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Assessment

Siloxanes Group

Chemical Abstracts Service Registry Numbers
107-46-0
141-62-8
141-63-9
541-05-9
2627-95-4

Environment and Climate Change Canada
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Synopsis

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted an assessment of five substances referred to collectively under the Chemicals Management Plan (CMP) as the Siloxanes Group. The Chemical Abstracts Service Registry Numbers (CAS RN[1]), their *Domestic Substances List* (DSL) names, and their common names are listed in the table below.

Of the two remaining substances out of the seven in the Siloxanes Group, one substance, cyclotetrasiloxane, 2,2,4,6,6,8-hexamethyl-4,8-diphenyl-, cis- (CAS RN 33204-76-1) was determined to be of low concern for risk to both the environment and human health and the decision for this substance is provided in a separate report.[2]

The other remaining substance, cyclosiloxanes, di-Me (CAS RN 69430-24-6), henceforth referred to as cyclomethicone, is a UVCB (unknown or variable composition, complex reaction products, or biological materials) primarily comprised of octamethylcyclotetrasiloxane (D4; CAS RN 556-67-2), decamethylcyclopentasiloxane (D5; CAS RN 541-02-6) and dodecamethylcyclohexasiloxane (D6; CAS RN 540-97-6), in varying proportions. Cyclomethicone is considered to have been addressed through the screening assessments of D4, D5, and D6 in 2008 and the revised conclusion regarding D5 in 2012. While it was concluded that D5 and D6 were not posing a risk to the environment or human health, it was concluded that D4 was posing a risk to the environment but not to human health. Given that the previous regulatory activities for D4 can also pertain to and address the use of mixtures containing D4[3], cyclomethicone will not be subject to further risk assessment work under the CMP at this time. Accordingly, this assessment addresses the five substances listed in the table below, hereinafter referred to as the Siloxanes Group.

Substances in the Siloxanes Group

CAS RN	DSL name	Common name (abbreviation)
107-46-0	Disiloxane, hexamethyl-	Hexamethyldisiloxane (L2)
141-62-8	Tetrasiloxane, decamethyl-	Decamethyltetrasiloxane (L4)
141-63-9	Pentasiloxane, dodecamethyl-	Dodecamethylpentasiloxane (L5)
541-05-9	Cyclotrisiloxane, hexamethyl-	Cyclotrisiloxane (D3)

[1] The Chemical Abstracts Service Registry Number (CAS RN) is the property of the American Chemical Society and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the Government of Canada when the information and the reports are required by law or administrative policy, is not permitted without the prior, written permission of the American Chemical Society.

[2] The conclusion for CAS RN 33204-76-1 is provided in the Rapid Screening of Substances with Limited General Population Exposure Screening Assessment.

[3] D4 management measures are provided in the Pollution Prevention Planning Notice with respect to D4 in Industrial Effluents.

2627-95-4	Disiloxane, 1,3-diethenyl-1,1,3,3-tetramethyl-	Divinyltetramethyldisiloxane (dvTMDS)

While L2, L5, and dvTMDS do not naturally occur in the environment, L4 and D3 are found in plants. According to information submitted in response to a CEPA section 71 survey, 1 000 kg to 100 000 kg for each of L2, L4, L5, D3 and dvTMDS were imported into Canada in 2008. In the same year, no Canadian manufacturing activity was reported for these five substances above the reporting threshold of 100 kg.

In Canada, L2 is used primarily as an intermediate, functional fluid, and solvent in products available to consumers such as cosmetics, electronics, medical devices, and anti-freeze and de-icing products. Exposures to L4 and L5 from cosmetics and to L5 from drugs were previously assessed through the assessment of dimethicone (CAS RN 9006-65-9).[4] There are no uses of L4 identified as an individual substance. L5 is also used primarily as a solvent and surface-active agent in industrial applications such as paints and coatings. D3 is used primarily as an intermediate, solvent, and emollient in products available to consumers such as cosmetics, and adhesives and sealants. DvTMDS is used as an intermediate in the manufacture of polymers and other organic compounds and may be used in food packaging materials.

The ecological risks of the substances in the Siloxanes Group were characterized using the ecological risk classification of organic substances (ERC), which is a risk-based approach that employs multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining the risk classification. Hazard profiles are based principally on metrics regarding mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity. Metrics considered in the exposure profiles include potential emission rate, overall persistence, and long-range transport potential. A risk matrix is used to assign a low, moderate or high level of potential concern for substances based on their hazard and exposure profiles. Based on the outcome of the ERC analysis, the substances in the Siloxanes Group are considered unlikely to be causing ecological harm.

Considering all available lines of evidence presented in this assessment, there is low risk of harm to the environment from substances in the Siloxanes Group. It is concluded that L2, L4, L5, D3 and dvTMDS in the Siloxanes Group do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are 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.

For the human health risk assessment, the linear siloxanes (L2, L4 and L5) were assessed together and D3 and dvTMDS were considered as individual substances. For

[4] The conclusion for CAS RN 9006-65-9 is provided in the Second Phase of Polymer Rapid Screening Assessment.

the general population of Canada, indoor air is the predominant source of exposure from environmental media to the linear siloxanes and D3. Oral exposure to L5 may occur from eating fish. Oral exposure to D3 may occur from eating fish and baked goods made in silicone baking moulds. Exposure to dvTMDS via environmental media is considered to be negligible and via food packaging materials is below 25 nanograms per kilogram of body weight per day (ng/kg bw/day). Amongst products available to consumers, the predominant sources of exposure are the use of self-care products that contain L2 and D3 (L2 may be present in nail polish drying drops and bandage adhesive remover, and D3 may be present in body makeup and diaper cream). The general population may also be exposed via inhalation to residual D3 from use of silicone baking moulds.

In laboratory studies, L2 affects the liver, testes, and lungs, whereas L4 affects the liver. L5 may have similar effects, on the basis of a read-across approach used to characterize its critical health effects. Laboratory studies also showed that D3 is associated with decreased food consumption, body weight, and liver weight.

For L2, L4, L5, and D3, estimates of exposure were derived based on levels of substances in environmental media including indoor air as the largest contributor for exposure. Estimates of exposure to products available to consumers were derived for L2 and D3.These estimates of exposure were compared with critical effect levels identified from laboratory studies and the margins of exposure are considered to be adequate to address uncertainties in the health effects and exposure databases.

Exposure of the general population to dvTMDS is not expected, and therefore the concern for human health is low. It was not identified as posing a high hazard to human health on the basis of classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity or reproductive toxicity.

The human health assessment took into consideration those groups of individuals within the Canadian population who, due to greater susceptibility or greater exposure, may be more vulnerable to experiencing adverse health effects from exposure to substances. Exposures to substances in this Siloxanes group were considered for all relevant age groups and life stages, including teens, children, toddlers, infants, and people of reproductive age, when applicable. A potential for increased susceptibility was not identified for a particular population or life stage. These subpopulations were taken into consideration in the risk assessment of substances in the Siloxanes Group.

Considering all the information presented in this assessment, it is concluded that L2, L4, L5, D3, and dvTMDS do not meet the criteria under paragraph 64(*c*) of CEPA as they are 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, it is concluded that L2, L4, L5, D3, and dvTMDS do not meet any of the criteria set out in section 64 of CEPA.

Table of contents

List of tables

1. Introduction

Pursuant to section 68 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health have conducted an assessment of five of seven substances referred to collectively under the Chemicals Management Plan (CMP) as the Siloxanes Group to determine whether these substances present or may present a risk to the environment or to human health. Substances in this group were identified as priorities for assessment as they met categorization criteria as described in ECCC, HC (modified 2017).

Of the two remaining substances out of the seven in the Siloxanes Group, one substance, cyclotetrasiloxane, 2,2,4,6,6,8-hexamethyl-4,8-diphenyl-, cis- (CAS RN[5] 33204-76-1), was considered in the Ecological Risk Classification of Organic Substances (ERC) Science Approach Document (ECCC 2016a) and via the approach applied in the Rapid Screening of Substances with Limited General Population Exposure (ECCC, HC 2018a) and was identified as being of low concern to both the environment and human health. As such, it is not further addressed in this report. Conclusions for this substance are provided in the Rapid Screening of Substances with Limited General Population Exposure Screening Assessment Report (ECCC, HC 2018a).

The other remaining substance, cyclomethicone (CAS RN 69430-24-6) is a UVCB (unknown or variable composition, complex reaction products, or biological materials), primarily comprised of octamethylcyclotetrasiloxane (D4; CAS RN 556-67-2), decamethylcyclopentasiloxane (D5; CAS RN 541-02-6) and dodecamethylcyclohexasiloxane (D6; CAS RN 540-97-6) in varying proportions (Johnson et al. 2012). Cyclomethicone is considered to have been addressed through the screening assessments of D4, D5, and D6 and the revised conclusion regarding D5 in 2012 (Environment Canada, Health Canada 2008a, 2008b, 2008c; Canada 2012a[6]). While it was concluded that D5 and D6 were not posing a risk to the environment or human health, it was concluded that D4 was posing a risk to the environment but not to human health. Given that the previous regulatory activities for D4 can also pertain to and address the use of mixtures containing D4 (Canada 2012b), cyclomethicone will not **be subject to further risk assessment work under the CMP at this time.**

[5] The Chemical Abstracts Service Registry Number (CAS RN) is the property of the American Chemical Society and any use or redistribution, except as required in supporting regulatory requirements and/or for reports to the Government of Canada when the information and the reports are required by law or administrative policy, is not permitted without the prior, written permission of the American Chemical Society.

[6] A revised ecological risk conclusion of D5 and a summary of the information on which the conclusion is based is found within this document.

The ecological risks of the five substances in the Siloxanes Group addressed in this document were characterized using the ERC approach (ECCC 2016a). The ERC describes the hazard of a substance using key metrics, including mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity, and considers the possible exposure of organisms in the aquatic and terrestrial environments on the basis of such factors as potential emission rates, overall persistence, and long-range transport potential in air. The various lines of evidence are combined to identify substances as warranting further evaluation of their potential to cause harm to the environment or as having a low likelihood of causing harm to the environment.

For the assessment of human health risk of the five substances addressed in this document, empirical data from key studies as well as results from models were used to reach proposed conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

Three substances in the Siloxanes Group (L2, L4, and L5) are also components of dimethicone (CAS RN 9006-65-9). Dimethicone is a mixture of fully methylated linear siloxane polymer end-blocked with trimethylsiloxy units (CIR 2003). The risk to ecological and human health of dimethicone was previously assessed in the second phase of polymer rapid screening of the CMP (ECCC, HC 2018b) and is not further addressed in this document. All cosmetic uses of L4 and L5 and all uses of L5 in drugs are notified to Health Canada (HC) as dimethicone, whereas L2 can be identified individually with a specific International Nomenclature of Cosmetic Ingredients (INCI) name (personal communication, emails from Consumer and Hazardous Product Safety Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau [ESRAB], HC, dated December 13 and 16, 2019; unreferenced). Therefore, exposures to L4 and L5 from cosmetics and to L5 from drugs were considered to be previously addressed (ECCC, HC 2018b) and are not further characterized in this assessment.

Three substances (L2, D3, dvTDMS) in the Siloxanes Group have been reviewed internationally through the Organisation for Economic Co-operation and Development (OECD) Cooperative Chemicals Assessment Programme and there are existing assessments available (OECD 2009, 2013, 2014). These assessments undergo rigorous review (including peer-review) and endorsement by international governmental authorities. Health Canada and Environment and Climate Change Canada are active participants in this process and consider these assessments to be reliable. There are also reviews available by the Australian Government Department of Health (AGDH 2018, 2019), and the Danish Environmental Protection Agency (EPA) (2014). These reviews were used to inform the health effects characterization in this assessment.

This assessment includes consideration of information on chemical properties, environmental fate, hazards, uses and exposures, including additional information submitted by stakeholders during the public comment period and identified up to September 2019 for the ecological portion and up to January 2022 for the health portion of this assessment.

This assessment was prepared by staff in the CEPA Risk Assessment Program at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The human health portions of this assessment have undergone external review and/or consultation. Comments on the technical portions relevant to human health were received from Dr. Herman Gibb, Dr. Joan Garey, Theresa Lopez and Jennifer Flippin of Tetra Tech. The ecological portion of this assessment is based on the ERC document (published July 30, 2016), which was subject to an external review as well as a 60-day public comment period. Additionally, the draft of this assessment (published June 1, 2019) was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

Assessments focus on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by considering scientific information, including information, if available, on subpopulations who may have greater susceptibility or greater exposure, vulnerable environments and cumulative effects[7], and by incorporating a weight of evidence approach and precaution.[8] This assessment presents the critical information and considerations on which the conclusions are based.

2. Identity of substances

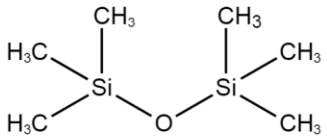
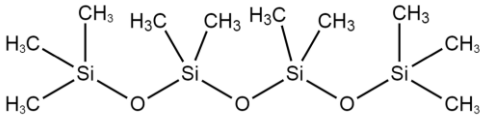
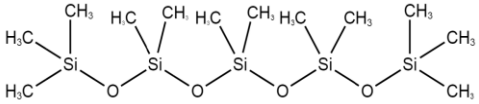
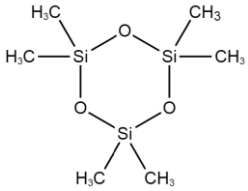
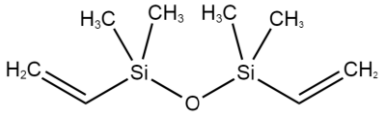
The CAS RNs, abbreviations, and *Domestic Substances List* (DSL) names for the individual substances in the Siloxanes Group are presented in Table 2-1.

For the purposes of this assessment, the five substances discussed are divided into the linear siloxanes (L2, L4, and L5) and two individual substances based on their chemical structure, properties, and/or toxicity.

Table 2-1. Substance identities of the Siloxanes Group

[7] The consideration of cumulative effects under CEPA may involve an analysis, characterization and possible quantification of the combined risks to health or the environment from exposure to multiple chemicals.

[8] A determination of whether one or more of the criteria of section 64 of CEPA 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 products available to consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other acts.

CAS RN (abbreviation)	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
107-46-0 (L2)	Disiloxane, hexamethyl- (hexamethyldisiloxane)	 $C_6H_{18}OSi_2$	162.38
141-62-8 (L4)	Tetrasiloxane, decamethyl- (decamethyltetrasiloxane)	 $C_{10}H_{30}O_3Si_4$	310.69
141-63-9 (L5)	Pentasiloxane, dodecamethyl- (dodecamethylpentasiloxane)	 $C_{12}H_{36}O_4Si_5$	384.84
541-05-9 (D3)	Cyclotrisiloxane, hexamethyl- (cyclotrisiloxane)	 $C_6H_{18}O_3Si_3$	222.46
2627-95-4 (dvTMDS)	Disiloxane, 1,3-diethenyl-1,1,3,3-tetramethyl- (divinyltetramethyldisiloxane)	 $C_8H_{18}OSi_2$	186.40

2.1 Selection of analogues

A read-across approach using data from analogues and the results of (quantitative) structure-activity relationship ([Q]SAR) models, where appropriate, have been used to inform the ecological and human health assessments.

For the human health effects assessment of the linear siloxanes, data from one or more substances were used to inform the other substances (Appendix A). In most cases, L2 was used for read-across to selected critical health effects for L4 and L5.

3. Physical and chemical properties

A summary of physical and chemical property data for the substances in the Siloxanes Group is presented in Table 3-1. Additional physical and chemical properties are provided in ECCC (2016b).

Table 3-1. Physical and chemical property values (at a standard temperature of 25°C) for the Siloxanes Group

Property[a]	L2	L4	L5	D3	dvTMDS
Physical state	liquid	liquid	liquid	solid	liquid
Melting point (°C)	-68.2	-73	-80	64	-99.7
Vapour pressure (Pa)	4 451 (at 20°C)	73	7.8	1156	1 655
Henry's law constant ($Pa \cdot m^3/mol$)	5.1×10^5	2.59×10^6	2.0×10^7	95 700 [modelled][b]	8.13×10^5 [modelled][c]
Water solubility (mg/L)	9.3×10^{-1}	6.74×10^{-3}	7.04×10^{-5}	1.6	0.207
Log K_{ow} (dimensionless)	5.2	8.21	9.41	4.38 [modelled]	5.36
Log K_{oc} (dimensionless)	2.53	5.16	6.3	2.92 [modelled][b]	3.20 [modelled][c]

Abbreviations: K_{ow}, octanol–water partition coefficient; K_{oc}, organic carbon–water partition coefficient.

[a] OECD (2013) and European Chemicals Agency (ECHA 2017b, 2017c, 2017d) for the linear siloxanes, OECD (2009) for D3, and OECD (2014) for dvTMDS unless otherwise stated. Experimental values unless otherwise indicated.

[b] SEHSC (2019a).

[c] SEHSC (2019b).

4. Sources and uses

While L2, L5, and dvTMDS do not naturally occur in the environment (Rücker and Kummerer 2015), L4 was found in *Pandanus amaryllifolius* leaves in Malaysia (Zakaria et al. 2020). Pandan leaves and essential oils extracted from pandan may be used in foods and traditional medicines (Zakaria et al. 2020). In Canada, dried pandan leaves tea may be publicly available for purchase online. D3 was found in essential oil extracted from *Camellia japonica* seeds (Ha et al. 2021). *Camellia japonica* is an evergreen tree with various uses, including in folk medicine, cosmetics, edible oil (extracted from seeds), and tea (using leaves) (Tamaru et al. 2013). In Canada, *Camellia japonica* oil may be present in cosmetics such as lip balm, face oil, and hair oil (personal communication, emails from the Consumer and Hazardous Product Safety

Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated May 18, 2022; unreferenced).

The substances in the Siloxanes Group have been included in a survey issued pursuant to section 71 of CEPA (Environment Canada 2009). Table 4-1 presents a summary of information reported on the total manufacture and total import quantities for the substances in the Siloxanes Group.

Table 4-1. Summary of information on Canadian manufacturing and imports of the Siloxanes Group

Substance	Total manufacture[a] (kg)	Total imports[a] (kg)
L2	< 100	15 500 – 80 000
L4	NR	29 200 – 92 000
L5	NR	13 200 – 57 000
D3	NR	1 000 – 100 000
dvTMDS	NR	1 000 – 100 000

Abbreviations: NR, not reported above the Domestic Substances List Inventory Update (DSL IU) reporting threshold of 100 kg.

[a] Values reflect quantities reported in response to a CEPA section 71 survey (Environment Canada 2009). See survey for specific inclusions and exclusions (Schedules 2 and 3).

According to the information submitted in response to a CEPA section 71 survey (Environment Canada 2009), L2 is primarily used in Canada as an intermediate, functional fluid, and solvent in products available to consumers such as cosmetics, anti-freeze and de-icing products, electronics, and medical devices. L2 is also used as an intermediate in the manufacture of polymers and other organic compounds. L5 is used primarily as a solvent and surface-active agent in industrial applications such as paints and coatings. D3 is used primarily as an intermediate, solvent, and emollient in products available to consumers such as cosmetics, and adhesives and sealants. DvTMDS is primarily used as an intermediate in the manufacture of polymers and other organic compounds, and there is no indication that it is used in products available to consumers in Canada (Environment Canada 2009). The OECD (2014) and the dossier submitted to ECHA under REACH (2017c) also reported that dvTMDS is not used in products available to consumers in Europe.

Additional uses of these substances in Canada are listed in Table 4-2. There were no other uses of L4 identified, other than those previously associated with dimethicone in cosmetics.

Table 4-2. Additional uses in Canada for L2, D3 and dvTMDS in the Siloxanes Group

Use	L2	D3	dvTMDS
Food packaging materials[a]	N	N	Y
Medicinal or non-medicinal ingredients in disinfectant, human or veterinary drug products[b]	N	Y[b]	N
Medicinal or non-medicinal ingredients in natural health products[c]	Y	N	N

Use	L2	D3	dvTMDS
Notified to be present in cosmetics under the *Cosmetic Regulations*[d]	Y	Y	N
Formulant in registered pest control products[e]	N	Y	N

Abbreviations: Y = use was reported for this substance; N = use was not reported for this substance.

[a] Personal communication, emails from the Food Directorate (FD), Health Canada (HC), to the Existing Substance Risk Assessment Bureau (ESRAB), HC, dated February 3, 2017, and June 2015 (Food Packaging/Incidental Additive result for dvTMDS only); unreferenced.

[b] Personal communication, emails from the Pharmaceutical Drugs Directorate (PDD), HC, to the ESRAB, HC, dated January 25, 2017 and June 2015; unreferenced. Although D3 is used in drug products in Canada, all products are discontinued.

[c] L2 and D3 are listed in the Natural Health Products Ingredients Database with a non-medicinal role for topical use only as skin-conditioning agents. However, only L2 is listed in the Licensed Natural Health Products Database as being present as a non-medicinal ingredient in natural health products for topical use. Personal communication, emails from the Natural and Non-prescription Health Products Directorate, HC, to the ESRAB, HC, dated January 30, 2017 and June 2015; unreferenced.

[d] Personal communication, emails from the Consumer and Hazardous Product Safety Directorate, HC, to the ESRAB, HC, dated January 31, 2017 and July 17, 2017; unreferenced.

[e] Personal communication, email from the Pest Management Regulatory Agency (PMRA), HC, to the ESRAB, HC, dated February 6, 2017 and June 2015; unreferenced. Although L4 and L5 are on the list of formulants that are found in pest control products currently registered in Canada, there is no record of current use of these substances.

L2 is used in cosmetics such as facial make-up, body lotion, nail polish drying drops and bandage adhesive remover according to the cosmetic notifications (personal communication, emails from the Consumer and Hazardous Product Safety Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 31, 2017 and July 17, 2017; unreferenced). Although L4 and L5 are on the list of formulants that are found in pest control products currently registered in Canada, there is no record of current use of these substances (personal communication, email from the Pest Management Regulatory Agency, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated February 6, 2017 and June 2015; unreferenced). Although L5 has previously been identified as an ingredient in sunscreens available to Canadian consumers (CPID 2001-2022; SDS 2012), the associated drug identification numbers (DINs) have been cancelled and the previously identified sunscreens containing L5 are no longer available in Canada (DPD [modified 2022]).

D3 can also exist as an impurity and residual in silicone polymers (personal communication, email from Medical Devices Bureau, Pharmaceutical Drugs Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 25, 2018; unreferenced). Globally, silicone elastomers (polymers with viscoelasticity) are used in a large number of biomedical applications including short- and long-term implants and prostheses, catheters, contact lenses and dentures (Will et al. 2007 cited in Environment Canada, Health Canada 2008a, 2008b, 2008c; Canada 2012a). These polymers are used in the manufacture of silicone breast implants (personal communication, email from the Medical Devices Bureau, Pharmaceutical Drugs Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 25, 2018; unreferenced). D3 is used in self-care products such as body makeup, face cream, fragrance, and diaper cream (Wang et al. 2009; personal communication, emails from the Consumer and Hazardous Product Safety

Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 31, 2017 and July 17, 2017; unreferenced). In a German study, although D3 was not detected as a component in silicone baking moulds manufactured in various countries, it was measured in indoor air and baked goods following use of silicone baking moulds (Fromme et al. 2019). D3 may be formed and released during the use of silicone-based products possibly due to the transformation of other cyclic volatile methyl siloxanes present in the products or during sample analysis (Kierkegaard and McLachlan 2013, Brothers et al. 2017) or it may be an impurity in siloxane polymers.

5. Potential to cause ecological harm

5.1 Characterization of Ecological Risk

The ecological risks of the substances in the Siloxanes Group were characterized using the ecological risk classification of organic substances (ERC) approach (ECCC 2016a). The ERC is a risk-based approach that considers multiple metrics for both hazard and exposure, with weighted consideration of multiple lines of evidence for determining risk classification. The various lines of evidence are combined to discriminate between substances of lower or higher potency and lower or higher potential for exposure in various media. This approach reduces the overall uncertainty with risk characterization compared to an approach that relies on a single metric in a single medium (for example, median lethal concentration) for characterization. The following summarizes the approach, which is described in detail in ECCC (2016a).

Data on physical-chemical properties, fate (chemical half-lives in various media and biota, partition coefficients, and fish bioconcentration), acute fish ecotoxicity, and chemical import or manufacture volume in Canada were collected from the scientific literature, from available empirical databases (for example, OECD QSAR Toolbox 2014), from responses to surveys issued pursuant to section 71 of CEPA, or they were generated using selected (Q)SAR or mass-balance fate and bioaccumulation models. These data were used as inputs to other mass-balance models or to complete the substance hazard and exposure profiles.

Hazard profiles were based principally on metrics regarding mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity. Exposure profiles were also based on multiple metrics, including potential emission rate, overall persistence, and long-range transport potential. Hazard and exposure profiles were compared to decision criteria in order to classify the hazard and exposure potentials for each organic substance as low, moderate, or high. Additional rules were applied (for example, classification consistency, margin of exposure) to refine the preliminary classifications of hazard or exposure.

A risk matrix was used to assign a low, moderate or high classification of potential risk for each substance on the basis of its hazard and exposure classifications. ERC classifications of potential risk were verified using a two-step approach. The first step

adjusted the risk classification outcomes from moderate or high to low for substances that had a low estimated rate of emission to water after wastewater treatment, representing a low potential for exposure. The second step reviewed low risk potential classification outcomes using relatively conservative, local-scale (that is, in the area immediately surrounding a point source of discharge) risk scenarios, designed to be protective of the environment, to determine whether the classification of potential risk should be increased.

ERC uses a weighted approach to minimize the potential for both over- and under-classification of hazard and exposure, and of subsequent risk. The balanced approaches for dealing with uncertainties are described in greater detail in ECCC (2016a). The following describes two of the more substantial areas of uncertainty. Error with empirical or modelled acute toxicity values could result in changes in classification of hazard, particularly metrics relying on tissue residue values (that is, mode of toxic action), many of which are predicted values from (Q)SAR models (OECD QSAR Toolbox 2014). However, the impact of this error is mitigated by the fact that overestimation of median lethality will result in a conservative (protective) tissue residue value used for critical body residue analysis. Error with underestimation of acute toxicity will be mitigated through the use of other hazard metrics such as structural profiling of mode of action, reactivity and/or estrogen binding affinity. Changes or errors in chemical quantity could result in differences in classification of exposure as the exposure and risk classifications are highly sensitive to emission rate and use quantity. The ERC classifications thus reflect exposure and risk in Canada on the basis of what is estimated to be the current use quantity, and may not reflect future trends.

Critical data and considerations used to develop the substance-specific profiles for the substances in the Siloxanes Group, and the hazard, exposure and risk classification results are presented in ECCC (2016b).

The hazard and exposure classifications for the five substances in the Siloxanes Group are summarized in Table 5-1.

Table 5-1. Ecological risk classification results for the substances in the Siloxanes Group

Common name (abbreviation)	ERC hazard classification	ERC exposure classification	ERC risk classification
Hexamethyldisiloxane (L2)	low	low	low
Decamethyltetrasiloxane (L4)	medium	low	low
Dodecamethylpentasiloxane (L5)	low	low	low
Cyclotrisiloxane (D3)	low	low	low
Divinyltetramethyldisiloxane (dvTMDS)	medium	low	low

On the basis of low hazard and low exposure classifications according to information considered under ERC, L2, L5, and D3 were classified as having a low potential for ecological risk. It is therefore unlikely that these substances are resulting in concerns for the environment in Canada.

According to information considered under ERC, L4 and dvTMDS were classified as having low exposure potentials. L4 and dvTMDS were classified as having moderate hazard potentials on the basis of a reactive mode of action and a moderate potential to cause adverse effects in aquatic food webs given their bioaccumulation potential. The potential effects and how they may manifest in the environment were not further investigated due to the low exposure of these substances. On the basis of current use patterns, these substances are unlikely to be resulting in concerns for the environment in Canada.

6. Potential to cause harm to human health

6.1 Exposure assessment

Exposure of the general population to substances in the Siloxanes Group can result from use of cosmetics and other products available to consumers, and their release to the environment during production, processing, use or disposal of the substances or products containing them. Due to their volatility and their use in cosmetics and other products available to consumers, inhalation and dermal absorption are considered to be the primary routes of exposure.

6.1.1 Environmental media and food

Linear siloxanes (L2, L4, L5)

There are no Canadian ambient air data for L2. The concentration of L2 in air was modelled using ChemCAN (2003), based on the total reported import and manufacture volumes in Canada (Environment Canada 2009). The predicted concentration of L2 in ambient air in Canada was 0.0015 µg/m^3.

L4 and L5 were measured at detection frequencies of 100% in ambient air in Toronto between 2010 and 2011 with maximum concentrations of 0.0065 µg/m^3 and 0.0048 µg/m^3, respectively (Ahrens et al. 2014). L4 and L5 were also measured in ambient air in eight locations across Canada with maximum concentrations of 0.00066 µg/m^3 and 0.00045 µg/m^3, respectively (Genualdi et al. 2011). From 2012 to 2013 and 2014 to 2015, L4 and L5 were measured in ambient air in nine locations across Canada with maximum concentrations of 0.0039 µg/m^3 and 0.0042 µg/m^3, respectively (Rauert et al. 2018).

L2, L4, and L5 have also been detected at higher concentrations in ambient air internationally (Kaj et al. 2005a, b; Genualdi et al. 2011; Kierkegaard and MacLachlan

2013; Gallego et al. 2017; ECHA 2018c). Between 2013 and 2015, Gallego et al. (2017) measured L2, L4, and L5 in ambient air in ten locations across Spain (sample size of 271), with maximum concentrations of 0.215 µg/m^3, 0.012 µg/m^3, and 0.066 µg/m^3, respectively. L2 was also measured in ambient air near houses in unspecified locations in Europe (sample size of 18) at a 90th percentile concentration of 0.2 µg/m^3 (ECHA 2018c).

The predicted concentration of L2 in ambient air in Canada (0.0015 µg/m^3) and the maximum measured ambient air concentrations of L4 (0.0065 µg/m^3) and L5 (0.0048 µg/m^3) in Canada (Ahrens et al. 2014) resulted in negligible (<2.5 ng/kg bw/day) exposure for the general population.

Levels of siloxanes measured in indoor air were generally higher than those detected in ambient air. In the Canadian Health Measures Survey (CHMS) Cycle 3 (Li et al. 2019) Indoor Air Study, L2, L4, and L5 were detected in indoor air samples, with median concentrations of 0.015 µg/m^3, 0.6 µg/m^3, and 0.19 µg/m^3, and 95th percentile concentrations 0.67 µg/m^3, 1.69 µg/m^3, and 0.9 µg/m^3, respectively. International indoor air values of L4 and L5 are also available from the United States (Tran and Kannan 2015), as well as L2, L4, and L5 values from abroad (Kaj et al. 2005b; Pieri et al. 2013; Katsoyiannis et al. 2014; Tran et al. 2017). The 95th percentile values for L2, L4, and L5 from the CHMS study (Li et al. 2019) were used to estimate general population exposures to indoor air (Tables B-2, B-3, B-4).

There were no Canadian drinking water or soil data identified for L2, L4, or L5. ChemCAN (2003) was used to derive concentrations of L2, L4, and L5 in surface water and soil using total reported import and manufacture volumes in Canada (Environment Canada 2009). The estimated concentration in surface water was used as a surrogate for drinking water data. The estimated concentrations of L2, L4, and L5 in drinking water and soil resulted in negligible exposures for the general population (Tables B-2, B-3, B-4).

Internationally, the siloxanes have been detected in surface water in Europe (NILU 2017; Companioni-Damas et al. 2012; Homem et al. 2017) and Japan (Horii et al. 2017). As part of the 2016 Norwegian environmental screening program, NILU (2017) monitored the occurrence of selected chemicals in the Norwegian indoor, marine and freshwater environments. In spring of 2015, L4 and L5 were measured in Lake Mjosa, Norway with mean concentrations of 0.0088 µg/L and 0.0075 µg/L, respectively, and maximum concentrations of 0.0244 µg/L and 0.0095 µg/L, respectively. In spring of 2011, L2, L4, and L5 were measured among two rivers in Spain with maximum concentrations of 0.00165 µg/L, 0.0008 µg/L, and 0.00394 µg/L, respectively (Companioni-Damas et al. 2012). In soil, L2, L4, and L5 were detected in Europe, Antarctica, and/or Japan (Kaj et al. 2005a, b; Companioni-Damas et al. 2012; Sanchis et al. 2015; ECHA 2018a, b).

No Canadian data on levels of linear siloxanes in dust were identified. In 2014, L4 and L5 were detected in floor dust samples from homes, labs, and offices in the US

with maximum concentrations of 34.2 µg/kg and 67 µg/kg, respectively (Tran et al. 2015). L4 and L5 have also been detected abroad in dust (Tran et al. 2015; Liu et al. 2018). Assuming these American dust concentrations would be similar to Canadian values, they would result in negligible human exposure.

Canadian occurrence data for siloxanes in retail foods were not identified. In Canada, L2, L4, and L5 were monitored but not detected in biota from the Gulf of St. Lawrence, St. Lawrence River, and Estuary and Lake Ontario in 2008 (Wang et al. 2017), and in freshwater fish from 16 water bodies across Canada in 2009 and 2010 (McGoldrick et al. 2014). L4 was monitored but not detected (method detection limit of 1.3 to 1.8 µg/kg wet weight [ww]) in any of the sampled fish and shellfish from Lake Ontario, Canada (ECHA 2018a), or in any of the biota samples from Lake Pepin, US, collected from 2011 to 2013 (ECHA 2018a). L5 was detected at concentrations ranging from 0.1 µg/kg (muscle) to 7.5 µg/kg (liver) in lake trout from Lake Michigan (Bordson et al. 2018). L5 was also monitored in fish from other Great Lakes from 2008 to 2012 but was not detected (McGoldrick and Murphy 2016). Internationally, L2 and L4 were monitored but not detected in fish in Sweden or Norway (Kaj et al. 2005a; ECHA 2018a). The maximum concentration of L5 reported in fish (Bordson et al. 2018) was selected for characterizing exposure from food (Table B-4).

In Germany, L2, L4 and L5 were monitored but not detected above the limit of quantification (0.25 µg/m^3) in indoor air while using silicone and metal moulds for baking (Fromme et al. 2019). L4 was found in pandan (*Pandanus amaryllifolius*) leaves in Malaysia at a maximum concentration of 0.54% (Zakaria et al. 2020). The concentration of L4 in dried tea leaves available in Canada is unclear, but based on the concentration of L4 measured in pandan leaves by Zakaria et al. (2020), exposure to L4 from ingestion of pandan leaf tea is expected to minimal. In the US, L5 was measured in chamber air after opening microwaved popcorn bags with concentrations ranging from 10 to 30 µg/m^3 (Rosati et al. 2007). Oral and inhalation exposures to L5 in the air from use of microwaved popcorn bags are expected to be less than from other products or environmental media.

No biomonitoring studies were identified in Canada for L2, L4, or L5. In 2004, the Swedish National Screening Program reported mean concentrations of L2 and L4 in human breast milk at 0.006 µg/L and 0.013 µg/L, respectively, while L5 was not detected (Kaj et al. 2005a).

D3

D3 was measured at a detection frequency of 100% in ambient air in Toronto between 2010 and 2011 with a maximum concentration of 0.0047 µg/m^3 (Ahrens et al. 2014). D3 was also measured in ambient air at several locations across Canada with a maximum concentration of 0.117 µg/m^3 (Genualdi et al. 2011). Rauert et al. (2018) measured D3 in ambient air in nine locations across Canada at a maximum concentration of 0.036 µg/m^3 in 2013 and 0.0071 µg/m^3 in 2015. In Spain, D3 was measured in ambient air

with average concentrations ranging from 0.039 to 1.358 µg/m^3 (Gallego et al. 2017). The maximum Canadian ambient air concentration of D3 (0.117 µg/m^3; Genualdi et al. 2011) was selected for characterizing exposure to D3 for the general population (Table B-5).

D3 was identified in indoor air from 37 of 50 homes from a Quebec City field study in homes of children with asthma between 2008 and 2010 (Won and Lusztyk 2011). The concentration of D3 ranged from 0.22 to 69.5 µg/m^3 (median 14.1 µg/m^3). This is higher than the D3 concentrations measured in the American studies. In the US, Tran and Kannan (2015) detected D3 in indoor air at concentrations ranging from 0.00346 to 0.0686 µg/m^3 (100% detection frequency) from 60 different locations including homes, offices and schools in 2014. Another study measured D3 at a maximum concentration of 9.3 µg/m^3 in indoor air of schools and early childhood education centers in the US from 2010 to 2011 (Bradman et al. 2015). D3 was also measured in indoor air elsewhere (Kaj et al. 2005b; Pieri et al. 2013; Katsoyiannis et al. 2014; Kang et al. 2017; Tran et al. 2017).

D3 emissions were also investigated from various sources that may impact D3 concentration in indoor air. D3 was detected in emission testing in a chamber setting of 58 building materials and furnishings used in Canadian homes (Won and Lusztyk 2011). These materials represent commonly used materials for building construction and furnishings that are expected to impact indoor levels of organic chemicals. In this emission study, D3 was detected at chamber air concentrations ranging from 0.03 to 45.68 µg/m^3 at 24 hours (median 0.37 µg/m^3, detection frequency of 72%) (Won and Lusztyk 2011). Davis et al. (2019) measured D3 emission from thermoplastic filaments during the last hour of 3D printing to capture the maximum chamber emissions from each filament in the US. Average emission yield of D3 normalized to the mass of the extruded filament material was determined to be highest from high impact polystyrene (HIPS) filaments (6.4 µg/g, sample size of 1), followed by acrylonitrile butadiene styrene (ABS) filaments (1.7 µg/g, sample size of 12). When converted to inhalation exposure level assuming a residential room setting, the exposure concentrations of D3 are 6.72 µg/m^3 from HIPS and 1.64 µg/m^3 from ABS.[9] Fromme et al. (2019) measured D3 in indoor air in Germany throughout the baking process using silicone and metal baking moulds. Indoor air concentrations of D3 80 minutes after use ranged from 0.4 to 18.2 µg/m^3 when using silicone baking moulds and from 0.8 to 2.2 µg/m^3 when using metal baking moulds, which was comparable to the background D3 concentration (1.1 to 1.9 µg/m^3) in indoor air. When amortized over 24 hours, the maximum concentration of D3 is 1.01 µg/m^3. The highest concentration of D3 (69.5 µg/m^3) reported from the Won and Lusztyk (2011)

[9] The estimated exposure concentration, C (µg/m^3), of a target emission for a particular room model was derived based on a steady state mass balance model using the following equation: C= ER×(A/V)×(1/N), where *ER* is the emission rate calculated in Davis et al. (2019), *A* is the number of printers in the modeled room, *V* (m^3) is the volume of the modeled room, and *N* (h^{-1}) is the air exchange rate of the modeled room. A residential room model was used assuming one 3D printer in a room, room volume of 20 m^3, and air exchange rate of 0.6/hour.

study was selected for characterizing exposure via indoor air in this assessment (Table B-5).

No Canadian data on levels of D3 in drinking water, soil, and dust were identified. The concentration of D3 in surface water and soils was modelled using ChemCAN (2003) and import quantities reported in Canada (Environment Canada 2009). The estimated concentration in surface water was used as a surrogate for drinking water data.The predicted concentrations of D3 in drinking water and soils in Canada resulted in negligible exposures for the general population (Table B-5).

Internationally, D3 was detected in the ng/L range in the river water in the US (Kaur et al. 2018). Sanchis et al. (2013) cited in Homem et al. (2017) reported the maximum concentration of D3 measured in river water in Sweden as 0.076 µg/L. D3 was detected in soil in Antarctica (Sanchis et al. 2015).

In the US, D3 was detected in floor dust samples from homes, labs, and offices in 2014 at a concentration ranging from less than 2 to 50.8 µg/kg (Tran et al. 2015). D3 has been detected abroad in dust (Tran et al. 2015; Liu et al. 2018). Assuming the American dust concentrations would be similar to Canadian values, they would result in negligible human exposure.

In Canada, D3 is not a permitted food additive, and there is no definitive information on its use in food packaging materials. While there is no Canadian occurrence data for D3 in retail foods, D3 was detected in the blood of harbour seals at a maximum concentration of 1.43 µg/kg ww from the Gulf of St. Lawrence and St. Lawrence River Estuary in 2008 (Wang et al. 2017). Another study measured D3 at concentrations ranging from 0.83 to 1.2 µg/kg ww in whole body homogenates of lake trout and walleye from 16 water bodies across Canada in 2009 and 2010 (McGoldrick et al. 2014). In addition, D3 was detected at concentrations ranging from less than 0.3 to 39 µg/kg ww in whole body lake trout and walleye in the Great Lakes from 2008 to 2012 (Great Lakes Environmental Data Base [GLENDA] cited in McGoldrick and Murphy 2016). D3 was also monitored, but not detected, in fish in Sweden and Norway (Kaj et al. 2005a).

Canadians may also be exposed to D3 in foods due to its migration from certain products available to consumers, such as silicone baking moulds used for home baking. In Germany, D3 was not detected as a component of silicone baking moulds but D3 was measured in the cakes that had been baked in 14 silicone moulds at concentrations ranging from less than 60 to 290 µg/kg (Fromme et al. 2019). The maximum concentration of D3 was found in the first batch of baked cakes and decreased upon repeated use of the silicone baking moulds, while it varied for other cyclic methyl siloxanes (Fromme et al. 2019). Canadians may also be exposed to D3 in foods from use of silicone baking moulds, and exposure is expected to decrease with use.

The maximum concentrations of D3 reported in freshwater fish (McGoldrick and Murphy 2016) and baked goods (Fromme et al. 2019) were selected for characterizing exposure via ingestion of food in this assessment (Table B-5).

Flassbeck et al. (2001) detected D3 in the plasma and blood of women who are or were exposed to silicone gel-filled breast implants in Germany. However, low molecular weight siloxanes including D3, are currently not detected in silicone breast implants sold in Canada (personal communication, email from the Medical Devices Bureau, Pharmaceutical Drugs Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 25, 2018; unreferenced).

DvTMDS

There was no information found on the presence of dvTMDS in environmental media or food. Since no monitoring data on dvTMDS have been identified, and dvTMDS is mainly used industrially as an intermediate for manufacturing other compounds or polymers and is not expected to remain after end use (Environment Canada 2009; ECHA 2017e; OECD 2014), its release to the environment is expected to be limited.

In Canada, dvTMDS may be present in certain food packaging materials with direct food contact based on its use in the manufacture of silicone materials and release coating. Dietary exposure to dvTMDS from this use is less than 25 ng/kg bw/day (personal communication, email from the Food Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated June 2015 and Jan 2018; unreferenced).

Intake based on environmental media, food and biomonitoring data

Overall, total daily intakes of L2, L4, L5, and D3 from environmental media and food have been estimated to range from 0.12 to 0.35 µg/kg bw/day, 0.29 to 0.89 µg/kg bw/day, 0.16 to 0.5 µg/kg bw/day, and 13 to 39.7 µg/kg bw/day, respectively, with infants and toddlers aged 6 months to 4 years having the highest intakes for all substances (Appendix B). Given the absence of measured Canadian drinking water, soil, and dust data, the negligible modelled Canadian drinking water and soil concentrations, and low international dust concentrations, exposures from drinking water, soil, and dust were not used to characterize risk for L2, L4, L5, and D3. Given inhalation exposure via indoor air is the primary contributor to total daily intake of L2, L4, L5, and D3, exposures from ambient air were not used to characterize risk for L2, L4, L5, and D3. Oral exposure to L5 may occur from eating fish. Oral exposure to D3 may occur from eating fish, and baked goods made in silicone baking moulds.

Exposure of the general population to dvTMDS from environmental media is considered to be negligible and exposure via food packaging materials is below 25 ng/kg bw/day.

6.1.2 Products available to consumers

L2 and D3 in the Siloxanes Group are used in a variety of products available to consumers that may result in exposure to the general population of Canada. Exposure of the general population to L4, L5 and dvTMDS from the use of products available to

consumers is not expected. Exposures to the general population from the use of products available to consumers were characterized using ConsExpo Web (2018) (Table C-1 in Appendix C). The estimates of exposure to L2 are summarized in Table 6-1. On the basis of a study of skin samples taken from six donors and exposed to L2 for 24 hours, L2 showed a very low dermal absorption potential (0.02%) in human skin (Dow Corning Corporation [DCC] 2000 cited in OECD 2013). Internal exposure estimates were derived using a dermal absorption of 0.02% for L2.

The estimates of exposure to D3 from use of cosmetics and other products available to consumers are presented in Table 6-2. Systemic exposures from dermal exposure for different sentinel scenarios were modelled using the maximum flux (Jmax) approach (Williams et al. 2016) (Appendix D). Inhalation exposure was modelled using ConsExpo Web (2018) (Table C-1 in Appendix C).

D3 can also exist as an impurity and residual in silicone polymers used in the manufacture of silicone breast implants. However, low molecular weight siloxanes (less than D8 and L6) are not detected (less than 1 µg/g of material) in silicone breast implants sold in Canada (personal communication, email from the Medical Devices Bureau, Pharmaceuticals Drugs Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 25, 2018; unreferenced). In addition, based on evidence provided in Canadian submissions for breast implants and from the literature review, there is no known scientific basis for any human health concerns for the trace amounts of low molecular weight siloxanes (including D3) in silicone breast implants (personal communication, email from the Medical Devices Bureau, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 25, 2018; unreferenced).

D3 was also reported at a concentration of 42% in an essential oil extracted from *Camellia japonica* seeds in South Korea, where the identity of D3 was confirmed via spectral matching with the US National Institute of Standards and Technology Database (Ha et al. 2021). The concentration of D3 in *Camellia japonica* oil extracted from *Camilla japonica* seeds in cosmetics available in Canada is unclear. Exposure to D3 from the use of products containing *Camellia japonica* oil is expected to be minimal.

Table 6-1. Estimated potential exposures to L2 from the use of cosmetics and other products available to consumers

Product scenario	Maximum concentration[a]	Dermal per event systemic exposure (mg/kg bw)	Inhalation mean event concentration (mg/m^3)[b]	Dermal daily systemic exposure (mg/kg bw/day)
Body lotion for face, neck and neckline (adults)	3%	0.000193	N/A	0.000193

Product scenario	Maximum concentration[a]	Dermal per event systemic exposure (mg/kg bw)	Inhalation mean event concentration (mg/m^3)[b]	Dermal daily systemic exposure (mg/kg bw/day)
Body lotion for face, neck and neckline (teens)	3%	0.000203	N/A	0.00016
Aerosol bandage adhesive remover (adults)	67%	0.00161	N/A	N/A
Aerosol bandage adhesive remover (teens)	67%	0.00192	N/A	N/A
Facial makeup (adults)	45%	0.000685	N/A	0.00085
Facial makeup (teens)	45%	0.000818	N/A	0.00101
Hair styling product	100%	0.000536	N/A	N/A
Nail polish drying drops (adults, teens)	100%	N/A	13.3	N/A
Aerosol bandage adhesive remover (adults, teens)	67%	N/A	0.729	N/A

Abbreviation: N/A, Not applicable.

[a] Personal communication, emails from the Consumer and Hazardous Product Safety Directorate (CHPSD), Health Canada (HC) to the Existing Substances Risk Assessment Bureau (ESRAB), HC, dated January 31, 2017 and July 17, 2017; unreferenced.

[b] Inhalation mean event concentrations are amortized over a 6-hour period by multiplying it by 'exposure duration/6-hour' to be aligned with the duration of treatment per day (via inhalation) in the toxicity study.

Table 6-2. Estimated potential exposures to D3 from the use of cosmetics and other products available to consumers

Product scenario (adult, unless otherwise indicated)	Maximum concentration	Dermal systemic exposure (mg/kg bw/ day)[a]	Inhalation mean event concentration (mg/m^3)
Body makeup	0.044%[b]	0.330	N/A
Face cream	0.1%[b]	0.0233	N/A
Fragrance	0.12 mg/g ww[c]	0.00366	N/A
Diaper cream (toddlers)	0.45 mg/g ww[c]	0.0678	N/A
Diaper cream (infants)	0.45 mg/g ww[c]	0.0893	N/A

Product scenario (adult, unless otherwise indicated)	Maximum concentration	Dermal systemic exposure (mg/kg bw/ day)[a]	Inhalation mean event concentration (mg/m^3)
Fragrance	0.12 mg/g ww[c]	N/A	2.24E-06[d]
Silicone baking moulds	Not detected[e]	N/A	0.0239 (measured)[e]

Abbreviation: N/A, Not applicable. ww, wet weight.

[a] Estimates of dermal systemic exposure to D3 are on day of exposure and estimated using Jmax method (Williams et al. 2016).

[b] Personal communication, emails from the Consumer and Hazardous Product Safety Directorate (CHPSD), Health Canada (HC) to the Existing Substances Risk Assessment Bureau (ESRAB), HC, dated January 31, 2017 and July 17, 2017; unreferenced.

[c] Wang et al. (2009).

[d] 6-hour TWA. Inhalation estimate for fragrance is an amortized concentration. Inhalation mean event concentration (0.000161 mg/m^3) is amortized over a 6-hour period by multiplying it with 'exposure time/6-hour' to be aligned with the duration of inhalation toxicity study.

[e] Fromme et al. (2019) measured D3 in indoor air throughout a baking process using silicone baking moulds and detected D3 at concentrations ranging from 1.4 to 23.9 µg/m^3 immediately after baking. In product analysis, D3 was not detected in the silicone baking moulds.

6.1.3 Consideration of subpopulations who may have greater exposure

There are groups of individuals within the Canadian population who, due to greater exposure, may be more vulnerable to experiencing adverse health effects from exposure to substances. The potential for elevated exposure within the Canadian population was examined. Exposure estimates are routinely assessed by age to take into consideration physical and behavioural differences during different stages of life. In this exposure assessment, exposures to Siloxanes from environmental media, food, and drinking water, and exposures to L2 and D3 from products available to consumers, were estimated for all relevant age groups, including teens, children, toddlers, infants, and people of reproductive age, when applicable. In the assessment of exposure from indoor air, outdoor air, and food young children (6 months to 4 years) had higher estimated exposure than adults. Formula-fed infants, in particular those consuming formula reconstituted with drinking water potentially containing elevated levels of these substances, had higher estimated exposure to Siloxanes than human-milk fed infants and than adults. These subpopulations were taken into account in the risk assessment outcomes of substances in the Siloxanes Group.

6.2 Health effects assessment

Linear siloxanes (L2, L4, L5)

For the three linear siloxanes substances, an international assessment was available for L2 (OECD 2013). L2 and L4 were also reviewed by AGDH (2018, 2019). There is a Danish EPA (2014) assessment of several siloxane substances, including L2, for the purpose of setting health-based criteria for ambient air. Additional information for L2, L4 and L5 was also identified from the published literature (up to September 2019), from

the ECHA database, or was submitted during the public comment period for this assessment.

A read-across approach was used, wherein data from one substance informed the human health effects assessments of other linear siloxanes substances. L2 was a potential structural analogue of L4 and L5 identified through the OECD QSAR toolbox (version 4.2). Differences in physical chemical properties between L2, L4, and L5 support the use of L2 toxicological data as protective of potential health effects from L4 and L5 exposures. For instance, L2 has a higher vapour pressure, as well as a lower molecular weight and lower log K_{ow} than L4 and L5, which suggest that L2 has a higher inhalation and lower dermal absorption potential than L4 and L5. In most cases, the information on L2 was used to predict health effects for L4 and L5 (Appendix A).

On the basis of inhalation dosing in rats, L2 was found to be mostly eliminated via exhalation and to a lesser extent in urine and faeces (Dow Corning Corporation [DCC] 2008 cited in OECD 2013; ECHA 2006a). Metabolic clearance of L2 was restricted to the liver and appeared to be initiated by a cytochrome P-450-mediated oxidation reaction (Dobrev et al. 2003). The major metabolite in urine was identified as 1,3-bis(hydroxymethyl)tetramethyldisiloxane (DCC 2001 cited in OECD 2013; ECHA 2006a). In a 14-day repeated dose study in rats (animals exposed nose-only 6 hours/day, 7 days/week to ^{14}C-L2), the majority of the radioactivity was eliminated from the body within 24 hours post-exposure (ECHA 2006a). In both the single day and repeated dose inhalation studies using L2, approximately 4% of the dose was retained in rat bodies (ECHA 2006a). For L5, 25% of an oral gavage dose in rats was absorbed in the gastrointestinal tract with 97% being eliminated after 48 hours. The dose was eliminated primarily via faeces and to a lesser extent via expired air and urine. Although no toxicokinetic data were identified for L4, read-across from L2 and L5 suggests that L4 would also be mostly eliminated via exhalation and excreted via faeces or urine after oral or inhalation dosing (DCC 1985; ECHA 1985).

No adverse effects were observed in rats administered L4 or L5 via gavage for seven days up to a limit dose of 1000 mg/kg bw/day (DCC 2009; ECHA 2009). No adverse effects were observed in rats administered L4 and L5 via gavage for 28 days (Dow Corning 1990 cited in OECD 2013; ECHA 2010d, 2017a). A no observed adverse effect level (NOAEL) of 25 mg/kg bw/day was determined in a 28-day rat gavage study, based on protoporphyrin accumulation observed in the liver of male animals administered 250 mg/kg bw/day of L4. At the next dose of 1000 mg/kg bw/day, bile duct proliferation and periportal chronic inflammation were observed. However, no adverse effects were observed in females administered doses up 1000 mg/kg bw/day (ECHA 2010a).

For L2, in a 28-day rat gavage study, there were no adverse effects in females but males administered 640 mg/kg bw/day had decreased food consumption and body weight gain, increased relative liver weights and hematological changes (increased white blood cell count, decreased mean corpuscular volume and hemoglobin), with a NOAEL of 160 mg/kg bw/day (ECHA 1994). Three-day and four-day gavage studies conducted in rats to determine estrogenic activity were also negative in animals

administered doses up to 1200 mg/kg bw/day of L2 (no effect on uterine weights) and in mice administered doses up to 1000 mg/kg bw/day of L4 (no effect on uterine weights and uterine peroxidase activity), respectively (McKim et al. 2001; He et al. 2003).

In a 1-year study described as a combined repeated dose/carcinogenicity study by the authors, rats were administered 0 or 500 mg/kg bw/day of L4 in the diet. There were decreased absolute and relative adrenal weights in both sexes and increased absolute and relative thyroid weights in males (DCC 1966a).

In an 8month study described as a combined repeated dose/carcinogenicity study by the authors, rabbits were administered 0 or 500 mg/kg bw/day of L4 in the diet. Effects were observed in the heart and kidney of females (increased pericardial fluid and chronic pyelitis of the kidney pelvis) and decreased relative liver weights and increased relative spleen weights were observed in males (DCC 1966b).

No adverse effects were observed in a 28-day dermal study, in which L2 was applied to the shaved backs of rats (under occlusion for 6 hours/day, 5 days/week) at doses up to 1000 mg/kg bw/day. Although statistically significant decreased liver and kidney weights relative to brain weight were observed in males at 1000 mg/kg bw/day, there were no accompanying histopathological effects observed in the liver, and the kidney weight change was considered to be related to male-specific alpha-2µ-globulin mediated effects, which were considered as not relevant to humans (DCC 1993b cited in OECD 2013).

In a 14-day rat inhalation study (animals exposed via their whole body for 6 hours/day, 5 days/week), a no observed adverse effect concentration (NOAEC) of 6652 mg/m^3 was determined for L2 based on lack of toxicological effects at the highest tested concentration. Although there was a dose-related increase in relative kidney weights in males at 3306 and 6652 mg/m^3, which correlated with an increase of hyaline droplet inclusions in the epithelial cells of the kidney proximal convoluted tubules, this condition is considered to be specific to male rats and not significant to human health (DCC 1992; ECHA 1992). In a 28-day rat inhalation study (animals exposed via nose-only for 6 hours/day, 5 days/week), a lowest observed adverse effect concentration (LOAEC) of 950 mg/m^3 (lowest concentration tested) was determined by the OECD for L2 based on clinical chemistry changes (increased phosphorus levels in females at all concentrations and in males at 3 380 mg/m^3 and higher) and changes in the lungs observed in both sexes (slight increases in interstitial inflammation, alveolar macrophage accumulation and leukocyte infiltration with increased incidence and severity at 59 260 mg/m^3) at all concentrations tested (from 950 to 59 260 mg/m^3) (DCC 1997c cited in OECD 2013).

Rats were exposed via inhalation (nose-only) for 6 hours/day, 5 days/week to L2 and L4 in two 90-day studies. For L2, a LOAEC of 140 mg/m^3 was determined based on an increased incidence of reduced testes size and/or flaccid testes in males, histopathological changes in the lungs (increased incidence and severity of multifocal, subpleural, subacute to chronic interstitial inflammation) and kidneys (proteinaceous casts and tubular degeneration) in both sexes, and histopathological changes in testes

(tubular atrophy) and vagina (mucification of the vaginal mucosa) at all concentrations (140 to 13 640 mg/m^3)(OECD 2013). After a one-month recovery period, inflammation in the lungs was still observed in exposed animals (DCC 1997b cited in OECD 2013). While effects in rats were observed at the lowest concentration of L2 tested in the 28- and 90-day nose-only inhalation studies, the effects observed at 140 mg/m^3 in the 90-day study were not observed in the 28-day study at 950 mg/m^3, suggesting that duration of exposure may be a factor. Other 90-day rat inhalation studies conducted with L2 and L4 (whole body exposure) resulted in NOAECs at the highest concentration tested: 33 100 mg/m^3 for L2 (Cassidy et al. 2001, DCC 1998, 2002 cited in OECD 2013) and 5080 mg/m^3 for L4 (ECHA 2010b).

In a 24-month inhalation study in rats exposed via their whole body for 6 hours/day, 5 days/week to L2 concentrations of 670 to 33 100 mg/m^3, a LOAEC of 670 mg/m^3 was determined based on increased incidence of enlarged testes and Leydig cell tumours in males. No adverse effects were observed in females up to the highest concentration tested (DCC 2005 cited in OECD 2013).

In vitro genotoxicity studies conducted with L2, L4, and L5 were negative in bacterial and mammalian cells (OECD 2013; ECHA 2005, 2010c, 2010e). In the only in vivo genotoxicity study, a micronucleus study, a negative result was observed in rats exposed to intraperitoneal doses of 255 to 1030 mg/kg bw L2 (Isquith et al. 1988; OECD 2013).

For L2, in both a 1-generation and a 2-generation reproductive toxicity study, animals were exposed via inhalation (whole body, 6 hours/day, 7 days/week) to concentrations of 670 to 33 100 mg/m^3. Neurotoxicity was examined in the 2-generation reproductive toxicity study in F1 adult females (functional observational battery) and at postnatal day (PND) 20 in F2 pups (functional observational battery, brain morphology). In the 2-generation reproductive toxicity study, there were liver effects (pigment accumulation, chronic inflammation, bile duct hyperplasia) at 10 600 mg/m^3 in the F1 generation adults, with a parental NOAEC of 2 700 mg/m^3. In the same study, there were decreased pup body weights (F1 and F2, PNDs 4 to 14) at 10 600 mg/m^3, with an offspring NOAEC at 2 700 mg/m^3 (identified by OECD as a developmental NOAEC). At 33 100 mg/m^3, F2 pups demonstrated decreased average and peak acoustic startle response in both sexes, lack of habituation in the locomotor activity assessments and delayed attainment of the surface righting response in females (WIL Research Laboratories Inc. 2006 cited in OECD 2013). The NOAEC for reproductive toxicity was 33 100 mg/m^3 in both studies; the NOAEC for parental and offspring toxicity in the 1-generation reproductive toxicity study was also set at 33 100 mg/m^3 (DCC 1999, WIL Research Laboratories 2000, 2006, and Siddiqui et al. 2000 cited in OECD 2013).

A developmental toxicity study was available in the L2 ECHA dossier (ECHA 2018d). Male and female rats were mated (24/sex/group) and the females exposed via inhalation (whole body, 6 hours/day) from gestation days (GDs) 6 to 20 to L2 concentrations of 0, 100, 1 000 or 3 000 ppm (equivalent to 0, 664, 6 641 or 19 923 mg/m^3, respectively). There were no effects in dams and an increased “mean litter

proportion" of 14th rudimentary ribs in fetuses at 19 923 mg/m^3 (35% per litter versus 5% per litter in controls) was reported. However, in the ECHA dossier, the submitter did not consider these effects to be toxicologically adverse and a maternal and developmental NOAEC of 19 923 mg/m^3 was identified at the highest dose tested (ECHA 2018d).

For L4, rats were exposed (6 hours/day, 7 days/week) to concentrations of 0 or 5080 mg/m^3 via inhalation (whole body) in a 1-generation reproductive toxicity study; males were exposed for 15 days prior to the mating period up to the day before necropsy (total 29 to 30 days); females were treated for 15 days prior to the mating period up to and including GD 19 (total approximately 42 to 49 days); dams and pups were sacrificed on PND 4. Adult males and females were subjected to a functional observational battery during the 4th week of exposure. There was no parental or offspring toxicity. However, the LOAEC for reproductive toxicity was 5080 mg/m^3 (only dose tested) based on failure to deliver litters in 3/10 dams (the uterus of these 3 dams was stained to enable counting of possible reabsorbed implant sites but reabsorption was not reported) (ECHA 2007a,b).

D3

A review by the OECD in 2009 informed the health effects characterization of cyclotrisiloxane (D3). There is also a Danish EPA (2014) assessment of several siloxane substances, including D3, which included the same information cited in OECD (2009). A literature search was conducted from the year prior to the publication of the OECD assessment to present and no new studies which would change the health effects characterization were identified.

In a 28-day gavage toxicity study in rats, increased relative and absolute liver weights were observed in both sexes, and decreased mean body weights and food consumption were observed in males, at the lowest dose tested of 1000 mg/kg bw/day (Crofoot et al. 1990 cited in Johnson et al. 2012). In a 14-day oral (gavage) study in rats designed to examine effects in the liver, although liver weights increased in males at 100 mg/kg bw/day and in both sexes above 400 mg/kg bw/day (at the next dose of 1600 mg/kg bw/day), there were no gross pathological changes (Dow Corning 1990 cited in OECD 2009). In the 14- and 28-day studies discussed above, the body and liver weight and food consumption changes may be reversible, based on the absence of gross pathological changes in the liver and similar trends in food consumption and body weight at 1000 mg/kg bw/day or above. However, in the absence of studies with additional analyses (that is, histopathology), 1000 mg/kg bw/day was selected as the lowest observed adverse effect level (LOAEL) for oral (and dermal) repeated dose studies. Repeated dose dermal toxicity studies were not identified for D3.

In a 28-day inhalation study in rats (nose-only exposure, 6 hours/day, 7 days/week), a NOAEC was established at 945 mg/m^3 on the basis of mortality in both sexes between days 13 and 16 and clinical signs of toxicity (dyspnea, ataxia, reduced reflexes and piloerection observed on days before death) in animals exposed to 9041 mg/m^3 (LPT 1992 cited in OECD 2009).

In a 90-day inhalation study in rats (10/sex/group exposed nose-only, 6 hours/day, 5 days/week), a NOAEC was established at the lowest tested concentration of 137 mg/m^3 (15 ppm) on the basis of a dose-related increase in relative liver weights and hepatocyte hypertrophy in animals exposed up to 22,750 mg/m^3 (2500 ppm). The authors suggested a NOAEC of 1365 mg/m^3 (150 ppm) based on overt toxicity and body weight effects at 5460 mg/m^3 (600 ppm) but did not provide any information to support this effect level (SEHSC 2019a).

In a combined repeated-dose/reproduction/developmental toxicity study, rats (10/sex/group) were exposed via inhalation (whole body exposure) to 0, 100, 500, or 2 500 ppm D3 vapour (reported as equivalent to 0, 610, 4 500 or 22 800 mg/m^3) for 6 hours/day, 7 days/week, for up to 46 days during mating and pregnancy (28 days in males and up to GD 19 in females) with parental males sacrificed on day 29 and parental females and pups sacrificed on PND 4 (DCC 2002 cited in OECD 2009). The lowest dose is considered equivalent to 910 mg/m^3, as reported by Johnson et al. (2012). There was an increased incidence of protein droplet nephropathy in males exposed to 4 500 and 22 800 mg/m^3. However, on the basis of both the OECD (2009) and Johnson et al. (2012) reviews, the protein droplet nephropathy is not considered to be relevant to human health, and the inhalation NOAEC for systemic toxicity is 4 500 mg/m^3 based on several effects observed in animals exposed to 22 800 mg/m^3 (decreased food consumption and body weights, increased liver weights, increased incidence of centrilobular hepatocellular hypertrophy and changes in clinical chemistry parameters in both sexes, and changes in seminal vesicles [decreased organ weight and increased incidence of organ atrophy], and decreased motor activity in the functional observational battery in males). The OECD identified a NOAEC for reproductive and developmental toxicity of 4 500 mg/m^3 based on decreased litter size and implantation sites in animals exposed to 22 800 mg/m^3, as well as a maternal NOAEC of 4 500 mg/m^3 based on decreased body weights in females exposed to 22 800 mg/m^3 (DCC 2002 cited in OECD 2009; Johnson et al. 2012).

In vitro genotoxicity studies showed positive and/or equivocal results for both chromosome aberration and DNA damage/repair in mouse lymphoma cells but negative in bacterial cells (Litton Bionetics Inc. 1978 cited in OECD 2009; Isquith et al. 1988 cited in Johnson et al. 2012), and positive results for DNA damage/repair in human breast epithelial cells (Farasani and Darbre 2017). Mutation potential was negative in mouse lymphoma cells and bacterial cells (*Salmonella typhimurium*) (Litton Bionetics Inc. 1978 and Dow Corning 1979 cited in OECD 2009; Isquith et al. 1988 cited in Johnson et al. 2012). Only one *in vivo* genotoxicity study was identified: a negative result was observed in rats exposed to intraperitoneal doses of 125 to 1080 mg/kg bw in a micronucleus study (Bioassay systems 1982 cited in OECD 2009; Isquith et al. 1988).

DvTMDS

No high hazard classifications by other national or international agencies for carcinogenicity, genotoxicity, developmental toxicity, or reproductive toxicity were identified for dvTMDS. It is also not on the ECHA's Candidate List of Substances of

Very High Concern for Authorisation (ECHA 2017f). Further investigation of the health effects is not warranted at this time given the negligible exposure of dvTMDS to the general Canadian population.

6.2.1 Consideration of subpopulations who may have greater susceptibility

There are groups of individuals within the Canadian population who, due to greater susceptibility, may be more vulnerable to experiencing adverse health effects from exposure to substances. The potential for susceptibility during different life stages or by sex are considered from the available studies. In this health effects assessment, studies included examinations of different sexes of laboratory animals, as well as developmental and neurotoxicity effects in the young, reproductive effects in pregnant animals, and carcinogenicity effects in older individuals. There was not a particular life stage or sex that was considered more susceptible based on the available information.

7. Characterization of risk to human health

Exposure may occur through air (L2, L4, L5, D3), food (D3), and consumer products (L2 and D3). Sentinel exposure scenarios resulting in the highest exposures for relevant age groups are presented to characterize risk. Table 7-1 to 7-4 provide relevant exposure estimates and critical effect levels, as well as resulting margins of exposure (MOEs) for L2, L4, L5 and D3. Critical effect levels are selected from a study, with considerations including the endpoint, exposure route and duration.

Table 7-1. Relevant exposure and critical effect levels for L2, as well as margins of exposure, for determination of risk

Exposure scenario	Exposure	Critical effect level	Critical health effect endpoint	MOE
Indoor air	0.0007 mg/m^3	LOAEC = 25 mg/m^3_{adj} in 90-day rat inhalation study (nose-only) using L2.[a]	Increased incidence of reduced testes size and/or flaccid testes in males and histopathological changes in the lungs and kidneys of both sexes, testes in males and vagina in females at all concentrations (25 to 2436 mg/m^3_{adj}).	36 000
Inhalation exposure to nail polish drying drops (per event, adults and teens)[b]	13.3 mg/m^3	NOAEC = 6652 mg/m^3 in 2-week rat inhalation study (whole body) using L2.	No adverse effects (highest dose tested).	500
Inhalation exposure to	0.729 mg/m^3[b]	NOAEC = 6652 mg/m^3	No adverse effects (highest dose tested).	9100

Exposure scenario	Exposure	Critical effect level	Critical health effect endpoint	MOE
bandage adhesive remover (per event, adults and teens)		in 2-week rat inhalation study (whole body) using L2.		

Abbreviations: MOE = Margin of exposure; adj = Adjusted to account for daily exposures of 24 hours.

[a] A LOAEC of 140 mg/m^3 was determined in this study. When exposure is amortized to 24 hours/day, 7 days/week, this LOAEC is adjusted to 25 mg/m^3.

[b] Exposure concentration was amortized over 6 hours.

For L2, with respect to inhalation exposure, comparison of critical effects to estimates of exposure concentrations in indoor air and from use of bandage adhesive remover and nail polish drying drops resulted in MOEs that are considered adequate to account for uncertainties in the health effects and exposure databases. The selected NOAEC of 6 652 mg/m^3 from a 2-week inhalation study is protective of potential developmental variations in the absence of maternal toxicity observed at 19 923 mg/m^3 L2 in a developmental toxicity inhalation study in rats (ECHA 2018d).

Dermal exposure to L2 from the use of cosmetics was also considered. No adverse health effects were observed in experimental animals whose skin was exposed to doses up to 1000 mg/kg bw/day of L2 under occlusion in a four-week dermal toxicity study (DCC 1993b cited in OECD 2013). As such, there is low potential risk to human health from dermal exposure to L2.

Table 7-2. Relevant exposure and critical effect level for L4, as well as margin of exposure, for determination of risk

Exposure scenario	Exposure	Critical effect level	Critical health effect endpoint	MOE
Indoor air	0.0017 mg/m^3	LOAEC = 25 mg/m$^3_{adj}$ in 90-day rat inhalation study (nose-only) using L2 (read-across)	Increased incidence of reduced testes size and/or flaccid testes in males and histopathological changes in the lungs and kidneys of both sexes, testes in males and vagina in females at all concentrations (140 to 13 640 mg/m^3).	15 000[a]

Abbreviations: MOE = Margin of exposure; adj = Adjusted to account for daily exposures of 24 hours.

[a] The LOAEC in the 90-day study in rats exposed to L4 was not selected for use in consideration of the study protocol (whole body exposure and daily exposure duration not specified). Comparison of exposure to the 24 hours/day time-weighted adjusted LOAEC of 1270 mg/m^3 in the 1-generation reproduction study (initially LOAEC of 5080 mg/m^3 based on increased failure to deliver litters) would result in a MOE of 747 000. This study was not selected for use, also in consideration of the study protocol (whole body exposure and shorter duration than the 90-day study using L2 [<=53 days]).

For L4, with respect to inhalation, comparison of the critical effect level and the estimate of exposure from indoor air resulted in an MOE that is considered adequate to account for uncertainties in the health effects and exposure databases.

Table 7-3. Relevant exposure and critical effect levels for L5, as well as margins of exposure, for determination of risk

Exposure scenario	Exposure	Critical effect level	Critical health effect endpoint	MOE
Indoor air	0.0009 mg/m^3	LOAEC = 25 mg/m^3_{adj} in 90-day rat inhalation study (nose-only) using L2 (read-across).	Increased incidence of reduced testes size and/or flaccid testes in males and histopathological changes in the lungs and kidneys of both sexes, testes in males and vagina in females at all concentrations (140 to 13 640 mg/m^3).	28 000

Abbreviation: MOE, Margin of exposure.

For L5, with respect to inhalation exposure, comparison of critical effects with estimates of exposure from indoor air resulted in MOEs that are considered adequate to account for uncertainties in the health effects and exposure databases.

Oral exposure to L5 from the potential ingestion of caught fish was also considered. No adverse health effects were observed in rats administered L5 up to a limit dose of 1000 mg/kg bw/day in a 7-day and 28-day oral gavage study (ECHA 2009, 2010d). As such, there is low potential risk to human health from oral exposure to L5.

Table 7-4. Relevant exposure and critical effect levels for D3, as well as margins of exposure, for determination of risk

Exposure scenario	Systemic exposure	Critical effect level	Critical health effect endpoint	MOE
Food (6 months to 4 years old)	0.0032 mg/kg bw/day	LOAEL = 1000 mg/kg bw/day (LDT) in 28-day rat gavage study.	Increased relative and absolute liver weights in both sexes and decreased mean body weights and food consumption in males.	310 000
Indoor air	0.0695 mg/m^3	NOAEC = 24.5 mg/m^3_{adj} in 90-day rat inhalation study (nose-only).[b]	Mortality and clinical signs of toxicity in males at 9041 mg/m^3.	350

Exposure scenario	Systemic exposure	Critical effect level	Critical health effect endpoint	MOE
Dermal exposure to body makeup (daily, adults)	0.330 mg/kg bw/day[a]	LOAEL = 1000 mg/kg bw/day (LDT) in 28-day rat gavage study.	Increased relative and absolute liver weights in both sexes and decreased mean body weights and food consumption in males.	3 000
Dermal exposure to diaper cream (daily, 0 to 6 months old)	0.0893 mg/kg bw/day[a]	LOAEL = 1000 mg/kg bw/day (LDT) in 28-day gavage rat study.	Increased relative and absolute liver weights in both sexes and decreased mean body weights and food consumption in males.	11 000
Inhalation exposure to silicone baking moulds (per event)[c]	0.0239 mg/m^3	NOAEC = 945 mg/m^3 in 28-day rat inhalation study (nose-only).	Mortality in both sexes and clinical signs of toxicity in animals at 9041 mg/m^3.	40 000

Abbreviations: MOE, Margin of exposure; LDT, lowest dose tested; adj, adjusted to account for daily exposures of 24 hours.

[a] Using the Jmax method.

[b] A NOAEC of 137 mg/m^3 was determined in this study. When exposure is amortized to 24 hours/day, this NOAEC is adjusted to 24.5 mg/m^3.

[c] Fromme et al. (2019) measured D3 in indoor air throughout a baking process using silicone baking moulds, but did not detect D3 in the silicone baking moulds in the product analysis.

For D3, the MOEs listed above for food (including caught fish and baked goods made in silicone baking moulds), indoor air, body makeup, diaper cream, and silicone baking moulds are all considered adequate to account for uncertainties in the health effects and exposure databases.

7.1 For dvTMDS, there is low concern for risk because exposure to the general population of Canada is not expected and there are no high hazard classifications for this substance. Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below. The achieved margins of exposure were considered adequate to address these uncertainties in the health effects and exposure databases.

Table 7-5. Sources of uncertainty in the risk characterization

Key sources of uncertainty	Impact
No dermal absorption data for D3.	+
D3 may be formed from other cyclic volatile methyl siloxanes, including during sample analysis.	+
No repeated dose dermal toxicity study for D3.	+/-

Key sources of uncertainty	Impact
No Canadian monitoring data in drinking water, soil, and dust for substances in the Siloxanes Group.	+/-
For L4, L5, and D3, there are no carcinogenicity studies by any route of exposure. For L4 and L5, there are no developmental studies by any route nor repeated dose studies by the dermal route. There is also no chronic oral or dermal study for L2.	+/-

+ = uncertainty with potential to cause over-estimation of exposure/risk; +/- = unknown potential to cause over or under estimation of risk.

8. Conclusion

Cyclomethicone is primarily comprised of D4, D5, and D6, three substances previously assessed under CEPA. Thus, cyclomethicone is considered to have been addressed through the screening assessments of D4, D5, and D6 in 2008 and through the revised conclusion regarding D5 in 2012. As such, this substance will not be subject to further risk assessment work at this time given previous regulatory activities.

Considering all available lines of evidence presented in this assessment, there is low risk of harm to the environment from L2, L4, L5, D3, and dvTMDS. It is concluded that the five substances in the Siloxanes Group do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are 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.

On the basis of the information presented in this assessment, it is concluded that the five substances in the Siloxanes Group do not meet the criteria under paragraph 64(*c*) of CEPA as they are 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, it is concluded that L2, L4, L5, D3, and dvTMDS do not meet any of the criteria set out in section 64 of CEPA.

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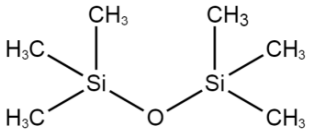
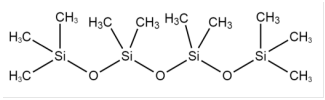
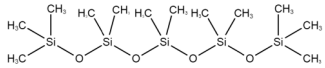
Appendices

Appendix A. Hazard summary and read-across within the linear siloxanes

Table A-1. Hazard information for linear siloxanes

Chemical name	L2	L4	L5
CAS RN	107-46-0	141-62-8	141-63-9
Role	Target substance	Target substance	Target substance
Chemical structure			
Vapour pressure (Pa at 25°C)	4451 (at 20°C)	73	7.8
Water solubility (mg/L)	9.3×10^{-1}	6.74×10^{-3}	7.04×10^{-5}
Log K_{OC} (dimensionless)	2.53	5.16	6.3
Toxico-kinetics and metabolism	L2 mostly eliminated via exhalation (50%) and to a lesser extent in urine (37%) with approximately 1% excreted in faeces; based on inhalation studies in rats (DCC 2008 cited in OECD 2013). Majority of radioactivity eliminated within first 24 hours in a 14-day inhalation study in rats; approximately 4% retained in body (ECHA 2006a).	Read-across from L2 and L5.	25% of single oral gavage dose in rats absorbed in gastrointestinal tract with 97% of it eliminated in faeces (74%) and expired air (appximately 23%) and < 3% recovered in urine (DCC 1985; ECHA 1985).

Chemical name	L2	L4	L5
CAS RN	107-46-0	141-62-8	141-63-9
Role	Target substance	Target substance	Target substance
Repeated dose toxicity (oral)	NOAEL = 160 mg/kg bw/day based on decreased food consumption and body weight gain, increased relative liver weights and changes in some hematological parameters in males at 640 mg/kg bw/day (HDT); 28 day gavage study in rats (ECHA 1994).	NOAEL = 25 mg/kg bw/day based on protoporphyrin accumulation in the liver of males at 250 mg/kg bw/day; 28 day gavage study in rats (ECHA 2010a). NOAEL = 1000 mg/kg bw/day (HDT); 7- and 28-day gavage study in rats (DCC 2009; ECHA 2010d). LOAEL (ODT) = 500 mg/kg bw/day based on decreased adrenal weights in both sexes and increased thyroid weights in males; 1-year dietary study in rats (DCC 1966a). LOAEL (ODT)= 500 mg/kg bw/day based on heart and kidney effects in females, decreased liver weights and increased spleen weights in males; 8-month dietary study in rabbits (DCC 1966b).	NOAEL = 1000 mg/kg bw/day (HDT); 7- and 28-day gavage study in rats (ECHA 2009, 2010d).
Repeated dose toxicity (dermal)	NOAEL = 1000 mg/kg bw/day (HDT); rats dosed under occlusion 6 h/day, 5 days/wk for 28 days (DCC 1993b cited in OECD 2013).	Read-across from L2.	NR.

Chemical name	L2	L4	L5
CAS RN	107-46-0	141-62-8	141-63-9
Role	Target substance	Target substance	Target substance
Repeated dose toxicity (inhalation)	NOAEC = 6652 mg/m^3 (HDT); 2-wk whole body rat 6 h/day, 5 days/wk (DCC 1992; ECHA 1992). LOAEC = 950 mg/m^3 based on clinical chemistry changes in females and histopathological changes in the lungs of both sexes; 4-wk nose-only rat 6 h/day, 5 days/wk (DCC 1997c cited in OECD 2013). LOAEC = 140 mg/m^3 based on increased incidence of reduced testes size and/or flaccid testes and histopathological changes in testes in males, histopathological changes in the vagina in females, and histopathological changes in the lungs and kidneys in both sexes; 13-wk nose-only rat 6 h/day, 5 days/wk (DCC 1997b cited in OECD 2013). NOAEC = 33 100 mg/m^3 (HDT); 13-wk whole body rat 6 h/day, 5 days/wk	NOAEC = 5080 mg/m^3 (HDT); 13-wk whole body rat 5 days/wk (duration of exposure/day not stated) (ECHA 2010b). Read-across from L2.	Read-across from L2.

Chemical name	L2	L4	L5
CAS RN	107-46-0	141-62-8	141-63-9
Role	Target substance	Target substance	Target substance
	(Caddidy et al. 2001; DCC 1998, 2002 cited in OECD 2013).		
Long-term toxicity (inhalation)	LOAEC = 670 mg/m^3 based on increased incidence of enlarged testes and Leydig cell tumours in males; 2-year whole body rat 6 h/day, 5 days/wk (DCC 2005 cited in OECD 2013).	NR	NR
Reproductive (inhalation)	NOAEC = 2700 mg/m^3 based on liver effects in F1 adults and decreased body weights in F1 and F2 pups at 10 600 mg/m^3; No reproductive effects up to the HDT (33 100 mg/m^3); 2-generation reproductive toxicity study in rats 6 h/day, 7 days/wk, whole body inhalation (WIL Research Laboratories 2006 cited in OECD 2013). NOAEC = 33 100 mg/m^3 (HDT) whole body 1-generation reproductive toxicity study in rats, 6 h/day, 7 days/wk (DCC 1990; WIL Research Laboratories 2000 and Siddiqui et al.	LOAEC = 5080 mg/m^3 (ODT) based on failure to deliver litters in 3/10 dams, in absence of other systemic effects in parental animals; 1-generation reproductive toxicity study in rats, 6 h/day, 7 days/wk, whole body inhalation (ECHA 2007a,b).	NR

Chemical name	L2	L4	L5
CAS RN	107-46-0	141-62-8	141-63-9
Role	Target substance	Target substance	Target substance
	2000 cited in OECD 2013).		
Develop-mental (inhalation)	Maternal and developmental NOAEC = 19 700 mg/m^3 (HDT) whole body developmental toxicity study in rats; 6 h/day, gestation days 6 to 20 (ECHA 2018d).	NR	NR
Genetic toxicity	Negative	Negative	Negative
Carcino-genicity (inhalation)	Some evidence of testicular carcinogenicity; 2-year whole body rat 6 h/day, 5 days/wk (DCC 2005 cited in OECD 2013).	NR	NR

Abbreviations: NR = Read-across not required for risk characterization; HDT = highest dose tested; LDT= lowest dose tested; ODT = only dose tested; K_{oc}, organic carbon–water partition coefficient; NOAEL, no observed adverse effect level; LOAEL, lowest observed adverse effect level; NOAEC, no observed adverse effect concentration; LOAEC, lowest observed adverse effect concentration; h = hours, wk = week.

Appendix B. Deterministic estimates of daily human exposure to siloxanes in environmental media and food

Table B-1. General human exposure factors for different age groups (Health Canada 1998)

Age Group	Body weight (kg)	Inhalation rate (m^3/day)	Drinking water intake (L/day)	Soil ingestion rate (mg/day)	Dust ingestion rate (mg/day)	Fish ingestion rate (g/day)
0 to 6 months (human milk-fed)	7.5	2.1	N/A	N/A	38	N/A
0 to 6 months (formula fed)	7.5	2.1	0.8	N/A	38	N/A
0 to 6 months (not formula fed)	7.5	2.1	0.3	N/A	38	N/A
6 months to 4 years	15.5	9.3	0.7	14	41	54.7
5 to 11 years	31.0	14.5	1.1	21	31	89.8
12 to 19 years	59.4	15.8	1.2	1.4	2.2	97.3
20 to 59 years	70.9	16.2	1.5	1.6	2.5	111.7
60+ years	72.0	14.3	1.6	1.5	2.5	72.9

Abbreviation: N/A, not applicable.

Table B-2. Estimates of daily intake (µg/kg bw/day) of L2 by various age groups

Route of exposure	0–6 months human milk-fed	0–6 months formula fed	0–6 months not formula fed	6 months –4 years	5–11 years	12–19 years	20–59 years	60+ years
Ambient Air[1]	5.3E-05	5.3E-05	5.3E-05	1.1E-04	8.8E-05	5.0E-05	4.3E-05	3.7E-05
Indoor Air[2]	1.6E-01	1.6E-01	1.6E-01	3.5E-01	2.7E-01	1.6E-01	1.3E-01	1.2E-01
Drinking Water[3]	N/A	3.3E-04	1.3E-04	1.4E-04	1.1E-04	6.3E-05	6.6E-05	7.0E-05
Soil[4]	N/A	N/A	N/A	5.3E-11	3.9E-11	1.4E-12	1.3E-12	1.2E-12
Total Intake	**1.6E-01**	**1.6E-01**	**1.6E-01**	**3.5E-01**	**2.7E-01**	**1.6E-01**	**1.3E-01**	**1.2E-01**

Abbreviation: N/A, not applicable.

[1] Ambient air intake was estimated using maximum estimated concentration of 0.0015 µg/m3 in ambient air, modelled using ChemCAN (2003).

[2] Indoor air intake was estimated using the highest measured concentration of 0.67 µg/m^3 from the Canadian Health Measures Survey (P95, Zhu 2017).

[3] Drinking water intake was estimated using maximum estimated concentration of 0.0031 µg/L in surface water, modelled using ChemCAN (2003).

[4] Soil intake was estimated using maximum estimated concentration of 5.82 x 10^{-5} µg/kg in soil, modelled using ChemCAN (2003).

Table B-3. Estimates of daily intake (µg/kg bw/day) of L4 by various age groups

Route of exposure	0–6 months human-milk fed	0–6 months formula fed	0–6 months not	6 months –4 years	5–11 years	12–19 years	20–59 years	60+ years

			formula fed					
Ambient Air[1]	2.3E-04	2.3E-04	2.3E-04	4.9E-04	3.8E-04	2.2E-04	1.9E-04	1.6E-04
Indoor Air[2]	4.1E-01	4.1E-01	4.1E-01	8.9E-01	6.9E-01	3.9E-01	3.4E-01	2.9E-01
Drinking Water[3]	N/A	1.0E-03	3.8E-04	4.3E-04	3.4E-04	1.9E-04	2.0E-04	2.1E-04
Soil[4]	N/A	N/A	N/A	9.9E-10	7.5E-10	2.6E-11	2.5E-11	2.3E-11
Dust[5]	1.7E-04	1.7E-04	1.7E-04	9.0E-05	3.4E-05	1.3E-06	1.2E-06	1.2E-06
Total Intake	**4.1E-01**	**4.2E-01**	**4.1E-01**	**8.9E-01**	**6.9E-01**	**3.9E-01**	**3.4E-01**	**2.9E-01**

Abbreviation: N/A, not applicable.
[1] Ambient air intake was estimated using highest measured concentration of 0.0065 µg/m^3 from a semi urban meteorological station in Toronto, Ontario (maximum, Ahrens et al. 2014).
[2] Indoor air intake was estimated using the highest measured concentration of 1.69 µg/m^3 from the Canadian Health Measures Survey (P95, Zhu 2017).
[3] Drinking water intake was estimated using maximum estimated concentration of 0.0095 µg/L in surface water, modelled using ChemCAN (2003).
[4] Soil intake was estimated using maximum estimated concentration of 0.0011 µg/kg in soil, modelled using ChemCAN (2003).
[5] Dust intake was estimated using the maximum measured concentration of 34.2 µg/kg from samples taken from the floors of homes, offices and labs in Albany, New York, US (Tran et al. 2015).

Table B-4. Estimates of daily intake (µg/kg bw/day) of L5 by various age groups

Route of exposure	0–6 months human-milk fed	0–6 months formula fed	0–6 months not formula fed	6 months –4 years	5–11 years	12–19 years	20–59 years	60+ years
Ambient Air[1]	1.7E-04	1.7E-04	1.7E-04	3.6E-04	2.8E-04	1.6E-04	1.4E-04	1.2E-04
Indoor Air[2]	2.2E-01	2.2E-01	2.2E-01	4.7E-01	3.7E-01	2.1E-01	1.8E-01	1.6E-01
Drinking Water[3]	N/A	6.3E-04	2.4E-04	2.7E-04	2.1E-04	1.2E-04	1.3E-04	1.3E-04
Food[4]	N/A	N/A	N/A	2.6E-02	2.2E-02	1.2E-02	1.2E-02	7.6E-03
Soil[5]	N/A	N/A	N/A	6.2E-10	4.7E-10	1.6E-11	1.6E-11	1.4E-11
Dust[6]	3.4E-04	3.4E-04	3.4E-04	1.8E-04	6.7E-05	2.5E-06	2.4E-06	2.3E-06
Total Intake	**2.2E-01**	**2.2E-01**	**2.2E-01**	**5.0E-01**	**3.9E-01**	**2.2E-01**	**1.9E-01**	**1.6E-01**

Abbreviation: N/A, not applicable.
[1] Ambient air intake was estimated using highest measured concentration of 0.0048 µg/m^3 from a semi urban meteorological station in Toronto, Ontario (maximum, Ahrens et al. 2014).
[2] Indoor air intake was estimated using the highest measured concentration of 0.9 µg/m^3 from the Canadian Health Measures Survey (P95, Zhu 2017).
[3] Drinking water intake was estimated using maximum estimated concentration of 0.0059 µg/L in surface water, modelled using ChemCAN (2003).
[4] Food intake was estimated using the maximum concentration of 7.5 µg/kg in the liver of lake trout from fish monitoring data in the US (Bordson et al. 2018).
[5] Soil intake was estimated using maximum estimated concentration of 0.00069 µg/kg in soil, modelled using ChemCAN (2003).
[6] Dust intake was estimated using the maximum measured concentration of 67 µg/kg from samples taken from the floors of homes, offices and labs in Albany, New York, US (Tran et al. 2015).

Table B-5. Estimates of daily intake (µg/kg bw/day) of D3 by various age groups

Route of exposure	0–6 months human-milk fed	0–6 months formula fed	0–6 months not formula fed	6 months –4 years	5–11 years	12–19 years	20–59 years	60+ years
Ambient Air[1]	4.1E-03	4.1E-03	4.1E-03	8.8E-03	6.8E-03	3.9E-03	3.3E-03	2.9E-03
Indoor Air[2]	1.7E+01	1.7E+01	1.7E+01	3.7E+01	2.8E+01	1.6E+01	1.4E+01	1.2E+01
Drinking Water[3]	N/A	6.0E-04	2.2E-04	2.5E-04	2.0E-04	1.1E-04	1.2E-04	1.2E-04
Food[4]	N/A	N/A	1.7	3.2	2.8	1.6	1.1	9.6E-01
Soil[5]	N/A	N/A	N/A	5.3E-11	4.0E-11	1.4E-12	1.3E-12	1.2E-12
Dust[6]	2.6E-04	2.6E-04	2.6E-04	1.3E-04	5.1E-05	1.9E-06	1.8E-06	1.8E-06
Total Intake	**1.7E+01**	**1.7E+01**	**1.9E+01**	**4.0E+01**	**3.1E+01**	**1.8E+01**	**1.5E+01**	**1.3E+01**

Abbreviation: N/A, not applicable.

[1] Ambient air intake was estimated using highest measured concentration of 0.117 µg/m^3 from Whistler, British Colombia (maximum, Genauldi et al. 2017).

[2] Indoor air intake was estimated using the highest measured concentration of 69.54 µg/m^3 from samples taken from homes in Quebec City (Won and Lusztyk 2011).

[3] Drinking water intake was estimated using maximum estimated concentration of 0.0056 µg/L in surface water, modelled using ChemCAN (2003).

[4] Food intake was estimated using the maximum concentration of 39 µg/kg ww from fish monitoring data in Canada (whole body homogenates of freshwater fishes) (McGoldrick and Murphy 2016), and the maximum concentration of 290 µg/kg reported in baked goods made in silicone baking moulds in Germany (Fromme et al. 2019).

[5] Soil intake was estimated using maximum estimated concentration of 0.000059 µg/kg in soil, modelled using ChemCAN (2003).

[6] Dust intake was estimated using the maximum measured concentration of 51 µg/kg from samples taken from the floors of homes, offices and labs in Albany, New York, US (Tran et al. 2015).

Appendix C. Parameters used to estimate human exposures

Exposure from the use of cosmetics and other products available to consumers was estimated using ConsExpo Web (2018). Exposure estimates were calculated based on default body weights of 70.9 kg, 59.4 kg, 31.0 kg, 15.5 kg, and 7.5 kg for adults (20 years and older), teens (12 to 19 years old), children (5 to 11 years old), toddlers (6 months to 4 years old), and infants (0 to 6 months old), respectively (Health Canada 1998). The parameters used in the estimation of inhalation and dermal exposures from the use of cosmetics and other products available to consumers are described in Table C-1. Unless specified, the defaults come from the relevant ConsExpo Fact Sheet for the scenario presented.

Table C-1. Exposure parameter inputs for cosmetics and other products available to consumers scenarios

Product scenario (substance)	**Assumptions[a]**
Body lotion for face, neck and neckline (L2)	Concentration of L2: 3%[b] Dermal - Direct contact, instant application model Frequency: 1 per day for adults, 0.8 per day for teens (Ficheux et al. 2015; Wu et al. 2010) Exposed area: 3820 cm² for adults, 3410 cm² for teens (considered surface area of face and half of body trunk based on product description; adjustment from Health Canada 1995) Product amount: 2.28 g/use for adults, 2.01 g/use for teens (Ficheux et al. 2016 and SA adjustment from adults) Absorption model: Fixed fraction Absorption fraction: 0.02%
Aerosol bandage adhesive remover (L2)	Concentration of L2: 67%[b] Frequency: 4 per month (professional judgement) Inhalation - Exposure to vapour, instantaneous release Exposure duration: 5 minutes (based on fragrance scenario) Product amount: 0.85 g [b] Room volume: 10 m³ Ventilation rate: 2 per hour Inhalation rate: 16.2 m³/hr Dermal - Direct contact, instant application Exposed area: 9 cm² (professional judgement) Product amount: 0.85 g [b] Absorption model: Fixed fraction Absorption fraction: 0.02%
Facial makeup	Concentration of L2: 45% [b]

(solid powder; L2)	Dermal - Direct contact, instant application model Frequency: 1.24 per day for adults and teens (Loretz et al. 2006) Exposed area: 637 cm^2 for adults and teens(Health Canada 1995) Product amount: 0.54 g/use for adults and teens (Loretz et al. 2006) Absorption model: Fixed fraction Absorption fraction: 0.02%
Hair styling product (hair gel; L2)	Concentration of L2: 100%[b] RF of 0.1 was applied (wash off), giving the final weight fraction of 10% (SCCS 2012) Dermal – Direct contact, instant application model Frequency: 16.4 per month Exposed area: 1092.5 cm^2 (Health Canada 1995) Product amount: 1.9 g/use for adults Absorption model: Fixed fraction Absorption fraction: 0.02%
Nail polish drying drops (top coat scenario; L2)	Concentration of L2: 100%[b] Inhalation – Exposure to vapour, evaporation model Frequency: 0.18 per day for adults, 0.2 per day for teens (Ficheux et al. 2014) Exposure duration: 18 minutes (Ficheux et al. 2014) Product amount: 0.33 g for adults and teens (Ficheux et al. 2014) Room volume: 1 m^3 (close to the face) Ventilation rate: 1 per hour Inhalation rate: 16.2 m^3/day for adults, 15.8 m^3/day for teens (Health Canada 1998) Mass transfer coefficient: 10 m/hr Release area mode: constant Release area: 26.2 cm^2 (based on data from Ficheux et al. 2014 and assumption that both finger- and toe-nails are painted) Molecular weight matrix: 124 g/mol
Body makeup (D3)	Concentration of D3: 0.044%[b] Dermal - Direct contact, instant application model (body lotion model was used) Frequency: 1 per day for adults (Ficheux et al. 2015; Wu et al. 2010) Exposed area: 9008 cm^2 for adults (considered SA of face, arms, and legs based on its use; Health Canada 1995) Product amount: 5.33 g/use for adults (adjusted based on the refined SA; Ficheux et al. 2016) Absorption model: Fixed fraction Absorption fraction: 100%
Face cream (D3)	Concentration of D3: 5% (MSDS 2010) Dermal – Direct contact, instant application model

	Frequency: 1.8 per day (Loretz et al. 2005) Exposed area: 638 cm^2 for adults, 730 cm^2 for teens (Health Canada 1995) Product amount: 1.2 g/use for adults and teens (Loretz et al. 2005) Absorption model: Fixed fraction Absorption fraction: 100%
Fragrance (D3)	Concentration of D3: 0.012% (converted from 0.12 mg/g ww, Wang et al. 2009) Frequency: 1.7 per day (Loretz et al. 2006) Inhalation – Exposure to spray, spraying model Spray duration: 0.08 minutes Exposure duration: 5 minutes Room volume: 10 m^3 Room height: 2.5 m Ventilation rate: 2 per hour Inhalation rate: 16.2 m^3/day (Health Canada 1998) Cloud volume: 0.0625 m^3 Mass generation rate: 0.1 g/s Airborne fraction: 0.02 Density non-volatile: 1.5 g/cm^3 Inhalation cut off diameter: 15 µm Median diameter: 2.7µm Arithmetic coefficient of variation: 0.73 Maximum diameter: 50 µm Dermal – Direct contact, instant application model Exposed area: 100 cm^2 Product amount: 0.33 g/use (Loretz et al. 2006) Absorption model: Fixed fraction Absorption fraction: 100%
Diaper cream (toddlers and infants; D3)	Concentration of D3: 0.045% (converted from 0.45 mg/g ww, Wang et al. 2009) Dermal – Direct contact, instant application model Frequency: 2.6 per day for toddlers and 1.1 per day for infants (Gomez-Berrada et al. 2013) Exposed area: 405 cm^2 for toddlers and 258 cm^2 for infants (calculated) Product amount: 2 g for toddlers and 2.6 g for infants (Gomez-Berrada et al. 2013) Absorption model: Fixed fraction Absorption fraction: 100%

[a] Unless specified, a retention factor of 1 was used
[b] Personal communication, emails from the Consumer and Hazardous Product Safety Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 31, 2017, July 17, 2017, and April 3, 2018; unreferenced.

Appendix D. Maximum flux (Jmax) approach for estimation of dermal systemic exposures to D3

The maximum flux (Jmax) approach as conducted in Williams et al. (2016) was used to estimate dermal systemic exposures to D3 from use of cosmetics and other products available to consumers. Face cream scenario is presented below as a representative for this approach. Exposure parameter assumptions for other products containing D3 are the same as described in Table C-1.

The equations used are provided below. Values for water solubility, log K_{ow}, and molecular weight (MW) were obtained from Table 3-1 of this assessment (where available, experimental values were used). A mass balance check was also done for this scenario; see Table D-2 below.

(1) Kp (Potts & Guy equation, based on aqueous vehicle):
Log Kp (in cm/h) = -2.71 + (0.71)(log K_{ow}) - (0.0061)(MW, in g/mol)

(2) Jmax:
Jmax (in mg/cm^2/h) = Kp (in cm/h) x Water solubility (in mg/cm^3)

(3) Maximum theoretical amount absorbed per day (Qmax):
Qmax (in mg) = Jmax (in mg/cm^2/h) x Surface area of skin contact (in cm^2) x Exposure duration (in h)

(4) Dermal Systemic Exposure = Qmax/BW

A mass balance check was conducted by comparing the Qmax to the total amount of the substance on the skin (Qapp).

(5) For mass balance check:
Qapp = Conc (mg/g) x Product Amount (Amt) x Exposure Frequency (F) X RF
(see individual exposure scenario in Table D-2 for specific values).

If the Qmax > Qapp, then Qapp (equivalent to 100% dermal absorption) was used to characterize the amount absorbed. Otherwise, Qmax was used.

Table D-1. Dermal exposure parameters for maximum flux approach for D3 in face cream (on a 'day of exposure' basis)[a]

Substance and sentinel exposure scenario	Age group(s)	Jmax (mg/cm^2/h)	Qmax (mg)
D3, face cream	Adult	0.0233	1.654

[a] See exposure scenarios in Table D-2 for frequency (F), if relevant.
[b] See Table D-2 for details on the per event and daily exposure scenarios.

Table D-2. Sentinel exposure scenario assumptions

Substance	Sentinel exposure scenario	Assumptions
D3	Face cream	Mass balance check (Qmax/Qapp): 0.766 Concentration (Conc): 0.1% = 1 mg/g[a] Age group: Adult Body weight (BW): 70.9 For Estimated Per Event Dermal Exposure: Frequency (F): 1.8 per day (Loretz et al. 2005) Product amount (Amt): 1.2 g/use (Loretz et al. 2005) Surface area of skin contact (SA): 638 cm² (Health Canada 1995) Retention factor (RF): 1 Exposure duration: 24 h/day Qapp - Leave on period: 2.16 mg

[a] Personal communication, emails from the Consumer and Hazardous Product Safety Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 31, 2017 and July 17, 2017; unreferenced.