	SciFinder: 73% ChemID: 83%
Decamethyl-tetrasiloxane 141-62-8 **L4**		**$C_{10}H_{30}O_3Si_4$** MW: 310.70 Low water solubility (6.7 µg/L)[e] Log K_{ow}: 7.2[f] Log K_{oc}: 4.3[b] D_{max}, D_{eff} (nm)[c]: 1.5, 1.0	SciFinder: 85% ChemID: 86%
Dodecamethyl-pentasiloxane 141-63-9 **L5**		**$C_{12}H_{36}O_4Si_5$** MW: 384.9 Low water solubility (0.07 µg/L)[e] Log K_{ow}: 7.8[f] Log K_{oc}: 5.2[b] D_{max}, D_{eff} (nm)[c]: 1.7, 1.1	SciFinder: ≥ 99% ChemID: 88%

Name / CAS RN / short name	**Structure**	**Molecular formula / molecular weight (g/mol) / chemical properties**	**Analogue identification method (% similar)**
Trisiloxane, 1,1,1,5,5,5-hexamethyl-3-phenyl-3-[(trimethylsilyl) oxy]- 2116-84-9 **PTS**		**$C_{15}H_{32}O_3Si_4$** MW: 372.76 Low water solubility (6.6 µg/L)[g] Log K_{ow}: 8.4[f] Log K_{oc}: 5.7[b] D_{max}, D_{eff} (nm)[c]: 1.2, 1.1	SciFinder: 66% ChemID: > 83%

Abbreviations: n/a, not applicable.

* PTS was not used in the human health effects assessment as the mammalian toxicity data associated with the other analogues were considered sufficient to fill in the data gaps.

[a] Table 2 of this report.

[b] Estimated using MCI method in KOCWIN (2008) given greater consistency of this method with empirical values for VMS in general.

[c] Conformational analysis performed using the MOPAC calculator and the BCF Baseline Model with Mitigating Factors (Dimitrov et al. 2005) in CPOPs (2008).

[d] Environment Canada, Health Canada 2014.

[e] SEHSC 2006.

[f] Estimated using the EVA method in KOWWIN (2008) and empirical log K_{ow} data for MDM of 6.6.

[g] Varaprath et al. 1996.

Appendix VI – Summary of Health Effects Information for M4Q

Table VI-1. Health Effects information for M4Q from animal and human studies

Endpoint	**Lowest effect levels[a]/results**
Acute toxicity	No studies were identified.
Short-term repeated-dose toxicity	**Oral NOAEL** = 1500 mg/kg-bw per day, based on no treatment-related effects on survival, body weight, food consumption, organ weights (kidney and liver), gross pathological changes and behavioural changes in male and female Sprague-Dawley rats (6 per group) dosed by gavage with 0 or 1500 mg/kg-bw per day, 5 days/week for 4 consecutive weeks (Dow Corning Corporation 1990). No other oral studies were identified. No inhalation or dermal studies were identified.
Subchronic toxicity	No studies were identified.
Chronic toxicity/ carcinogenicity	No studies were identified.
Reproductive toxicity	No studies were identified.
Developmental toxicity	No studies were identified.
Genotoxicity and related endpoints: *in vivo*	No studies were identified.
Genotoxicity and related endpoints: *in vitro*	No studies were identified.
Sensitization	No studies were identified.
Irritation	**Skin irritation:** No studies were identified. **Eye irritation:** No studies were identified.
Human studies	No studies were identified.

[a] Definitions; LD_{50}: median lethal dose; LOEL/LOEC = lowest-observed-effect level/concentration; LOAEL/LOAEC = lowest-observed-adverse-effect level/concentration; NOAEL/NOAEC = no-observed-adverse-effect level/concentration.

Appendix VII – Summary of Health Effects Information for Analogues Considered in This Assessment

Table VII-1. Health effects information for MDM from animal and human studies

Endpoint	LD_{50}/LC_{50} or lowest/no effect levels[a]/results
Acute toxicity	**Oral LD_{50}** (rat) = > 2000 mg/kg-bw (Dow Corning Corporation 2006) **Inhalation LC_{50}** (rat, 4h) = > 2350 ppm (22 600 mg/m^3) (Dow Corning Corporation 2004) **Dermal LD_{50}** (rat) = > 2000 mg/kg-bw (Dow Corning Corporation 1999)
Short-term repeated-dose toxicity	**Inhalation LOAEC =** 7740 mg/m^3, based on significant increases in serum cholesterol in males, significant increases in absolute and relative liver weights in females and hyaline droplet nephropathy, which was consistent in appearance with alpha-2μ nephropathy, in male Sprague-Dawley rats (10/sex/group) exposed via whole-body inhalation to 0, 7.74, 15.5 or 31.0 mg/L (equal to 0, 7740, 15 500 or 31 000 mg/m^3), 6 h/day, 7 days/week, for 28–29 days in a combined repeated-dose/reproductive/developmental toxicity study. Significant increases in serum cholesterol and increases in relative liver weight were also observed in females at 15 500 mg/m^3 and in males at 31 000 mg/m^3. Other observations included centrilobular hypertrophy, which was considered an adaptative change, in females exposed to 7740 mg/m^3 and above and in males exposed at the highest dose, and hepatic protoporphyrinosis in males at 15 500 mg/m^3 and above. No treatment-related effects on body weight, food consumption and neurobehavioral responses were noted (Dow Corning Corporation 2007). **Oral LOAEL** = 250 mg/kg-bw per day, based on significant increase in liver weight in both sexes in Sprague-Dawley rats (5 per group) dosed by gavage at 0, 5, 25, 250 and 1000 mg/kg-bw per day for 28 days. This increase was accompanied with hepatocellular hypertrophy and protoporphyrin accumulation with associated bile duct proliferation and periportal chronic inflammation in males at 250 and 1000 mg/kg-bw per day and in females at the highest dose only. After a 14-day recovery period, hepatocellular hypertrophy showed complete regression while protoporphyrin accumulation and periportal chronic inflammation was still present in both sexes at 1000 mg/kg-bw per day. An increase incidence and severity of hyaline droplets and higher levels of alpha-2μ-globulin was observed in males at 25 mg/kg-bw per day and above and at all dose levels, respectively. However, hyaline deposits showed complete regression at the end of the recovery period. Thyroid gland follicular cell hypertrophy of minimal severity was observed in both sexes at 1000 mg/kg-bw per day. A reduction in body weight gain was also noted in males at the highest dose at the end of the treatment period (Harland Laboratories Ltd 2010). No dermal studies were identified.

Endpoint	**LD_{50}/LC_{50} or lowest/no effect levels[a]/results**
Subchronic toxicity	**Inhalation LOAEL** = 31 000 mg/m^3, based on protoporphyrin accumulations along with secondary effects of cholangitis/pericholangitis and bile duct proliferation in both sexes in Sprague-Dawley rats (number of animals per group unknown) exposed via whole-body inhalation to 0, 95, 400 or 3200 ppm (equal to 0, 919, 3870 or 31 000 mg/m^3), 6 h/day, 7 days/week, for 90 days. By the end of the 28-day recovery period, partial recovery was observed. Centrilobular hepatocellular hypertrophy associated with a change in organ weight was also observed in males at 3870 mg/m^3 and in both sexes at the highest concentration. This was reversible and considered to represent an adaptative process due to enzyme-induction rather than to be a toxic effect. In the kidney, hyaline droplets and higher levels of alpha-2µ-globulin was observed in males. There was evidence of incomplete recovery at the highest dose (SEHSC 2011). No oral or dermal studies were identified.
Chronic toxicity/ carcinogenicity	No studies were identified.
Reproductive toxicity	**NOAEC for reproductive toxicity =** 31 000 mg/m^3 based on no treatment-related reproductive toxicity observed in a combined repeated-dose/reproductive/ developmental toxicity screening test in which rats (10/sex/concentration) were exposed via whole-body inhalation to 0, 7.74, 15.5 or 31.0 mg/L (equal to 0, 7740, 15 500 or 31 000 mg/m^3), 6 h/day, 7 days/week for 28 or 42 days (males treated 14 days prior to mating and 14 days after mating; females treated from 14 days prior to mating until gestation day 19). Reproductive parameters evaluated during the study included evidence of mating, pregnancy, duration of gestation, macroscopic observations at necropsy such as determination of the number of implantation sites and corpora lutea, litter size and weight, sex ratios, pup viability and litter weight gain. Systemic toxicity in parents is reported in the short-term toxicity section (Dow Corning Corporation 2007). No other reproductive toxicity studies were identified.
Developmental toxicity	**NOAEC for developmental toxicity =** 31 000 mg/m^3 based on no evidence of treatment-related developmental toxicity observed in fetuses in a combined repeated-dose/reproductive/ developmental toxicity screening test in which rats (10/sex/concentration) were exposed via whole-body inhalation to 0, 7.74, 15.5 or 31.0 mg/L (equal to 0, 7740, 15 500 or 31 000 mg/m^3), 6 h/day, 7 days/week for 28 or 42 days (males treated 14 days prior to mating and 14 days after mating; females treated from 14 days prior to mating until gestation day 19). Developmental parameters evaluated during the study included macroscopic observations of the fetuses for any external, visceral or skeletal abnormalities. LOEC for maternal toxicity = 7740 mg/m^3, based on significant increases in liver weights accompanied with centrilobular hypertrophy (Dow Corning Corporation 2007). No other developmental toxicity studies were identified.
Genotoxicity and related endpoints: *in vivo*	No studies were identified.
Genotoxicity and related endpoints: *in vitro*	**Mutagenicity in bacteria** **Negative:** *Salmonella typhimurium*, strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation (Seifried et al. 2006). **Negative:** *Salmonella typhimurium*, strains TA98, TA100, TA1535 and TA1537, with and without metabolic activation (BioReliance 2008). **Negative:** *E. coli*, strain WP2uvrA, with and without metabolic activation (BioReliance 2008).

Endpoint	LD_{50}/LC_{50} or lowest/no effect levels[a]/results
	Chromosome aberration assay **Negative:** Chinese hamster ovary (CHO) cells, with and without metabolic activation (BioReliance 2009). **Mammalian cell mutation assay** **Positive:** Mouse lymphoma L5178Y TK+/- in absence of metabolic activation (Seifried et al. 2006) **Negative:** Mouse lymphoma L5178Y TK+/- in presence of metabolic activation (Seifried et al. 2006)
Irritation	**Skin irritation:** No dermal irritation was observed following a single semi-occlusive application of Dow Corning 200® Fluid 1cSt. (MDM) to intact rabbit skin (3, New Zealand white) for 4 hours (Dow Corning Corporation 1999). Tx-1302 A (MDM) was applied to 3 albino rabbits (sex not specified) under a 1 inch by 1 inch cotton pad on the shaved abdomen and held by a cloth bandage. Ten applications were made over a 14-day period. Minimal to moderate irritation to the skin was noted (Dow Corning Corporation 1994a). **Eye irritation:** No studies were identified.
Human studies Sensitization	In a human patch test, 103 subjects (male and female) were exposed to the test material (MDM) for two phases. The first phase (induction) consisted of nine consecutive patch applications of 0.2 mL of test material to the same site every 48 hours under semi-occlusive wraps; the patches were removed after 24 hours of exposure. After a 12- to 14-day rest period, the same dose method was used on a previously unexposed site (challenge phase) and the volunteers removed the patches after 24 hours. None of the subjects exhibited signs of irritation or sensitization to MDM during any part of the study (Dow Corning Corporation 1998).

[a] See Table VI-1 for footnotes.

Table VII-2. Health effects information for L4 from animal and human studies

Endpoint	Lowest/no effect levels[a]/results
Acute toxicity	No studies were identified.
Short-term repeated-dose toxicity	**Oral LOAEL** = 25 mg/kg-bw per day, based on increased incidence and severity of perilobular fatty change in female Sprague-Dawley rats (5 per group) dosed by gavage with 0, 25, 250 or 1000 mg/kg-bw per day for 28 days. This increase in incidence and severity was still present after a 14-day recovery period for the females treated with the highest dose in comparison with the controls. Also, an increase in absolute and relative liver weights was observed in males. This increase was accompanied with liver effects such as brown pigment in intrahepatic bile ducts at the highest and intermediate dose and bile duct proliferation, chronic inflammation and hepatocellular hypertrophy at the highest dose, which were not present in the control group males. While increases in absolute and relative liver weights were also observed in females at 250 mg/kg-bw per day and above, bile duct pigment accumulation and associated bile duct proliferation/chronic inflammation were not present in treated females at any dose level. There were also statistically significant increases in group mean locomotor activity (early intervals and/or total session) at the highest dose in males and females (Dow Corning Corporation 2009a).

Endpoint	Lowest/no effect levels[a]/results
	Oral LOEL = 1500 mg/kg-bw per day, based on increase in relative kidney weight in male Sprague-Dawley rats (6 per group) dosed by gavage with 0 or 1500 mg/kg-bw per day 5 days/week for 4 consecutive weeks. No mortality, change in general appearance, behavioural abnormalities and other signs of toxicity were observed in both males and females (Dow Corning Corporation 1990). **Dermal NOAEL =** 1000 mg/kg-bw per day based on no significant adverse effects with respect to body weight, mortality and behavioural reactions and no evidence of testicular atrophy and reduced testicular function in male New Zealand albino rabbits (10 per group) exposed dermally to 0 or 1000 mg/kg-bw per day, once daily, for 28 consecutive days (Hobbs et al. 1972). No other dermal studies were identified. No inhalation studies were identified.
Subchronic toxicity	**Oral NOAEL =** 500 mg/kg-bw per day based on no treatment-related effects on growth, physiological status, organ weights or gross and microscopic appearance of tissues (all organ systems) in albino rats (5/sex/dose) exposed via the diet to 0 or 1% 200 Fluid 1.5 cs (decamethyltetrasiloxane) (equivalent to 0 or 500 mg/kg-bw per day, using a dose conversion by Health Canada 1995), for 1 year (Dow Corning Corporation 1966). **Other oral NOAEL =** 500 mg/kg-bw per day based on no treatment-related effects on hematological and urinalysis parameters, organ weights and gross or microscopic appearance of tissues from all organ systems in albino rabbits (3 males and females per dose) exposed via the diet to 0 or 1% 200 Fluid 1.5 cs (decamethyltetrasiloxane) (equivalent to 0 or 500 mg/kg-bw per day, using a dose conversion by Health Canada 1995), for 8 months (Dow Corning Corporation 1965). No inhalation or dermal studies were identified.
Chronic toxicity/ carcinogenicity	No studies were identified.
Reproductive toxicity	No studies were identified.
Developmental toxicity	No studies were identified.
Genotoxicity and related endpoints: *in vivo*	No studies were identified.
Genotoxicity and related endpoints: *in vitro*	No studies were identified.
Sensitization	No studies were identified.

Endpoint	Lowest/no effect levels[a]/results
Irritation	**Skin irritation:** No studies were identified. **Eye irritation:** 0.1 mL of undiluted decamethyltetrasiloxane was applied to the right eye of 5 albino rabbits (left eye served as a control). The cornea, iris and palpebral conjunctiva were examined and irritation was graded at 1, 24, 48, 72, 96 hours and 7 days following exposure. The test substance was reported to be practically non-irritating to the eye (Industrial Bio-Test Laboratories, Inc. 1964).
Human studies	No studies were identified.

[a] See Table VI-1 for footnotes.

Table VII-3. Health effects information for L5 from animal and human studies

Endpoint	Lowest/no effect levels[a]/results
Acute toxicity	No studies were identified.
Short-term repeated-dose toxicity	**Oral LOAEL** = 25 mg/kg-bw per day, based on significant increase in absolute and relative liver weight accompanied with liver lesions such as periportal hepatocellular vacuolation in female Sprague-Dawley rats (5 per group) dosed by gavage with 0, 25, 250 or 1000 mg/kg-bw per day for 28 days. Increased absolute and relative liver weight and periportal hepatocellular vacuolation were observed in males only at 250 and 1000 mg/kg-bw per day. Bile duct proliferation was noted in males at 1000 mg/kg-bw per day and in females at 250 mg/kg-bw per day and above. Accentuated lobular pattern was also noted on the liver of the males treated at the highest dose (Dow Corning Corporation 2009b). **Oral NOAEL** = 1500 mg/kg-bw per day, based on no treatment-related effects on survival, body weight, food consumption, organ weights (kidney and liver), gross pathological changes and behavioural changes in Sprague-Dawley rats (6/sex/dose) dosed by gavage with 0 or 1500 mg/kg-bw per day, 5 days/week for 4 consecutive weeks (Dow Corning Corporation 1990). No inhalation or dermal studies were identified.
Subchronic toxicity	No studies were identified.
Chronic toxicity/ carcinogenicity	No studies were identified.
Reproductive toxicity	No studies were identified.
Developmental toxicity	No studies were identified.
Genotoxicity and related endpoints: *in vivo*	No studies were identified.
Genotoxicity and related endpoints: *in vitro*	**Mutagenicity in bacteria** **Negative:** *Salmonella typhimurium*, strains TA98, TA100, TA1535, TA1537 and TA1538, with and without metabolic activation (Dow Corning Corporation 1979).
Sensitization	No studies were identified.

Endpoint	Lowest/no effect levels[a]/results
Irritation	**Skin irritation:** No studies were identified. **Eye irritation:** 0.1 mL of undiluted test substance containing dodecamethylpentasiloxane was instilled into the eyes of two albino rabbits. After a one-minute contact period, the left eye of each rabbit was rinsed with tap water. Examinations were conducted at 1, 24, 48, 72 and 96 hours, and 7 days following instillation. Iritis and conjunctivitis were reported in both washed and unwashed eyes at 1 hour post instillation but had resolved by 48 hours. The test fluid was classified as mildly irritating to both rinsed and unwashed eyes (Industrial Bio-Test Laboratories, Inc. 1967).
Human studies	No studies were identified.

[a] See Table VI-1 for footnotes.