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Canada

Draft Screening Assessment

Aliphatic Amines Group

Environment and Climate Change Canada
Health Canada

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Synopsis

Pursuant to section 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA), the Minister of the Environment and the Minister of Health have conducted a screening assessment of 13 of 19 substances referred to collectively under the Chemicals Management Plan as the Aliphatic Amines Group. These 19 substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA or were considered a priority on the basis of other human health concerns. Four of the 19 substances were determined to be of low concern through other approaches, and decisions for these substances are provided in separate reports.[1,2] In addition, 2 of the 19 substances have been moved from the Aliphatic Amines Group into other groups under the Chemicals Management Plan.[3] Accordingly, this screening assessment addresses the 13 substances listed in the table below and hereinafter referred to as the Aliphatic Amines Group. The Chemical Abstracts Service Registry Numbers (CAS RN[4]), their *Domestic Substances List* (DSL) names and their common names (abbreviations) are listed in the table below.

Substances in the Aliphatic Amines Group

CAS RN	DSL name	Common name (abbreviations)	Subgroup
103-83-3[a]	Benzenemethanamine, N,N-dimethyl-	Dimethylbenzylamine	Short-chain
107-15-3	1,2-Ethanediamine	Ethylenediamine	Short-chain
111-40-0	1,2-Ethanediamine, N-(2-aminoethyl)-	Diethylenetriamine	Short-chain
112-69-6	1-Hexadecanamine, N,N-dimethyl-	Hexadecyldimethylamine	Long-chain
124-30-1	1-Octadecanamine	Octadecylamine	Long-chain
124-40-3	Methanamine, N-methyl-	Dimethylamine	Short-chain
61788-46-3[b]	Amines, coco alkyl	Cocoamine	Long-chain

[1] Conclusions for the substance bearing CAS RN 68955-53-3 are provided in the Substances Identified as Being of Low Concern using the Ecological Risk Classification of Organic Substances and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Screening Assessment.

[2] Conclusions for substances bearing CAS RNs 112-90-3, 80939-62-4 and 90367-27-4 are provided in the Rapid Screening of Substances with Limited General Population Exposure Screening Assessment.

[3] The substances bearing CAS RNs 108-91-8 and 58713-21-6 have been moved from the Aliphatic Amines Group into the Sodium Cyclamate and Cyclohexylamine Group (formerly known as Sulfamic Acid, Cyclohexyl-, Monosodium Salt) and the Hexamethylenetriamine Group, respectively.

[4] 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.

CAS RN	DSL name	Common name (abbreviations)	Subgroup
61789-79-5[a,b]	Amines, bis(hydrogenated tallow alkyl)	Bis(hydrogenated tallow alkyl) amines (BHTAA)	Long-chain
61790-59-8[b]	Amines, hydrogenated tallow alkyl, acetates	Hydrogenated tallow alkyl amines acetates (HTAAA)	Long-chain
61790-60-1[b]	Amines, tallow alkyl, acetates	Tallow alkyl amines acetates (TAAA)	Long-chain
61791-55-7[b]	Amines, N-tallow alkyltrimethylenedi-	N-tallow alkyltrimethylenediamines (TAPDA)	Long-chain
68479-04-9[b]	1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-, branched	1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-, branched (DPDAB)	Long-chain
68783-25-5[b]	Amines, N,N,N’-trimethyl-N’-tallow alkyltrimethylenedi-	N,N,N'-trimethyl-N'-tallow alkyltrimethylenediamines (TMTADA)	Long-chain

[a] This substance was not identified under subsection 73(1) of CEPA but was included in this assessment as it was considered a priority on the basis of other human health concerns.
[b] This CAS RN is a UVCB (unknown or variable composition, complex reaction products, or biological materials).

The 13 substances in the Aliphatic Amines Group were organized into two subgroups based on carbon chain length: short-chain aliphatic amines (alkyl-chain <8 carbon atoms) and long-chain aliphatic amines (alkyl-chain ≥8 carbon atoms). Functionally, long-chain, but not short-chain, aliphatic amines are surface-active compounds (surfactants).

According to information submitted in response to a CEPA section 71 survey, for the reporting year 2011, 4 substances in the Aliphatic Amines Group (cocoamine, BHTAA, HTAAA, and TAAA) were manufactured in Canada at quantities between 10 000 and 170 000 kg, whereas TAPDA was manufactured at quantities between 100 000 and 1 000 000 kg. The other 8 substances in the Aliphatic Amines Group were not manufactured in Canada at quantities above the reporting threshold of 100 kg. In 2011, dimethylamine was imported into Canada at a quantity greater than 10 million kg. Ethylenediamine, diethylenetriamine, octadecylamine, cocoamine, and DPDAB were imported into Canada in quantities between 100 000 and 1 000 000 kg. In 2011, dimethylbenzylamine, hexadecyldimethylamine, BHTAA, and TAPDA were imported into Canada in quantities between 10 000 to 100 000 kg/year, while 7 900 kg of TMTADA were imported. The remaining aliphatic amines (HTAAA and TAAA) were not reported to be imported at quantities above 100 kg.

Major industrial uses of long-chain aliphatic amines include polyurethane foam production, formulation of cleaning products and personal care products, flotation in mineral extraction, and formulation of asphalt emulsions. Aliphatic amines are also used as intermediates in the production of various other chemicals with diverse applications. According to information submitted in response to a CEPA section 71 survey, aliphatic amines are used in a variety of consumer, commercial and industrial products in

Canada. Consumer uses include automotive care, pest control, building and construction materials, cleaning and furnishing care, personal care, paints and coatings, automotive, aircraft and transportation, laundry and dishwashing, and drugs. In Canada, ethylenediamine, diethylenetriamine, dimethylamine, and BHTAA may be used as components in food packaging materials, while octadecylamine and cocoamine may be used as components in incidental additives used in food processing establishments. Ethylenediamine and octadecylamine were identified as ingredients in human drug products in Canada. Hexadecyldimethylamine was identified as a non-medicinal ingredient (NMI) in natural health products in Canada while octadecylamine and cocoamine were notified to be present in cosmetics in Canada. Ethylenediamine, dimethylamine, hexadecyldimethylamine, cocoamine, HTAAA, and TAPDA were identified as formulants in pest control products registered in Canada.

The ecological risks of the four short-chain aliphatic amine substances were characterized individually 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 risk classification. Based on the outcome of the ERC analysis, dimethylbenzylamine, ethylenediamine, diethylenetriamine and dimethylamine are considered unlikely to be causing ecological harm.

The ecological risk of the nine long-chain aliphatic amines was assessed using a class-based approach, which considers all long-chain aliphatic amines that are captured within the monoamine and diamine subclasses. A class-based approach is appropriate as long-chain aliphatic amines are cationic surfactants with similar reactivity and ecotoxicity, and they may co-occur in and impact the environment collectively.

Monoamine subclass:

- Monoamines that include one or two long-chain alkyls (C_8-C_{22} linear or branched, saturated or unsaturated) attached to the nitrogen, with the remaining one or two substituents being any combination of hydrogen atoms or methyl groups;
- Ethers of 1-propaneamine, N-methylpropanamine or N,N-dimethylpropanamine with one long-chain alkyl (C_8-C_{22} linear or branched, saturated or unsaturated);

Diamine subclass:

- 1,3-propanediamines and N- and N'-methylated-1,3-propanediamines with one long-chain alkyl (C_8-C_{22} linear or branched, saturated or unsaturated); and
- Ethers of 1,3-propanediamine and N- and N'-methylated-1,3-propanediamines with one long-chain alkyl (C_8-C_{22} linear or branched, saturated or unsaturated).

The description of the alkyl-chain length in the definition above refers to the number of carbon atoms in the long alkyl-chain(s) (after the last functional group in the case of diamines and ethers). This definition includes long-chain aliphatic amines alone or as part of a salt.

Long-chain aliphatic amines may be released to the Canadian environment from the formulation, manufacture and consumer use of products containing these substances, as well as from their uses in various industrial processes. Releases to aquatic and terrestrial environments are expected from both diffuse and point sources. The long-chain aliphatic amines are expected to be positively charged at environmentally relevant pH. When released to the aquatic environment, long-chain aliphatic amines will tend to sorb to dissolved and suspended solids. Therefore, these substances may potentially be transported in the water column or settle to bed sediment. Long-chain aliphatic amines do not persist in water, sediment or soil. Long-chain aliphatic amines with alkyl-chains less than C_{14} have low to moderate potential for bioaccumulation in aquatic organisms, and those with alkyl-chains of C_{14} and longer have high potential to bioaccumulate.

Experimental data on ecological toxicity for the long-chain aliphatic amines show they have the potential to cause adverse effects in aquatic, sediment, and soil-dwelling organisms at low concentrations. Quantitative ecological exposure scenarios were developed for the most relevant uses and potential releases of long-chain aliphatic amines including production and processing, polyurethane foam production, down-the-drain release of amine derivatives, use as a flotation agent for mineral extraction, and biosolids application to land. Qualitative ecological exposure scenarios were developed for asphalt emulsion and for fertilizer application and formulation. Predicted exposure concentrations were adjusted for sorption to organic matter in the water column. Risk quotient analyses were conducted to compare the estimated concentrations in aquatic and soil compartments to adverse effect concentrations in aquatic and soil-dwelling organisms. Scenarios for production, processing, production of polyurethane foam (polyol blend), down-the-drain release of amine derivatives, flotation treatment in mineral extraction, formulation of asphalt emulsion, and formulation of fertilizers indicate that long-chain aliphatic amines pose a risk to aquatic organisms, whereas the scenario for polyurethane foam production (flexible polyurethane foam) is unlikely to pose a risk. The scenario for the application of biosolids to land indicates that long-chain aliphatic amines are unlikely to pose a risk to soil-dwelling organisms.

Considering all available lines of evidence presented in this draft screening assessment, there is risk of harm to the environment from long-chain aliphatic amines. It is proposed to conclude that long-chain aliphatic amines, including the nine long-chain aliphatic amines in this assessment, meet the criteria under paragraph 64(*a*) of CEPA as they are entering or may enter 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. However, it is proposed to conclude that long-chain aliphatic amines, including the nine long-chain aliphatic amines in this assessment, do not meet the criteria under paragraph 64(*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends. It is also proposed to conclude that the short-chain aliphatic amines dimethylbenzylamine, diethylenetriamine, dimethylamine, and ethylenediamine 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.

The human health assessment in this report considers each short- and long-chain aliphatic amine in the Aliphatic Amines Group separately due to differences in critical health effects observed. The health effects datasets for some of the short-chain aliphatic amines were limited, and read-across approaches were used. General toxicity (e.g., significantly reduced body weight, reduced food consumption, salivation) was identified to be the critical effect associated with exposure to dimethylbenzylamine and dimethylamine. For ethylenediamine, critical effects on the liver, kidneys, lungs, adrenal glands, and effects on blood chemistry were identified. For diethylenetriamine, increased duration of gestation and post-implantation loss were identified as the critical effects. For all of the short-chain aliphatic amines, comparison of levels to which the general population may be exposed from sources, such as products available to consumers, food, and/or environmental media to the critical effect levels resulted in margins of exposure that are considered adequate to address uncertainties in the health effects and exposure databases.

The health effects datasets for some of the long-chain aliphatic amines were limited, and read-across approaches were used. Effects on certain lymph nodes were identified to be the critical effects for hexadecyldimethylamine and BHTAA. For octadecylamine and cocoamine, these effects were also accompanied by general toxicity and effects on the gastrointestinal (GI) tract. In addition to the effects mentioned above (i.e., lymph nodes, general toxicity, GI tract), inflammatory effects were also identified for DPDAB.

Potential exposure of Canadians to hexadecyldimethylamine, octadecylamine, cocoamine, and BHTAA can occur from non-prescription drugs, cosmetics, natural health products, products available to consumers, material containing the substance, environmental media, incidental additives, and food packaging materials. Comparison of the exposure estimates for each substance to critical effect levels resulted in margins that are considered to be adequate to address the uncertainties in the health effects and exposure databases.

For DPDAB, comparison of the potential exposure of Canadians from a two-component marine epoxy adhesive product available to consumers to the critical effect level resulted in a margin that is considered potentially inadequate to address the uncertainties in the health effects and exposure databases.

With respect to the long-chain aliphatic amines HTAAA, TAAA, TAPDA, and TMTADA, their potential to cause harm to human health was evaluated by the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances, which is based on the potential hazard of similar chemical structures, as well as chemical-specific genotoxicity data, when available. The exposure estimates generated for HTAAA, TAAA, TAPDA, and TMTADA were lower than the TTC values, indicating a low

probability of risk to human health. Therefore, HTAAA, TAAA, TAPDA, and TMTADA are considered to be a low concern for human health at current levels of exposure.

On the basis of the information presented in this draft screening assessment, it is proposed to conclude that DPDAB meets the criteria under paragraph 64(*c*) of CEPA as it is entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

On the basis of the information presented in this draft screening assessment, it is proposed to conclude that dimethylbenzylamine, ethylenediamine, diethylenetriamine, dimethylamine, hexadecyldimethylamine, octadecylamine, cocoamine, BHTAA, HTAAA, TAAA, TAPDA, and TMTADA 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.

It is therefore proposed to conclude that all long-chain aliphatic amines, including hexadecyldimethylamine, octadecylamine, cocoamine, BHTAA, HTAAA, TAAA, TAPDA, DPDAB and TMTADA, meet one or more of the criteria set out in section 64 of CEPA, and that the four short-chain aliphatic amines, dimethylbenzylamine, ethylenediamine, diethylenetriamine and dimethylamine, do not meet any of the criteria set out in section 64 of CEPA.

It is also proposed that long-chain aliphatic amines with C_{14} or greater alkyl-chains meet the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA, but those with alkyl-chains less than C_{14} do not, and that long-chain aliphatic amines do not meet the persistence criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA**.**

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1. Introduction

Pursuant to section 68 or 74 of the *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999), the Minister of the Environment and the Minister of Health have conducted a screening assessment of 13 of 19 substances referred to collectively under the Chemicals Management Plan as the Aliphatic Amines Group, to determine whether these 13 substances present or may present a risk to the environment or to human health. The 19 substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA or were considered a priority on the basis of other human health concerns (ECCC, HC [modified 2017]).

Two of the 19 substances (Chemical Abstracts Service Registry Number (CAS RN)[5] 108-91-8, cyclohexanamine; and CAS RN 58713-21-6, 1,3,5,7-tetraazatricyclo[3.3.1.1^{3},7]decane, hydrochloride) have been moved from the Aliphatic Amines Group to the Sodium Cyclamate and Cyclohexylamine Group and the Hexamethylenetriamine Group, respectively. They are not further addressed in this assessment.

Another 4 of the 19 substances (CAS RNs are listed in Table 1-1) were considered in the Ecological Risk Classification of Organic Substances (ERC) Science Approach Document (ECCC 2016a) and in either the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Science Approach Document (Health Canada 2016) or via the approach applied in the Rapid Screening of Substances with Limited General Population Exposure (ECCC, HC 2018a) and were identified as being of low concern to both human health and the environment. Conclusions for these 4 substances are provided in the Substances Identified as Being of Low Concern Using the Ecological Risk Classification of Organic Substances and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Screening Assessment (ECCC, HC 2018b) and the Rapid Screening of Substances with Limited General Population Exposure Screening Assessment (ECCC, HC 2018a). Therefore, these 4 substances are not further addressed in this report, although, CAS RNs 112-90-3 and 68955-53-3 are used as read-across in the ecological assessment and are considered for their potential contribution to the risk of long-chain aliphatic amines.

Table 1-1. Substances in the Aliphatic Amines Group that were addressed under other approaches

CAS RN	*Domestic Substances List* name	Approach under which the substance was addressed	References
112-90-3	9-Octadecen-1-amine, (Z)-	ERC/ Rapid Screening	ECCC, HC 2018a

[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.

CAS RN	*Domestic Substances List* name	Approach under which the substance was addressed	References
68955-53-3	Amines, C_{12-14}-tert-alkyl	ERC/TTC	ECCC, HC 2018b
80939-62-4	Amines, C_{11-14}-branched alkyl, monohexyl and dihexyl phosphates	ERC/ Rapid Screening	ECCC, HC 2018a
90367-27-4	Ethanol, 2,2'-[[3-[(2-hydroxyethyl)amino]propyl]imino] bis-, N-tallow alkyl derivs.	ERC/ Rapid Screening	ECCC, HC 2018a

The 13 substances addressed in this screening assessment will hereinafter be referred to as the Aliphatic Amines Group. This group is composed of two subgroups: short-chain and long-chain aliphatic amines. For the purpose of the Aliphatic Amines Group assessment, short-chain aliphatic amines are considered to be those where no alkyl substituent exceeds seven carbon atoms, whereas long-chain aliphatic amines have at least 1 alkyl chain of 8 or more carbon atoms.

Some substances in the Aliphatic Amines Group (i.e. ethylenediamine and dimethylamine) have been reviewed internationally through the OECD Cooperative Chemicals Assessment Programme, and there are OECD SIDS Initial Assessment Report (SIARs) and/or SIDS Initial Assessment Profiles (SIAPs) available. 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. The European Union has also assessed some substances in the Aliphatic Amines Group (i.e., octadecylamine and cocoamine). The information from these assessments was taken into consideration in this screening assessment, where applicable.

Four of the 13 substances in the Aliphatic Amines Group are short-chain aliphatic amines (dimethylbenzylamine, ethylenediamine, diethylenetriamine, dimethylamine) that were identified as having a low potential to cause ecological harm based on the ERC approach (ECCC 2016a; Appendix A). These results are considered in support of the conclusions made under section 64 of CEPA in this screening assessment.

Another 4 of the substances in the Aliphatic Amines Group (HTAAA, TAAA, TAPDA and TMTADA) were included in the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Science Approach Document (Health Canada 2016). In the TTC-based approach, Health Canada used a structure-based decision tree and chemical-specific data on genotoxicity (e.g., Ames test), when available, to assign a human exposure threshold value for a chemical, below which there is a low probability of risk to human health (i.e., TTC value). For each substance in the TTC-based approach, potential exposure of the Canadian general population was characterized and compared to the TTC value assigned to the substance. HTAAA, TAAA, TAPDA and TMTADA were associated with exposure lower than their assigned TTC value.

Therefore, these substances are considered to be a low concern for human health at current levels of exposure. These results are considered in support of the conclusions made under section 64 of CEPA in this screening assessment.

A class-based approach was taken for the ecological assessment of the 9 long-chain aliphatic amines in the Aliphatic Amines Group. This approach considers all long-chain aliphatic amines captured within the definition in Section 2.1 to be part of the long-chain aliphatic amines class for the reason that all are considered to have similar reactivity and ecotoxicity and may co-occur in and impact the environment collectively. Therefore, all long-chain aliphatic amines are considered to contribute to the ecological risk collectively and are assessed as a class rather than as individual substances defined by CAS RNs.

With respect to the human health assessment, substances in the Aliphatic Amines Group were assessed individually by CAS RN, as there were differences in the types of critical health effects observed.

This draft screening assessment includes consideration of information on chemical properties, environmental fate, hazards, uses, and exposures, including additional information submitted by stakeholders. Relevant data were identified up to November 2019. 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.

This draft screening 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 ecological and human health portions of this assessment have undergone external review and/or consultation. Comments on the technical portions relevant to the environment were received from James Armitage (AES Armitage Environmental Services, Inc.) and Steven Droge (University of Amsterdam). Comments on the technical portions relevant to human health were received from Jennifer Flippin, Theresa Lopez, and Joan Garey, all affiliates of Tetra Tech. Substances assessed in either the TTC or ERC approach documents (Health Canada 2016; ECCC 2016a) were subject to an external review and a 60-day public comment period. The draft Rapid Screening of Substances with Limited General Population Exposure (published June 10, 2017) was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

This draft screening assessment focuses on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by examining scientific

information and incorporating a weight-of-evidence approach and precaution.[6] This draft screening assessment presents the critical information and considerations on which the proposed conclusions are based.

2. Identity of substances

Aliphatic amines are organic chemicals composed of one or more amine functional groups, each substituted with up to three aliphatic (alkyl[7]) chains attached directly to the nitrogen atom (see Appendix B for further description of aliphatic amine chemistry). The aliphatic chains vary in length, and can be cyclic, branched, or linear. An ether functional group may also be present in which case they are also known as "ether amines."

For the purpose of the Aliphatic Amines Group assessment, short-chain aliphatic amines are considered to be those where no alkyl substituent exceeds seven carbon atoms, whereas long-chain aliphatic amines have at least one alkyl chain of eight or more carbon atoms. The basis for this subgrouping is that long-chain, but not short-chain, aliphatic amines are surface-active compounds (surfactants).

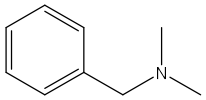
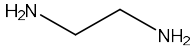
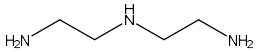
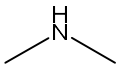
Aliphatic amines may be described according to the number of amine functional groups (e.g., as monoamines, diamines or triamines) or number of organic substituents associated with the amine functional group (e.g., primary, secondary or tertiary amine). When the substituents are alkyl groups, the amine is described as a mono-, di- or trialkyl amine (Appendix B). In this assessment, dialkyl amines with two equal alkyl-chain lengths are described as "$2xC_{number}$", where C_{number} is the number of carbons in the alkyl-chain (e.g., a dialkyl with 2 alkyl chains of 8 carbon atoms each is described as $2xC_8$). It is, however, possible that a dialkylamine may have long alkyl-chains of differing lengths.

The substance identities for the 13 substances in the Aliphatic Amines Group are presented in Tables 2-1 and 2-2 for short- and long-chain aliphatic amines, respectively.

[6] 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.

[7] An aryl group may be attached to the alkyl group, as in CAS RN 103-83-3, but the aryl group cannot be attached directly to the nitrogen atom.

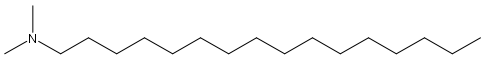
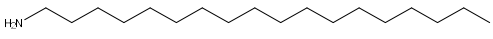
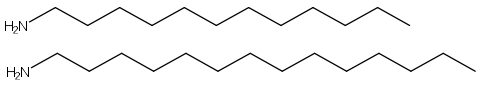
Table 2-1. Substance identities for short-chain aliphatic amines

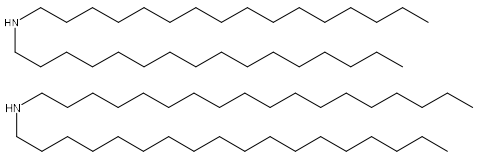
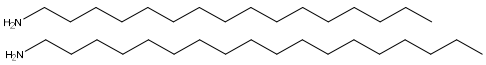
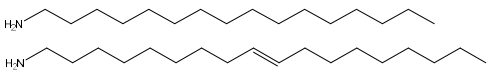
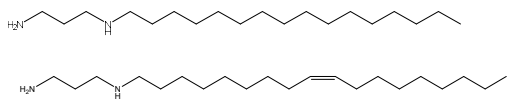
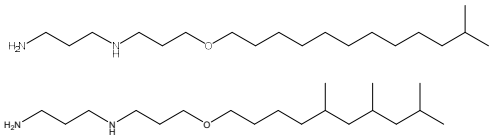
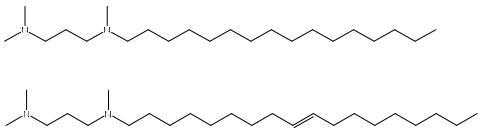
CAS RN	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
103-83-3	Benzenemethanamine, N,N-dimethyl (dimethylbenzylamine)[a]	 $C_9H_{13}N$	135
107-15-3	1,2-Ethanediamine (ethylenediamine)[a]	 $C_2H_8N_2$	60
111-40-0	1,2-Ethanediamine, N-(2-aminoethyl)-(diethylenetriamine)[a]	 $C_4H_{13}N_3$	103
124-40-3	Methanamine, N-methyl-(dimethylamine)[a]	 C_2H_7N	45

[a] Substance evaluated in this assessment report by Health Canada; previously identified as a low ecological concern through the ERC approach (ECCC 2016a)

Seven of the long-chain aliphatic amine substances (Table 2-2) are UVCBs (unknown or variable composition complex reaction products and biological material). These materials are derived from natural sources or complex reactions and cannot be characterized in terms of constituent chemical compounds because their composition is too complex or variable. A UVCB is not an intentional mixture of discrete substances and for the purposes of this assessment is considered a single substance. Two possible representative structures for predominant alkyl-chain lengths of the UVCBs are shown in Table 2-2. For more information on the substance identities of long-chain aliphatic amines see ECCC 2021.

Table 2-2. Substance identities for long-chain aliphatic amines

CAS RN	DSL name (common name)	Chemical structure and molecular formula[a]	Alkyl-chain length[b]
112-69-6	1-Hexadecanamine, N,N-dimethyl-(hexadecyldimethylamine)[c]	 $C_{18}H_{39}N$ (270 g/mol)	C_{16}
124-30-1	1-Octadecanamine (octadecylamine)[c]	 $C_{18}H_{39}N$ (270 g/mol)	C_{18}
61788-46-3	Amines, coco alkyl (cocoamine)[c]	 Representative structures (UVCB)	C_8-C_{18}

CAS RN	DSL name (common name)	Chemical structure and molecular formula[a]	Alkyl-chain length[b]
61789-79-5	Amines, bis (hydrogenated tallow alkyl) (BHTAA)[c]	 Representative structures (UVCB)	2xC_{14}-C_{18}
61790-59-8	Amines, hydrogenated tallow alkyl, acetates (HTAAA)[d,e]	 Representative structures (UVCB)[e]	C_{14}-C_{18}
61790-60-1	Amines, tallow alkyl, acetates (TAAA)[d,e]	 Representative structures (UVCB)[e]	C_{14}-C_{18}
61791-55-7	Amines, N-tallow alkyltrimethylenedi- (TAPDA)[d]	 Representative structures (UVCB)	C_{14}-C_{18}
68479-04-9	1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-, branched (DPDAB)[c]	 Representative structures (UVCB)	C_{11}-C_{14}
68783-25-5	Amines, N,N,N'-trimethyl-N'-tallow alkyltrimethylenedi- (TMTADA)[d]	 Representative structures (UVCB)	C_{16}-C_{18}

[a] Additional representative structures to those given for UVCBs may be available and used in some modelling.
[b] For UVCBs, alkyl-chain length is listed for all possible representative structures, while the images represent the predominant alkyl-chain lengths.
[c] Substance evaluated in this assessment report by Environment and Climate Change Canada and Health Canada.
[d] Substance evaluated in this assessment report by Environment and Climate Change Canada; previously identified as low concern for human health.
[e] Note that the chemical structures shown do not include the acetate counter ion.

A class-based approach was taken for the ecological assessment, which includes the nine long-chain aliphatic amines in the Aliphatic Amines Group identified in Table 2-2. This approach considers all long-chain aliphatic amines captured within the two subclasses below to be part of the long-chain aliphatic amines class. A definition based on chemical formulae is found in Appendix B.

Monoamine subclass:

- Monoamines that include one or two long-chain alkyls (C_8-C_{22} linear or branched, saturated or unsaturated) attached to the nitrogen, with the remaining one or two substituents being any combination of hydrogen atoms or methyl groups; and
- Ethers of 1-propaneamine, N-methylpropanamine or N,N-dimethylpropanamine with one long-chain alkyl (C_8-C_{22} linear or branched, saturated or unsaturated).

Diamine subclass:

- 1,3-propanediamines and N- and N'-methylated-1,3-propanediamines with one long-chain alkyl (C_8-C_{22} linear or branched, saturated or unsaturated); and
- Ethers of 1,3-propanediamine and N- and N'-methylated-1,3-propanediamines with one long-chain alkyl (C_8-C_{22} linear or branched, saturated or unsaturated).

The description of the alkyl-chain length in the definition above refers to the number of carbon atoms in the long alkyl chain(s) (after the last functional group in the case of diamines and ethers). This definition includes long-chain aliphatic amines alone or as part of a salt. A non-exhaustive list of substances on the *Domestic Substances List* that meet this class definition is provided in Appendix C.

With respect to the human health assessment, substances in the Aliphatic Amines Group were assessed individually by CAS RN, as there were differences in the types of critical health effects observed. Some of the substances were associated with limited to no health effects data. In these cases, a read-across approach was applied, whereby data from similar chemicals (on the basis of chemical structure, physical-chemical properties, toxicokinetics, and reactivity) were taken into consideration and used to inform the assessment.

2.1 Selection of analogues and use of (Q)SAR models

A read-across approach using data from analogues and the results of (quantitative) structure-activity relationship ((Q)SAR) models, where appropriate, has been used to inform the ecological and human health assessments. Analogues were selected that were structurally similar and/or functionally similar to substances within this group (e.g., based on physical-chemical properties, toxicokinetics, reactivity) and that had relevant empirical data that could be used to read across to substances with limited empirical data. The applicability of (Q)SAR models was determined on a case-by-case basis. Details of the read-across data and (Q)SAR models chosen to inform the ecological and human health assessments of the Aliphatic Amines Group are further discussed below.

2.1.1 Analogues used for the ecological assessment

The identity of analogue substances used in the ecological assessment of long-chain aliphatic amines is presented in Table 2-3, while the identity of long-chain aliphatic amines that were used as read across can be found in ECCC (2021).

Table 2-3. Identity of quaternary ammonium compounds used as analogues for long-chain aliphatic amines and the parameters they informed

CAS RN	Alkyl-chain length	Substance name (chemical group)	Fate data	Ecotoxicity data
1125503-33-4	C_{12-14}	HYEQS	N	Y
71808-53-2	C_{12-18}	Quaternary ammonium compounds, C_{12-18}-alkylbis(hydroxyethyl)methyl, chlorides	Y	N
57-09-5	C_{16}	Cetyltrimethylammonium bromide	Y	N
N/A	C_{16-18}	C_{16-18} trimethyl ammonium chloride	Y	N
107-64-2	C_{18}	1-Octadecanaminium, N,N-dimethyl-N-octadecyl-, chloride	Y	N
7173-51-5	$2xC_{10}$	1-Decanaminium, N-decyl-N,N-dimethyl-, chloride	Y	Y
68607-24-9	C_{20-22}	Quaternary ammonium compounds, C_{20-22} alkyltrimethyl, chlorides	N	Y
N/A	C_{22}	C_{22} trimethyl ammonium chloride	Y	N

Abbreviations: Y, yes; N, no; N/A, not available

2.1.2 Analogues used for the human health assessment

A read-across approach using data from analogues was applied to inform the human health assessments for hexadecyldimethylamine, octadecylamine, and DPDAB. Appendix D provides further details on the factors considered in the identification of analogues. A list of analogues used to inform this assessment for hexadecyldimethylamine, octadecylamine, and DPDAB is presented in Tables 2-4 to 2-6, respectively. For further information on the physical-chemical properties of the analogues, refer to Appendix E. Details of the health effects data from these analogues are further discussed in the relevant sections of this report.

Table 2-4. Identity of analogues used to inform the assessment for hexadecyldimethylamine

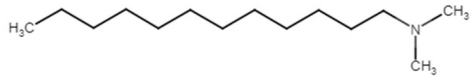
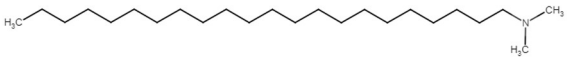
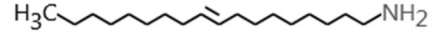
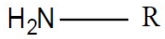
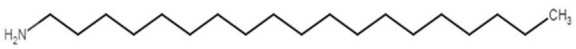
CAS RN	Common name	Chemical structure and molecular formula
112-18-5	Dodecyl-dimethylamine	 $C_{14}H_{31}N$
21542-96-1	N,N-dimethyl-docosylamine	 $C_{24}H_{51}N$

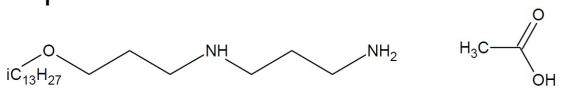
Table 2-5. Identities of analogues used to inform the assessment for octadecylamine

CAS RN	Common name	Chemical structure and molecular formula
112-90-3	(Z)-octadec-9-enylamine	 $C_{18}H_{37}N$
61790-33-8[a]	Amines tallow alkyl	

		 R = tallow alkyl
68037-92-3[a]	C_{16-22}-alkyl amines	Representative structure:  $C_{19}H_{41}N$

[a] This substance is a UVCB.

Table 2-6. Identities of analogues used to inform the assessment for DPDAB

CAS RN	Common name	Chemical structure and molecular formula
Unknown CAS RN EC number 931-295-2[a]	1,3-propanediamine, N-[3-((C_{11-14}, C_{13}-rich)oxy) branched acetate	Representative structure:  $C_{19}H_{42}N_2O \cdot C_2H_4O_2$

[a] This substance is a UVCB.

3. Physical and chemical properties

Information on the physical and chemical properties for each substance in the Aliphatic Amines Group was obtained for the temperature range of 20 to 25 °C, unless otherwise specified. When experimental information was limited or not available for a property, data from analogues were used for read-across, and/or (Q)SAR models were used to generate predicted values for the substance.

3.1 Short-chain aliphatic amines

A summary of physical and chemical property data for short-chain aliphatic amines in the Aliphatic Amines Group is presented in Table 3-1.

Table 3-1. Physical and chemical properties for short-chain aliphatic amines

Property	Dimethyl-benzylamine	Ethylene-diamine	Diethylene-triamine	Dimethyl-amine
Physical state	Liquid[a]	Liquid	Liquid	Gas
Vapour pressure (Pa)	214[b]	1.61×10^{3}[b]	30.93[b]	2.03×10^{6}[b]
Water solubility (mg/L)	12 000[c]	1.0×10^{6} [b]	"miscible"[b]	1.63×10^{6} [b,d]
log K_{ow}	1.98[b]	-2.04[b]	-1.58[e]	-0.38[b]
pK_a	8.91[c]	7.6-10.7[b,f]	4.9-10.1[f,g]	10.73[b]
Melting point (°C)	-75	8.5[b]	-39[f]	-92.2[b]
Boiling point (°C)	181	117[b]	207[f]	6.8[b]

Abbreviations: K_{ow}, octanol-water partition coefficient; pK_a, dissociation constant
[a] ECHA c2007-2018a, CAS RN 103-83-3
[b] PubChem 2004-2020
[c] PhysProp c2013

[d] Temperature at 40°C
[e] ECHA c2007-2018b, CAS RN 111-40-0
[f] pK_a1 (the constant for dissociation of the 1st proton) or pK_a2 (2nd proton), not the overall pK_a
[g] pK_a1 (the constant for dissociation of the 1st proton), pK_a2 (2nd proton), or pK_a3 (3rd proton), not the overall pK_a

3.2 Long-chain aliphatic amines

A summary of physical and chemical property data for long-chain aliphatic amines in the Aliphatic Amines Group is presented in Tables 3-2 and 3-3. Data on vapour pressure, melting point, and boiling point are provided in ECCC (2021).

3.2.1 Dissociation constants

All of the long-chain aliphatic amines have at least one dissociation constant (pK_a) of 10 or above (Table 3-3), indicating that at environmentally relevant pH levels, they will predominantly be present in the protonated form.

3.2.2 Water solubility and critical micelle concentration

In general, long-chain aliphatic amines have moderate water solubility (WS). However, the WS of long-chain aliphatic amines is pH-dependent with WS being greater for the charged species than for the neutral species. Experimental and modelled WS data for long-chain aliphatic amines are summarized in Table 3-3.

Critical micelle concentration (CMC) is a relevant property for surfactants, such as long-chain aliphatic amines. Above the CMC, the concentration of freely dissolved individual molecules in solution are nearly constant (Gecol 2006); thus, the CMC can be considered a water solubility limit (ECHA 2017). CMCs for four long-chain aliphatic amines with alkyl chains of C_8 to C_{12} ranged from 0.0003 to 0.4 mol/L (Hoffman et al. 1942; Hoerr and Ralston 1943; Thorsteinsdóttir et al. 1995). This is similar to CMCs observed with quaternary ammonium compounds (QACs) with alkyl-chain lengths ranging from C_8 to C_{18} (CMCs of 0.001 to 0.1 mol/L; Rosen and Kunjappu 2012). Based on the CMCs of Rosen and Kunjappu (2012), the CMCs for long-chain aliphatic amines are calculated to be 40 mg/L or greater.

3.2.3 Distribution coefficients

Long-chain aliphatic amines are surfactants, and as such, they do not partition between octanol and water phases but rather tend to accumulate at the interface between phases and to emulsify the octanol-water system (Miller and McWilliams 2010, 2012). Therefore, this parameter will not be considered within the assessment of long-chain aliphatic amines, as there are no reliable experimental or modelled K_{ow} values. Instead, the solids-water distribution coefficient (K_d), an organic carbon-water distribution coefficient specific to cations ($K_{oc\text{-}cation}$), a distribution coefficient for ionic interactions with clays (K_{CEC}), and the membrane-water partition coefficient (K_{mw}) will be used to characterize the distribution of long-chain aliphatic amines in the environment.

To account for differences in distribution coefficients, the monoamines and diamines subclasses were divided into the following alkyl-chain categories: C_8-C_{14}, C_{15}-C_{18}, C_{19}-C_{22}, and C_{22} or greater. For the purpose of describing the impact of the alkyl-chain length on fate, monoamines with two C_8 or longer alkyl chains are considered to have an alkyl-chain length corresponding to the sum of the two long-chain alkyl groups.[8]

3.2.3.1 Solids-water, organic carbon-water, and clay distribution coefficients

Organic cations that are charged at environmentally relevant pH, such as aliphatic amines, sorb via ionic and non-ionic interactions with negatively charged cation exchange sites in both organic matter and clays (Droge and Goss 2013a, 2013b). Models have been developed based on volume and charged surface area to estimate partition coefficients for cationic interactions between organic cations and organic carbon ($K_{OC\text{-}cationic}$, in L/kg) and between organic cations and clay ($K_{CECclay}$, in L/mol_{Charge}) (Droge and Goss 2013a, 2013b, 2013c). Estimated $K_{OC\text{-}cationic}$ and K_{CEC} may be used to estimate the distribution coefficient, K_d,[9] for a soil or sediment according to the following equation (Droge and Goss 2013b):

$$K_d = K_{CEC,clay} \cdot (CEC_{medium} - 3.4 \cdot f_{oc}) + K_{OC\text{-}cationic} \cdot f_{oc}$$

where CEC_{medium} is the cation exchange capacity (CEC) of the medium (e.g., soil or sediment), CEC_{clay} is the cation exchange capacity of the clay present in the medium, and f_{oc} is the fraction of organic carbon in the medium.

Estimated log $K_{OC\text{-}cationic}$, log K_{CEC} and log K_d values for various C_8 to C_{36} monoamines and C_8 to C_{22} diamines using the natural standard LUFA2.2 soil are listed in Table 3-2.

Table 3-2. Modelled organic carbon-water, clay, and solids-water distribution coefficients for long-chain aliphatic amines

Amine number	Alkyl-chain length category	log $K_{OC\text{-}cationic}$[a]	log $K_{CECclay}$[b]	log K_d[c,d]
Monoamines	C_8-C_{14}	2.5–4.0	2.1–4.1	1.1–2.7
Monoamines	C_{15}-C_{18}	4.0–4.9	3.3–4.8	2.6–3.5
Monoamines	C_{19}-C_{22}	4.9–5.8	4.0–5.4	3.4–4.2
Monoamines	C_{23} to C_{36}[d]	5.9–8.4	5.0–7.1	4.2–6.7
Diamines	C_8-C_{14}	3.5-–5.0	2.7–3.9	1.9–3.3
Diamines	C_{15}-C_{18}	5.0–5.8	3.9–5.4	3.3–4.2
Diamines	C_{19}-C_{22}[e]	5.9–6.7	4.6–5.3	4.2–4.9

[8] For example, a long-chain aliphatic amine with two C_8 alkyl chains (i.e., 2xC_8) would be considered to be equivalent to a C_{16} alkyl chain and considered with the C_{15}-C_{18} alkyl-chain category for monoamines.

[9] K_d is a partition (or distribution) coefficient describing the distribution of a chemical species between a solid and aqueous matrix after equilibration. K_d is an important parameter for describing the substance mobility in the environment and its distribution between aqueous and soil or sediment compartments.

[a] Droge and Goss 2013a
[b] Droge and Goss 2013b
[c] LUFA2.2 soil is a sandy loam with the following physical properties used for modelling: 1.7% OC and cation exchange capacity of 0.092 mol_C/kg dry weight (dw) (LUFA Speyer 2018).
[d] The C_{24} to C_{36} alkyl-chain lengths represent C_{12} to C_{18} dialkyl amines as the sum of the two alkyl chains are considered for placement in the alkyl-chain length categories. There is some uncertainty in the calculated log K values as no long-chain dialkyl amines were used in the development of the model and only the C_{24} representative structure (i.e., dialkyl amine with two C_{12} alkyl-chains) was within the domain for volume and charge surface area of the model.
[e] There is some uncertainty in the calculated log K values for the diamine C_{19} to C_{22} category as only one C_{19} representative structure was within the model domain for volume and charge surface area.

The data in Table 3-2 demonstrate that diamines generally have a slightly greater sorptive capacity (i.e., higher partition coefficients) than monoamines with similar alkyl-chain lengths and that sorption increases with increasing alkyl-chain length. In addition, calculated $K_{OC\text{-}cationic}$ values indicate that dialkyl monoamines (i.e., two long alkyl chains bound to one amine) have similar log $K_{OC\text{-}cationic}$ values when the sum of the two alkyl chains is comparable to that of a similar monoalkyl-chain monoamine (ECCC 2021).

3.2.3.2 Membrane partitioning coefficients

Long-chain aliphatic amines can sorb to biological membranes and have a relatively high affinity to cell membranes compared to storage lipids, due to favourable electrostatic and hydrophobic interactions in the cell membrane phospholipid biolayers (Droge 2017). In order to consider ionic interactions of the cationic aliphatic amine with anionic phosphate groups in cell membranes (Timmer and Droge 2017), the membrane-water partition coefficient (K_{mw}) is used. This may be experimentally-derived using a solid supported phospholipid membrane (SSLM) assay (Timmer and Droge 2017) or modelled using the quantum chemistry-based model COSMOmic (Bitterman et al. 2014, 2016; COSMOmic c2015-2018). The log K_{mw} values for C_8 to C_{12} long-chain aliphatic monoamines that were experimentally derived from SSLM assays ranged from 2.35 to 5.58 (Timmer and Droge 2017) and were noted to increase with increasing alkyl chain length (ECCC 2021), but to decrease with increased methylation of the amine group (e.g., log K_{mw} decreased in order of primary > secondary > tertiary amine, see Appendix B).

For the COSMOmic model, the $K_{DMPC\text{-}W}$ (L-*α*-dimyristoyl phosphatidyl choline (DMCP)-water partition coefficient) is determined as a surrogate for K_{mw}. Log $K_{DMPC\text{-}W}$ values were determined for a number of the long-chain aliphatic amines in the Aliphatic Amines Group (see Table 3-3) (Droge 2017). Timmer and Droge (2017) also reported log $K_{DMPC\text{-}W}$ values for a number of C_8 to C_{18} primary, secondary and tertiary long-chain aliphatic amines, including one dialkyl monoamine (ECCC 2021). The log $K_{DMPC\text{-}W}$ value for the $2xC_8$ dialkyl amine was lower than that of a C_{16} aliphatic amine, likely due to steric effects affecting partitioning of the dialkyl amine into membranes (Timmer and Droge 2017).

Table 3-3. Dissociation constant, physical state, water solubility, and DMPC-water partition coefficient ($K_{DMPC\text{-}W}$) data for long-chain aliphatic amines in the Aliphatic Amines Group

Chemical name (alkyl-chain length)	pK_a[a]	Physical state	Experimental water solubility (mg/L)	Modelled water solubility (mg/L)[a]	Log K_{DMPC-W} [b]
Hexadecyldimethyl-amine (C_{16})	10.0	Liquid[c]	18[d]	5.1	8.22
Octadecylamine (C_{18})	10.6	Solid[e]	NA	1.6	8.56
Cocamine (C_8-C_{18})	10.6	Liquid[f]	(C_8-C_{10}) 200-550; (C_{12}-C_{14}) 42-78; (C_{16}-C_{18}) 1.6-6[g]	(C_8-C_{18}) 1.6–19000	5.35
BHTAA (2xC_{14}-C_{18})	10.6	Solid[h]	< 0.1[i]	NA	NA
HTAAA (C_{14}-C_{18})	10.6	Solid[j]	130[k]	(C_{14}-C_{18}) 1.6–42	7.65
TAAA (C_{14}-C_{18})	10.6	Solid[l,m]	540[n]	(C_{14}-C_{18}) 42–130	7.43
TAPDA (C_{14}-C_{18})	8.7, 10.7[d]	Paste[l]	NA	(C_{18}) 850–9700	6.44–7.85
DPDAB (C_{11}-C_{14})	8.4, 10.3[d]	Liquid[n]	1300[o]	(C_9-C_{11}) 6900–19000	3.94–6.30
TMTADA (C_{16}-C_{18})	7.8, 9.7[d]	Liquid[m]	NA	(C_{14}-C_{18}) 60–850	7.64–8.34

Abbreviations: pKa, dissociation constant; NA, not available
[a] ACD/Percepta c1997-2012 (modelling done with representative structures at pH 8). pKa values in table from ACD/Percepta are an average of two values.
[b] Determined using COSMOmic c2015-2018, as reported in Droge 2017. .
[c] SDS 2014a
[d] ECHA c2007-2018d, CAS RN 124-30-1 (water solubility test conducted at pH 7.1)
[e] SDS 2019
[f] EC 2008
[g] ECHA c2007-2018e, CAS RN 111-86-4 (conducted at pH 7-11); Christie and Crisp 1967 (pH unknown)
[h] ECHA c2007-2018e, CAS RN 111-86-4
[i] ECHA c2007-2018c, CAS RN 112-69-6 (pH unknown)
[j] SDS 2017a
[k] SDS 2014b (pH unknown)
[l] Akzo Nobel 2010
[m] SDS 2014c
[n] ECHA c2007-2018f, CAS RN 1273322-47-6 (the pH at which the water solubility was tested at is unknown)
[o] ECHA c2007-2018g, EC 931-295-2 (conducted at pH 7)

4. Sources and uses

All of the substances in the Aliphatic Amines Group have been included in surveys issued pursuant to a CEPA section 71 notice (Canada 2012). Tables 4-1 and 4-2 present a summary of information reported on the total manufacture and total import quantities for short-chain aliphatic amines and long-chain aliphatic amines in the Aliphatic Amines Group, respectively. Data on the nine long-chain aliphatic amines in the Aliphatic Amines Group were used to describe the sources and uses of these specific long-chain aliphatic amines. These data, together with data from other sources, were also used to describe the uses of the class of long-chain aliphatic amines in general. Manufacturing quantities for the aliphatic amines ranged from below the reporting threshold of 100 kg/year to 1 000 000 kg/year. Import quantities ranged from below the reporting threshold of 100 kg/year to 1 000 000 kg/year. Additional follow up

information for import volumes of dimethylamine indicates that import volumes were greater than 10 000 000 kg in 2011 (personal communication, Aliphatic Amines voluntary data gathering, Existing Substances Risk Assessment Bureau [ESRAB], Health Canada [HC], 2018; unreferenced).

Table 4-1. Summary of information on Canadian manufacturing and imports of the short-chain aliphatic amines (Environment Canada 2013)

Chemical name	Total manufacture (kg)[a]	Total import (kg)[a]
Dimethylbenzylamine	NR	77 317
Ethylenediamine	NR	100 000 – 1 000 000
Diethylenetriamine	NR	100 000 – 1 000 000
Dimethylamine	NR	[31 305] 1.9×10^{7}[b]

Abbreviations: NR, not reported

[a] Values reflect quantities reported in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3). Exact values are provided when they are non-confidential. Confidential quantities are presented as a range of values.

[b] Updated value replacing original import quantity that was submitted under a CEPA section 71 survey (Aliphatic Amines voluntary data gathering, Health Canada, 2018; unreferenced).

Table 4-2. Summary of information on Canadian manufacturing and imports of the long-chain aliphatic amines (Environment Canada 2013)

Chemical name	Total manufacture (kg)[a]	Total import (kg)[a]
Hexadecyldimethylamine	NR	58 884
Octadecylamine	NR	[100 000–1 000 000] 1 000–10 000[b]
Cocoamine	38 000	125 329
BHTAA	170 000	55 000
HTAAA	120 000	NR
TAAA	29 000	NR
TAPDA	100 000–1 000 000	10 000–100 000
DPDAB	NR	100 000–1 000 000
TMTADA	NR	7 900

Abbreviations: NR, not reported

[a] Values reflect quantities reported in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3). Exact values are provided when they are non-confidential. Confidential quantities are presented as a range of values.

[b] Updated value replacing original import quantity that was submitted under a CEPA section 71 survey (Aliphatic Amines voluntary data gathering, Health Canada, 2018; unreferenced).

Table 4-3 presents a summary of the major uses of both short- and long-chain aliphatic amines, according to information submitted in response to a CEPA section 71 survey (Environment Canada 2013).

Table 4-3. Summary of the major uses of aliphatic amines in Canada (Environment Canada 2013)

Major uses[a]	Short-chain aliphatic amines	Long-chain aliphatic amines
Adhesives and sealants	Diethylenetriamine, Dimethylbenzylamine	HTAAA, TAAA, TAPDA
Paints and coatings	Diethylenetriamine, Dimethylbenzylamine, Ethylenediamine	BHTAA, Cocoamine, HTAAA, TAPDA
Water treatment	Dimethylamine, Ethylenediamine	BHTAA, Cocoamine, HTAAA, TAPDA
Cleaning and furnishing care	N/A	Cocoamine, Octadecylamine, TAPDA
Laundry and dishwashing	Ethylenediamine	Hexadecyldimethylamine
Automotive care	N/A	Cocoamine, Hexadecyldimethylamine
Personal care	N/A	Hexadecyldimethylamine
Pest control	Dimethylamine, Ethylenediamine	N/A
Fabric, textile, and leather products	N/A	BHTAA, Cocoamine, Hexadecyldimethylamine, HTAAA, TAPDA
Lubricants and greases	Ethylenediamine	BHTAA, Cocoamine, HTAAA, Octadecylamine, TAPDA
Building or construction materials	Dimethylbenzylamine	Cocoamine, Hexadecyldimethylamine, TAPDA, TMTADA
Agricultural products, mixtures or manufactured items (non-pesticidal)	N/A	Cocoamine, Octadecylamine
Oil and natural gas extraction	Diethylenetriamine Dimethylbenzylamine	Cocoamine, TAPDA
Fuels and related products, mixtures, or manufactured items	Ethylenediamine	Hexadecyldimethylamine
Plastic and rubber materials	N/A	Hexadecyldimethylamine
Foam seating and bedding	N/A	Hexadecyldimethylamine
Furniture and furnishings	N/A	Hexadecyldimethylamine
Metal materials	N/A	DPDAB
Drugs	Ethylenediamine	N/A
Automotive, aircraft, and transportation	Ethylenediamine	N/A

Abbreviations: N/A, not applicable (no uses were reported)
[a] Non-confidential uses, based on commercial/consumer codes, reported in response to a CEPA section 71 survey (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

Table 4-4 presents additional use information on short and long-chain aliphatic amines in Canada derived from other sources.

Table 4-4. Additional uses in Canada for short-chain and long-chain aliphatic amines

Use	Short-chain aliphatic amines	Long-chain aliphatic amines
Food packaging materials[a]	Diethylenetriamine Dimethylamine Ethylenediamine	BHTAA
Incidental additives[a,b]	N/A	Cocoamine, Octadecylamine
Medicinal or non-medicinal ingredients in disinfectant, human or veterinary drug products[c]	Ethylenediamine	Octadecylamine
Medicinal or non-medicinal ingredients in licensed natural health products[d,e]	N/A	Hexadecyldimethylamine
Present in cosmetics, based on notifications submitted under the *Cosmetic Regulations*[f]	N/A	Cocoamine, Octadecylamine
Formulant in registered pest control products[g]	Dimethylamine Ethylenediamine	Cocoamine, Hexadecyldimethylamine, HTAAA, TAPDA

Abbreviations: N/A, not applicable (no uses reported for these substances)
[a] Personal communication, e-mail from Food Directorate, HC, to the Existing Substances Risk Assessment Bureau, HC, dated January 10, 2017; unreferenced
[b] While not defined under the Food and Drugs Act (FDA), incidental additives may be regarded, for administrative purposes, as those substances which are used in food processing plants and which may potentially become adventitious residues in foods (e.g., cleaners, sanitizers) (Health Canada 2010)
[c] DPD [modified 2017]; Personal communication, e-mail from Therapeutic Products Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated December 16, 2016; unreferenced
[d] NHPID [modified 2019]
[e] LNHPD [modified 2016]
[f] Personal communication, e-mails from Consumer and Hazardous Products Safety Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated Dec 14, 2016 and Dec 14, 2017; unreferenced
[g] Personal communication, e-mail from Pest Management Regulatory Agency, HC to the Existing Substances Risk Assessment Bureau, HC, dated December 21, 2016 and January 27, 2020; unreferenced

4.1 Short-chain aliphatic amines

Major uses of the short-chain aliphatic amines are listed in Table 4-3 and Table 4-4. In addition, dimethylbenzylamine is used in polyurethane foam (PUF) applications in Canada (Environment Canada 2013). Specifically, dimethylbenzylamine has been reported to be used as a catalyst in PUF systems (Havermans and Houtzager 2014). Dimethylbenzylamine has been detected in air in car interiors, with the foam-based car seating being identified as a potential source (Rampfl et al. 2008). A two-component marine epoxy product sold in Canada has been found to contain dimethylbenzylamine (SDS 2014d). Dimethylbenzylamine has been qualitatively identified as naturally occurring in black tea (Vitzthum et al. 1975).

In the uses outlined in Table 4-3, ethylenediamine functions as a corrosion inhibitor, plating agent, surface treating agent, additive, and bleaching agent (Environment Canada 2013). Ethylenediamine is also used as a chemical intermediate (PubChem 2004-2020). Ethylenediamine is described as a prohibited ingredient on Health Canada's Cosmetic Ingredient Hotlist (Health Canada [modified 2018]). In Canada, ethylenediamine is used as an ingredient in a prescription intravenous respiratory smooth muscle relaxant pro-drug, aminophylline (personal communication, e-mail from the Therapeutic Products Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated December 16, 2016; unreferenced). Ethylenediamine is a formulant in pest control products registered in Canada. The Canadian Food Inspection Agency (CFIA) monitors pesticide residues and metabolites in food, including ethylenediamine (CFIA 2019).

In addition to the uses outlined in Table 4-3, diethylenetriamine has been identified in a two-component epoxy glue product and in a two-component marine epoxy filler product available to consumers in Canada (SDS 2015; SDS 2018a).

Dimethylamine occurs naturally in many types of foods, such as various fruits, vegetables, meats, fish, and dairy products (VCF 2018; Pfundstein et al. 1991), and it has been identified as being ubiquitous in water and human urine. In addition, dimethylamine is naturally occurring in cigarette smoke and animal waste (PubChem 2004-2020). The presence of dimethylamine in urine is a result of endogenous formation via biochemical pathways or from exogenous sources such as diet (Zhang et al. 1995).

Dimethylamine is described as a prohibited ingredient on Health Canada's Cosmetic Ingredient Hotlist (Health Canada [modified 2018]).

4.2 Long-chain aliphatic amines

Information on the uses of long-chain aliphatic amines in Canada was obtained in part through a survey issued pursuant to a CEPA section 71 notice (Canada 2012) and a questionnaire to specific companies and industry associations (ECCC 2016b). The ecological assessment of long-chain aliphatic amines also considers use information from other sources, including uses reported in other jurisdictions and in published articles.

A large proportion of long-chain aliphatic amines serve as intermediates in the derivation of other chemical substances, such as aliphatic amine ethoxylates or amides (BUA 1994; EC 2008), that have a wide range of industrial and commercial uses (e.g., antistatic agents for plastic formulations, auxiliary agents in textile industry, additives in laundry and dishwashing products). Chemicals derived from long-chain aliphatic amines contain unreacted residual long-chain aliphatic amines, which may be released into the environment during the use of products containing them. For example, aliphatic amine ethoxylates and diamines derived from primary monoamines may contain about 0.2% to 2.2% and about 7.5%, respectively, of unreacted primary monoamines (EC 2008). Of

the long-chain aliphatic amines in the Aliphatic Amines Group, cocoamine and BHTAA were identified as being used as intermediates in Canada. In Europe, octadecylamine, cocoamine, tallow alkyl amine, hydrogenated tallow alkyl amine (CAS RN 61790-33-8) and oleylamine (CAS RN 112-90-3) have identified uses as intermediates (EC 2008). In addition, Roose et al. (2015) identified secondary amines as being mainly used as intermediates.

Hexadecyldimethylamine is imported into Canada as a process regulator/aid in polyurethane foam production, particularly in the production of foam seating and bedding (e.g., automotive seating) (ECCC 2016b). It is not known whether other long-chain aliphatic amines are similarly used.

Several long-chain aliphatic amines are used as flotation agents for mineral extraction (e.g., iron ore, potash, feldspar, zinc oxide, kaolin, etc.) (Akzo Nobel 2010; Nouryon 2019). Specifically, DPDAB was identified as being used as a flotation agent in Canada (SDS 2017b; Evonik 2019). According to Akzo Nobel (2010) and Nouryon (2019; formerly Akzo Nobel Specialty Chemicals), cocoamine and HTAAA from the Aliphatic Amines Group, as well as hydrogenated tallow alkylamines (CAS RN 61788-45-2), tallow alkyl amine (CAS RN 61790-33-8), oleylamine (CAS RN 112-90-3), N-tallow-1,3-diaminopropane (CAS RN 7173-62-8) and N-tallow-1,3-diaminopropane distillates (CAS RN 61790-59-8) are also used as flotation agents. Two propane diamine ethers similar to DPDAB, namely N-(3-(tridecyloxy)propyl)-1,3-propane diamine and N-(3-(tridecyloxy)propyl)-1,3-propane diamine acetate, are used as flotation agents (Olsvik et al. 2015). In Europe, cocoamine, tallow alkyl amine, hydrogenated tallow alkyl amine (CAS RN 61788-45-2) and octadecenylamine have been identified as being used in mineral flotation (EC 2008).

Long-chain primary amines, diamines, and ether amines are used to emulsify asphalt. The long-chain aliphatic amine products are used at low concentrations (0.2% to 2.0 wt% of the emulsion) for slow, medium, and rapid setting cationic asphalt emulsions (Roose et al. 2015).

Some long-chain primary amines are used as anti-caking agents in fertilizers, while others are used in mineral products (Roose et al. 2015). In Canada, octadecylamine is identified as being used as an anti-caking agent (ECCC 2016b). Cocoamine, tallow alkyl amine, and hydrogenated tallow alkyl amine are also identified as being used for this purpose (Akzo Nobel 2010; Nouryon 2019; EC 2008; Strathdee et al. 1982).

In North America, a number of long-chain aliphatic monoamines and diamines have been identified as being available for use as corrosion inhibitors, including octadecylamine and cocoamine from the Aliphatic Amines Group. Other aliphatic amines with this use are octadecyldimethylamine (CAS RN 124-28-7), dimethyl hydrogenated tallow alkyl amine (CAS RN 61788-95-2), dicocoalkylamine (CAS RN 61789-76-2), and oleyl-1,3-propanediamine (CAS RN 7173-62-8) (Nouryon c2019).

In Canada, various consumer uses have been identified for the long-chain aliphatic amines in the Aliphatic Amines Group in Canada. Hexadecyldimethylamine (identified as dimethyl palmitamine) is listed on the Natural Health Products Ingredients Database as an NMI with the function of antistatic agent (NHPID [modified 2019]), and it is listed in the Licensed Natural Health Products Database as an NMI in two topical rinse-off acne facial cleansers (LNHPD [modified 2018]). Octadecylamine (INCI name: stearamine) and cocoamine have identified uses in cosmetics based on notifications submitted to Health Canada under the *Cosmetic Regulations* (personal communication, e-mail from the Consumer and Hazardous Products Safety Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated December 14, 2016; unreferenced). Octadecylamine is reported to be an incidental additive, where it is used as an additive in boiler water. Cocoamine may be used as an incidental additive component in cleaners and lubricants used in food processing establishments. BHTAA is used as a component in stabilizers for use in polypropylene and high density polyethylene intended to be used in food packaging applications (personal communication, e-mail from the Food Directorate, HC, to the Existing Substances Risk Assessment Bureau, HC, dated January 10, 2017; unreferenced). Hexadecyldimethylamine, cocoamine, HTAAA, and TAPDA were identified as formulants in Canada (personal communication, e-mail from the Pest Management Regulatory Agency, HC, to the Existing Substances Risk Assessment Bureau, HC, dated December 21, 2016 and January 27, 2020; unreferenced). DPDAB has been reported in the hardener of a two-component marine epoxy adhesive product available to the general public in Canada (personal communication, Aliphatic Amines voluntary data gathering, Existing Substances Risk Assessment Bureau, HC 2018; unreferenced).

5. Releases to the environment

Due to the variety of uses for short and long-chain aliphatic amines, both diffuse and point source releases to the Canadian environment are expected. Point source releases (e.g., from industrial facilities) may occur during the manufacturing, formulation or industrial use stages. Releases of short-chain aliphatic amines to the environment are expected through wastewater and releases to air from use in industry as intermediates and processing aids. For most long-chain aliphatic amines, releases to the environment are expected to occur primarily to water through wastewater treatment systems[10] (WWTS), with some releases to water directly from industrial sites. Releases of long-chain aliphatic amines to soil may occur via the application of biosolids from WWTS, or through the use of primary long-chain aliphatic amines in fertilizer formulations.

[10] In this assessment, the term “wastewater treatment system” refers to a system that collects domestic, commercial and/or institutional household sewage and possibly industrial wastewater (following discharge to the sewer), typically for treatment and eventual discharge to the environment. Unless otherwise stated, the term wastewater treatment system makes no distinction of ownership or operator type (municipal, provincial, federal, indigenous, private, partnerships). Systems located at industrial operations and specifically designed to treat industrial effluents will be identified by the terms “on-site wastewater treatment systems” and/or “industrial wastewater treatment systems.”

6. Environmental fate and behaviour

The short-chain aliphatic amines from the Aliphatic Amines Group were determined through ERC to have low potential to cause ecological harm due to low overall persistence, low reported use volumes, and low potential for long-range transport in air (ECCC 2016b). Therefore, this section focuses on the long-chain aliphatic amines as a class.

6.1 Environmental distribution

Present fugacity models are generally not appropriate for ionizing and surface-active substances (Mackay et al. 2009) and therefore were not used for describing the distribution of long-chain aliphatic amines among the environmental compartments (air, water, soil, sediments, and biota). Instead, descriptions of the fate and behaviour of long-chain aliphatic amines were based on their physical and chemical properties, including their partition coefficients.

Long-chain aliphatic amines are not expected to be released to air given their intended uses and physical-chemical properties. These substances have very low to moderate vapour pressure for the neutral form. When present as cations, as expected at environmentally relevant pH (6-9), long-chain aliphatic amines are not expected to volatilize (Trapp et al. 2010). Therefore, Henry's law constant is not considered to be relevant to long-chain aliphatic amines (ECCC 2021), and the potential for long-range atmospheric transport is expected to be very low. This assertion is further supported by the estimated half-lives for reaction with OH radicals and ozone, which indicate that even if these substances did partition to air, they would not remain there for long (see section 6.2.4).

Given the reported uses of long-chain aliphatic amines, it is expected that these substances may be released to surface water, generally following wastewater treatment. Based on studies with QACs, it is expected that long-chain aliphatic amines will be removed either via sorption to sewage sludge or via degradation during wastewater treatment, with sorption outcompeting biodegradation (Tezel et al. 2006). Studies on the sorption of QACs to sewage sludge indicate that sorption is rapid (within hours) and increases with increasing alkyl-chain length (Ismail et al. 2010). However, aliphatic amines sorbed to sludge organic matter that are released to receiving waters may also desorb, with the magnitude of desorption expected to decrease with increasing alkyl-chain length (Ismail et al. 2010). Ismail et al. (2010) noted that dodecyl trimethyl ammonium chloride, a C_{12} QAC similar to dodecylamine, was only 13% sorbed to sludge while hexadecyl trimethyl ammonium chloride, a C_{16} QAC similar to hexadecylamine, was 88% sorbed. However, 40% of the C_{12} QAC desorbed from sludge in 10 days, as compared to only 5% of the C_{16} QAC.

Once released to surface waters, the high pK_a values of long-chain aliphatic amines (10.0 to 10.7; see Table 3-3) indicate that the cationic form will be the dominant species in water. When low concentrations are released to water, long-chain aliphatic amines

are expected to be dissolved in water based on their low- to moderate-water solubilities and their estimated critical micelle concentrations of 40 mg/L or greater. In water, they are also expected to sorb to various sorbents, such as suspended solids, dissolved and particulate organic carbon, and sediments, which will reduce their bioavailability. Sorption occurs via both ionic and non-ionic interactions at cation exchange sites on the sorbents and not by sorption into hydrophobic regions of organic matter. While the molar density of the ion-exchange sites determines the maximum sorption capacity of sorbents, the hydrophobic properties of the surfactant (e.g., alkyl-chain length) largely determine the overall sorption affinities to these sites (Droge and Goss 2013a). Sorption affinity to organic matter in water is described by the $K_{OC\text{-}cationic}$ as discussed in Section 3.2.5. Since alkyl-chain length impacts sorption affinity and thus behaviour in the environment, long-chain aliphatic amines were grouped into smaller alkyl-chain categories to describe their environmental behaviour. These categories include: C_8-C_{14} (including smaller long-chain aliphatic amines and the predominant components of cocoamines); C_{15}-C_{18} (including the predominant components of amines derived from tallow and soya); C_{19}-C_{22} (including a predominant component of amines derived from rapeseed); and C_{24} and greater. Long-chain aliphatic amines with two long alkyl chains were placed in the category corresponding to the sum of their two long alkyl chains (e.g., a 2xC_8 dialkylamine was considered with C_{16} monoamines) as their sorption properties were more similar to others in the same alkyl-chain length category. Using modelled $K_{OC\text{-}cationic}$ and the median total organic carbon (TOC) content for Canadian waterways, the fraction of long-chain aliphatic amines freely dissolved were determined for 43 representative monoamines and 26 representative diamines (Table 6-1). The fraction freely dissolved ($f_{dissolved}$) is determined as:

$$f_{\text{dissolved}}(\%) = \frac{1}{1 + \mathrm{K}_{OC-cation} \times \left[TOC\,\frac{kg}{L}\right]}\; x\; 100$$

where $K_{OC\text{-}cation}$ is the estimated organic carbon partition coefficient for cations and TOC is the concentration of total organic carbon in kg/L. The derivation of the TOC value (1.305×10^{-5} kg/L = 13.05 mg/L) is described in ECCC (2021).

A single value of the percent freely dissolved for each alkyl-chain length category was determined as the midpoint of the lowest and highest freely dissolved values calculated for a range of representative structures. The percent freely dissolved when in water with a TOC of 13.05 mg/L is presented in Table 6-1. Further information is available in ECCC 2021.

Table 6-1. Percentage of long-chain aliphatic amines freely dissolved in surface water having a median total organic carbon concentration of 13.05 mg TOC/L

Amine number	Alkyl-chain length category	Range of % freely dissolved (midpoint)[a]
Monoamines	C_8-C_{14}	87.8 – 99.6 (93.7)
Monoamines	C_{15}-C_{18}	50.1 – 87.6 (68.8)
Monoamines	C_{19}-C_{22}	11.9 – 49.3 (30.6)

Amine number	Alkyl-chain length category	Range of % freely dissolved (midpoint)[a]
Monoamines	C_{24} ($2xC_{12}$)	9.5
Monoamines	C_{26} ($2xC_{13}$)	3.7
Monoamines	C_{28} ($2xC_{14}$) and C_{36} ($2xC_{18}$)	1.4 or less
Diamines	C_8-C_{14}	45.5 – 95.7 (70.6)
Diamines	C_{15}-C_{18}	10.2 – 41 (25.6)
Diamines	C_{19}-C_{22}	1.5 – 8.7 (5.1)

Abbreviations: TOC, total organic carbon.
[a] The midpoint is the average of the lowest and highest value for representative structures in the range

While the fraction freely dissolved can be quite high for lower alkyl-chain lengths, it decreases as the alkyl-chain length increases such that the amines with the longest alkyl chains are mainly sorbed. Diamines tend to sorb more for a given alkyl-chain length than monoamines. The fate of long-chain aliphatic amines in sediments and soils will be determined by their sorption characteristics. The modelled partition coefficient for solids-water in soil (K_d) includes both sorption to clays (K_{CEC}) and organic matter ($K_{OC\text{-}cationic}$) and thus is dependent on the cation exchange capacity (e.g., type and amount of clay), organic carbon fraction, salinity of the system, and specific aliphatic amine. Diamines generally have a slightly greater K_d than monoamines, and sorption increases for both with an increase in alkyl-chain length (Table 3-2, Section 3.2.3). Long-chain aliphatic amines with lower alkyl-chain lengths are expected to be more mobile than those with very high alkyl-chain lengths, which are expected to be immobile. Long-chain aliphatic amines are also expected to sorb much less to low organic carbon sandy soil or sediment than to high organic carbon clay soil or sediment.

Long-chain aliphatic amines are expected to settle out of the water column to sediment when sorbed to organic carbon or clays in the water column, and to sorb to bottom sediment directly. As noted, this will vary widely depending on the alkyl-chain length and the characteristics of the sediment. Where input into a water body is continuous, such as near wastewater discharge sites, these substances may accumulate in sediments depending on the rate of flux to sediment as compared to losses due to biodegradation. Long-chain aliphatic amines will be predominantly protonated in soils; therefore, when released to soil (e.g., via the application of sludge/biosolids or mineral potassium fertilizers on agricultural lands), long-chain aliphatic amines will sorb to both organic matter and clays in soils mainly via ionic and non-ionic interactions at cationic exchange sites (Droge and Goss 2013a, 2013b).

In addition to sorbing to organic carbon and clays in the water column, sediments, and soils, aliphatic amines will also partition to organisms. Long-chain aliphatic amines have high empirical and modelled membrane-water partition coefficients, indicating strong sorption to membranes (see section 3.2.3). Some organisms, such as algae, have negatively charged cell walls that may increase sorption (van Wijk et al. 2009; Zhang et al. 2015).

6.2 Environmental persistence

6.2.1 Biodegradation in water

Biodegradability data for long-chain aliphatic amines are available from screening tests following OECD guidelines 301 for ready biodegradability. Biodegradability data for 22 long-chain aliphatic amines range from 3% to 91% (ECCC 2021), where the percentage represents the biodegraded quantity of the test substance after 28 days. Biodegradation in water is determined by assessing parameters such as DOC production, CO_2 evolution or O_2 consumption. Ready biodegradability tests with a biodegraded quantity of 40% or greater indicate that there is high confidence that the half-lives are less than 182 days, signifying that the test substance is unlikely to persist in water.

ECCC (2021) includes results from 40 studies with ready biodegradability tests, where 9 of these studies achieved biodegradation quantities less than 40%. Some studies with substances having the ether functional group show low biodegradability, which may be due to the ether functional group and/or the concentration of test substance used (2 to 100 mg/L). Concentrations of the QAC analogue cetyltrimethylammonium bromide (CTAB, C_{16}-QAC) above 0.3 mg/L negatively affected the degradation of the reference compound aniline (Timmer et al. 2019) and EC (2008) determined a predicted no-effect concentration of 0.55 mg/L for microbial activity, suggesting that long-chain aliphatic amine concentrations of 2 mg/L or greater might inhibit biodegradation. However, some aliphatic amines demonstrate high biodegradation at concentrations above 2 mg/L, so it is unclear as to why the biodegradation rates vary. Ultimate biodegradation half-life predictions for 44 representative structures of long-chain aliphatic amines ranged from 13 to 269 days with all but one value below 150 days (CATALOGIC 2014), indicating that long-chain aliphatic amines are not likely to persist in water. While both tert-alkyl amines and aliphatic amine ethers were included in the modelling, the representative structures of the amine ethers were not highly branched; therefore, the CATALOGIC results may not be comparable to the experimental data on aliphatic amine ethers (ECCC 2021).

Many of the tests with primary long-chain aliphatic amines began with a lag phase of several days, then a quick increase in degradation with up to 50% to 60% of total mineralization, followed by a third phase where further degradation increased quite slowly. It was hypothesized that the third phase was caused by reduced bioavailability of the test substances to microorganisms due to adsorption of aliphatic amines on laboratory glassware (EC 2008) or sludge, thus reducing the bioavailability of the substance for biodegradation. In addition, the high toxicity of aliphatic amines to microorganisms could cause lower than expected biodegradation. Toxicity and the resulting inhibition in degradation may decrease as the aliphatic amines biodegrade, which could explain why the lag phase of up to 7 days was followed by increased degradation (Timmer et al. 2019).

In terms of the metabolic pathways, EC (2008) presented the results of Yoshimura et al. (1980) who suggested that primary alkyl amines are biodegraded through one of two

pathways: (1) oxidative deamination (producing the corresponding fatty acid and ammonia) or (2) ω-oxidation on the terminal methyl group (producing ω-amino fatty acid), followed by β-oxidation in either case. The initial reaction step of either oxidative deamination or ω-oxidation would lead to a loss of surfactant properties and, therefore, to a loss of toxicity, while further degradation involving β-oxidation would lead to total mineralization (van Ginkel 1996). Ratledge (1994) confirmed that unsaturated alkyl-chains degrade through similar reactions.

The experimental and model results indicate that long-chain aliphatic amines are not persistent in water. While there are uncertainties regarding long-chain aliphatic amines with ether or tert-alkyl functional groups, the CATALOGIC (2014) model indicates that they are unlikely to persist in the aquatic environment.

6.2.2 Biodegradation in soils

Data on the degradation of ^{14}C-radiolabelled hexadecanamine and two ^{14}C-radiolabelled analogue substances (both quaternary ammonium compounds) in soils were found (ECHA c2007-2018c, c2007-2018d). The formation of radioactive carbon dioxide ($^{14}CO_2$) was determined, and DT_{50}[11] values (i.e., time required for 50% reduction of the initial concentration of a parent compound) were calculated (Table 6-2). The relatively high percentage of the formation of radioactive $^{14}CO_2$ indicates that biodegradation is a predominant process in the dissipation of these substances and therefore that soil microorganisms are capable of degrading long-chain aliphatic amines. This, plus the short calculated DT_{50} values, indicate that long-chain aliphatic amines are not persistent in soils. This also showed that the relatively large sorbed fractions of aliphatic amines in these soils were readily bioaccessible.

Table 6-2. Experimental biodegradation of aliphatic amines and analogues in soils[a]

Common name	$^{14}CO_2$ formation (%)[a]	DT_{50} (days)
[^{14}C] 1-Hexadecanamine	55-59	8.1-9.0[b]
[^{14}C] Quaternary ammonium compounds, C_{12}-C_{18} alkyl (hydroxyethyl)dimethyl, chlorides	55-59	6.0-13.6[b]
[^{14}C] 1-Hexadecanamine	44-48	8.7-9.9[c]

[11] DT_x does not differentiate between transfer processes and degradation processes (FOCUS 2006). Importantly, the DT_{50} should be distinguished from half-life; the half-life, $t_{1/2}$=ln(2)/k, indicates the time required to reduce the concentration by 50% from any concentration point in time. It is an intuitive way to express the rate of decline of first-order degradation. In contrast, the DT_{50} is the time required for the concentration to decline to half of the initial value. For non-first-order decay, the time to reach half the concentration from any other concentration point on the curve will be different (Bohaty et al. 2015).

Common name	$^{14}CO_2$ formation (%)[a]	DT_{50} (days)
[^{14}C]C_{22} Trimethyl ammonium chloride	63-73	23-41[d]

[a] Formation of radioactive $^{14}CO_2$ (% of the applied radioactivity in soils by the end of the study)
[b] Soils are silty clay loam, loam, and sandy loam
[c] Soils are silty loam, loam, and sandy loam
[d] Soils are silty loam, clay, and loam

Half-lives between 16 and 150 days have been modelled for aliphatic amines in water (see section 6.2.1). Half-lives in soil are expected to be the same on the basis of the extrapolation ratio of 1:1:4 for water to soil to sediment given by Boethling et al. (1995).

6.2.3 Biodegradation in sediments

No studies on the aerobic biodegradation of aliphatic amines in sediments have been located. Therefore, the biodegradation results for long-chain aliphatic amines in soils under aerobic conditions (see section 6.2.2) can be extrapolated to the top layer of sediments. Thus, under aerobic conditions, long-chain aliphatic amines are not expected to persist in fresh sediments.

No tests on the biodegradation of long-chain aliphatic amines in sediments under anaerobic conditions are available. Studies on similar alkyl QACs indicated low to no biodegradation under anaerobic conditions (Zhang et al. 2015; Tezel et al. 2006) and elevated concentrations of quaternary ammonium compounds in hypoxic surficial sediments (Lara-Martin et al. 2010). Therefore, it is presumed that long-chain aliphatic amines are persistent in sediments under anaerobic conditions.

6.2.4 Abiotic degradation

Long-chain aliphatic amines are unlikely to undergo photolytic degradation in water (including water treatment in open water lagoons) because of the lack of aromatic rings, heteroatoms, and other functional chromophore groups capable of absorbing light energy directly or via reactions with photo-generated transient species. Furthermore, hydrolytic degradation is not expected because the substances lack hydrolysable groups.

In the atmosphere, long-chain aliphatic amines are likely to be degraded due to reactions with hydroxyl radicals and with ozone. The half-lives of long-chain aliphatic amines in air were 3.2 hours or less and 2.1 hours or less for reactions with hydroxyl radicals and ozone, respectively (EPI Suite c2000-2012). However, long-chain aliphatic amines are expected to have limited presence in air (see section 6.1).

6.3 Potential for bioaccumulation

6.3.1 Bioaccumulation in aquatic organisms

Long-chain aliphatic amines can interact both ionically and non-ionically with organic matter, including organisms. Their cationic amine functional group can sorb strongly to negative charges on surfaces, such as cell membranes (Gecol 2006; Droge 2017), while their hydrophobic aliphatic chains can interact non-ionically with membranes (Droge 2017). Sorption to algae was identified as an important sink for long-chain aliphatic amines in a static toxicity test (ECHA c2007-2018h), and relatively high concentrations of hexadecylamine were measured in fish mucous and scales in an 11-month chronic study (Akzo Nobel 2006). This sorption to surfaces is especially important for smaller organisms such as daphnids and unicellular algae, which have a much higher surface-to-volume ratio than larger organisms such as fish. Indeed, long-chain aliphatic amines affect daphnids and algae at much lower concentrations than fish (see section 7.1.2).

While long-chain aliphatic amines do sorb to surfaces, they can also enter the organism, as noted by research sponsored by the European Chemical Industry Council (CEFIC) on the bioaccumulation of surfactants including C_9 to C_{16} long-chain aliphatic amines. As part of this research, a study on the uptake and tissue-distribution of surfactants by rainbow trout was conducted (McLachlan 2018). In this study, rainbow trout were exposed for 7 days to constant concentrations of two mixtures of long-chain aliphatic amines and QACs and the concentration of each individual substance in the mixture was determined in mucous, skin, gills, liver and muscle tissues. The nominal test concentrations for each individual substance in the mixture ranged from 2.5 to 50 µg/L. The results indicate that long-chain aliphatic amines are distributed among all of the tissues considered. The highest concentrations of individual substances were noted in fish livers, followed by gills and then skin. Muscle tissue, which included much of the subcutaneous fat, generally had low concentrations (McLachlan 2018), indicating that adipose tissue is not a major sink for these substances. On a percentage of total body burden basis, long-chain aliphatic amines on or in the gills, skin and mucous were generally the highest (40% to 70%) (McLachlan 2018), demonstrating the importance of sorption onto or into surface tissues. The 7-day BCFs for individual aliphatic amines ranged from approximately 3 to 1000 L/kg wet weight (ww) (McLachlan 2018). More recently, McLachlan et al. (2019) presented preliminary data from a 14-day BCF study conducted as a continuation of this project. BCFs greater than 5000 L/kg ww were determined for C_{16} primary and secondary amines and a C_{14} tertiary amine, while C_{13}-primary and -tertiary amines had BCFs over 1000 L/kg ww, indicating that some longer-chain aliphatic amines have high bioaccumulation potential. The bioaccumulation potential of aliphatic amines with alkyl chains longer than C_{16} is unknown, but as 14-day BCFs increased with increasing alkyl-chain length (McLachlan et al. 2019), it is presumed that they will also be bioaccumulative.

Only one steady-state bioaccumulation study was located on the bioaccumulation of long-chain aliphatic amines in fish. BCF values for hexadecylamine (C_{16}-primary amine)

were experimentally determined in a long-term, 11-month study (in which steady-state was reached) that was conducted by Akzo Nobel (2006) and is briefly described in EC (2008). Common carp (*Cyprinus carpio*) were exposed to a nominal water concentration of 3 µg/L hexadecylamine, with measured concentrations of 50% to 80% of the nominal concentration. After 11 months of exposure, the whole-fish body burden ranged from 1500 to 3600 µg/kg, while in the mucous and scales, the concentrations of hexadecylamine were 8000 to 15 000 µg/kg. After removing the mucous and scales and washing the fish with chloroform (to remove physically adsorbed hexadecylamine; ECHA 2011), the residual concentrations in the body were 650 to 850 µg/kg. Following a second rinsing procedure with acidified methanol (to remove ionically bound hexadecylamine; ECHA 2011), the concentrations dropped to 280 to 600 µg/kg. These analytical results indicate that both physical adsorption and ionic binding to the organism's surfaces occurred. Considering the measured exposure concentrations (50% of the nominal) of hexadecylamine and the whole-fish body burden, the experimental BCF was 2400 L/kg (i.e., log BCF=3.4), indicating a moderate potential for bioaccumulation. Lower BCFs would be calculated if certain tissues were not included (e.g., mucous and/or scales) (EC 2008). This is lower than the 14-day BCFs determined by McLachlan et al. (2019) for a C_{16} primary amine. However, it is noted that growth dilution does not appear to have been considered in the determination of the whole-body BCF even though growth of the fish is expected over the 11-month test duration (ECHA 2011). Growth dilution would cause the concentration of hexadecylamine to diminish over time, resulting in an underestimation of the BCF.

Experimental bioaccumulation studies are available for dialkyl quaternary ammonium compounds, which are read-across for dialkyl long-chain aliphatic amines. These indicate a low potential for bioaccumulation, with BCFs of 256 L/kg or less (ECCC 2021), comparable to the low 14-day BCFs for a C_{10} and C_{14} monoalkyl QAC (< 100 L/kg ww) determined by McLachlan et al. (2019). No comparable data on long-chain dialkyl aliphatic amines were found. Krop and de Voogt (2007) show that monoalkyl trimethyl QACs, with alkyl chains of C_{12} or less, have BCF values of approximately 100 L/kg or less (Versteeg and Shorter 1992; Schlechtriem et al. 2014). This is similar to the low 14-day BCFs (< 60 L/kg) noted for C_{10} and C_{14} monoalkyl trimethyl QACs by McLachlan et al. (2019). Schlechtriem et al. (2014) estimated the BCF for a $C_{16\text{-}18}$ monoalkyl trimethyl QAC as 1960 L/kg, which, compared to McLachlan et al. (2019), is much higher than the BCF for the C_{14} QAC but lower than the BCFs for C_{16} aliphatic amines. The preliminary results of McLachlan et al. (2019) suggest that the bioaccumulation of QACs is dominated by surface sorption, which differs from the uptake observed with long-chain aliphatic amines. Given that longer QACs (e.g., C_{15} or higher) were not tested by McLachlan et al. (2019), it is difficult to compare with the BCF values estimated by Schlechtriem et al. (2014). The lack of comparable data and possible differences in uptake of QACs versus aliphatic amines results in uncertainty as to the extent that QAC bioaccumulation data can be read-across to aliphatic amines.

Rainbow trout *in vitro* liver S9 tests demonstrated that aliphatic amines may be readily biotransformed, although substantially lower rates were observed for primary amines (Chen et al. 2016). This study included a $2xC_6$ dialkylamine as a test substance, which,

while not technically a long-chain aliphatic amine, demonstrated the capacity of trout liver to metabolize dialkylamine structures. The data suggest that N-dealkylation is a major biotransformation pathway in trout, with de-methylation resulting in the conversion of tertiary amines to secondary amines, which in turn are transformed to primary amines (Chen et al. 2016). A more complete metabolic pathway is available for primary aliphatic amines in mammals: (1) oxidative deamination by monoamine oxidase forming ammonia and the corresponding alkyl amine aldehyde, (2) oxidation of the aldehyde by aldehyde dehydrogenases to carboxylic acids, followed by (3) β-oxidation of the carboxylic acids to carbon dioxide (EC 2008).

While some studies on long-chain aliphatic amines and QAC analogues indicate low to moderate potential for bioaccumulation of long-chain aliphatic amines, preliminary results from one study with 14-day BCFs indicate that aliphatic amines with $C_{14\text{-}16}$ alkyl chains can be highly bioaccumulative with BCFs greater than 5000 L/kg ww. It is presumed that aliphatic amines with longer chains will also have BCFs greater than 5000 L/kg ww. Studies with dialkyl QACs suggest that dialkyl amines might similarly have low bioaccumulation potential; however, there is some uncertainty as to whether QACs are bioaccumulated in a similar manner as aliphatic amines.

In summary, the available data show that long-chain aliphatic amines with alkyl chains shorter than C_{14} have low to moderate potential for bioaccumulation in aquatic organisms, and those with alkyl chains of C_{14} and longer have high potential to bioaccumulate.

6.3.2 Bioaccumulation in sediment-dwelling organisms

For sediment-dwelling organisms, no bioaccumulation data for aliphatic amines are available. However, there are data for the analogue dimethyldioctadecylammonium chloride (DODMAC; $2xC_{16\text{-}18}$). Comber et al. (2008) measured the route of uptake for DODMAC in *Lumbriculus variegatus* (Oligochaete) and demonstrated the relative importance of uptake via ingestion (86%) compared with direct contact with sediment and via pore water (14%). The overall tendency of DODMAC to bioaccumulate on a dry weight basis was low, with measured biota-sediment accumulation factors (BSAF) of 0.22 for *L. variegatus* and 0.78 for *Tubifex tubifex* (Oligochaete) (Comber et al. 2008). This is similar to the low bioaccumulation potential of dialkyl QACs noted with fish. However, there is some uncertainty in the extent that QAC bioaccumulation data can be extrapolated to aliphatic amines. As other aliphatic amines (e.g., those with alkyl chains of C_{14} and longer) were found to have a high potential to bioaccumulate in fish, it is assumed that bioaccumulation of these aliphatic amines will be similarly high in sediment-dwelling organisms.

7. Potential to cause ecological harm

7.1 Ecological effects assessment

Given that the short-chain aliphatic amines from the Aliphatic Amines Group were determined through ERC to have low potential to cause ecological harm, this section focuses on the long-chain aliphatic amines as a class.

7.1.1 Mode/mechanism of action

Some experimental evidence is available which suggests that long-chain aliphatic amines have a non-specific narcotic mode of action [MoA]. For example, Bernhard and Dyer (2005) found that cellular residue levels for a number of individual surfactants and their mixtures corresponded closely to *in vivo* body burdens (2 to 8 mmol/kg) associated with non-polar organic or narcosis-acting compounds in a hepatic fish cell line, suggesting that long-chain aliphatic amines act through a narcotic MoA. Nonetheless, a narcotic MoA would involve disruption of cell membranes. However, Wood et al. (1996) found no gross external disruptions to gill lamellae while studying the influence of the QAC didecyldimethylammonium chloride (DDAC) on the physiology of rainbow trout.

Structure-property model predictions also tend to suggest that aliphatic amines are narcotic chemicals with non-specific MoAs. For example, various models—Verhaar et al. (1992), TEST (2016), ASTER (1999), OASIS MoA profiler (Dimitrov et al. 2003), and US EPA MOATox (Barron et al. 2015)—classify long-chain aliphatic amines from the Aliphatic Amines Group as narcotic substances. However, there are exceptions in that tallow alkyl amines (CAS RNs 61790-59-8 and 61790-60-1) are classified as more reactive substances (i.e., reactive unspecified) by OASIS. There is further uncertainty in that these models consider acute aquatic toxicity data to inform their predictions, and it is unknown if this can be extrapolated to chronic tests or to organisms such as algae.

In terms of algal toxicity, Rieb and Grimme (1993) examined whether the impact of surfactants on algae depends on a common MoA using *Chlorella fusca*. The authors found that the toxicity of both non-ionic and cationic surfactants to *C. fusca* was due to a non-specific MoA, while the QAC cetyltrimethylammonium chloride exhibited a more specific MoA by interfering with cell reproduction processes. Indeed, aliphatic amines are expected to interact both ionically and non-ionically with membranes, and there is uncertainty in how these separate interactions relate to narcosis in algal species.

While there is evidence to suggest that long-chain aliphatic amines have a non-specific narcotic MoA, there is uncertainty as to whether this MoA could be expected for all organisms or whether some may be more susceptible to these substances due to specific ionic interactions.

7.1.2 Effects on aquatic organisms

7.1.2.1 Factors influencing aquatic toxicity

There are few studies in the published literature on the ecotoxicity of long-chain aliphatic amines. However, the European Chemicals Agency (ECHA) provides numerous summaries for unpublished acute and chronic aquatic toxicity studies with fish, invertebrates, and algae for a large number of long-chain aliphatic amines. These substances are difficult to test because of their surface-active properties, which result in molecules migrating to air/water and solid/water interfaces (including the test vessel surface) and at higher concentrations, developing micelles (Karsa 2006). Based on the molar CMCs presented in section 3.2.2, the CMC can be as low as 40 mg/L, which is used as a solubility limit. In addition, the cationic amine functional group will adsorb to negatively charged surfaces (Gecol 2006), including dissolved and particulate organic matter that is present in test water, as well as cell membranes.

Aquatic ecotoxicity data are available from studies conducted with both laboratory and natural river water. Natural river water contains both dissolved and particulate organic matter and, as noted in section 6.1, long-chain aliphatic amines may sorb to such matter, thus reducing their bioavailability to test organisms. Consequently, for the same species, toxicity values from tests with laboratory water are expected to be lower (i.e., higher apparent toxicity) than from tests with natural river water, and this is generally observed. In addition, the toxicity of the long-chain aliphatic amine oleylamine was noted to decrease in the presence of added humic acids (ECHA c2007-2018c). However, Chen et al. (2014) determined that although the toxicity of a C_{12} monoalkyl QAC to *Daphnia magna* decreased with increasing humic acid, the toxicity on a freely dissolved basis remained constant. It is therefore expected that the toxicity of long-chain aliphatic amines will also remain constant on a freely dissolved basis.

7.1.2.2 Nominal vs. measured toxicity values

Very few studies for long-chain aliphatic amines have toxicity values based on analytically measured concentrations. A number of studies analytically measured some test concentrations, yet did not use these measured concentrations in the determination of the toxicity value. Rather, toxicity values were determined using nominal concentrations according to the bulk approach proposed by ECETOC (2003). ECETOC (2003) advocates that the toxicity of strongly adsorbing substances, such as long-chain aliphatic amines, should be determined in modified ecotoxicity tests using humic acid, natural waters (containing dissolved and particulate organic matter) or effluents in order to mimic the fate of the substance in the environment. The resulting toxicity value should then be based on the total or “bulk” concentration (i.e., nominal concentration including both the dissolved and sorbed substance).

However, there are concerns with this approach for long-chain aliphatic amines. Aliphatic amines sorbed to organic matter in the test water and to test vessels/glassware are not bioavailable to the test organism. Therefore, nominal

concentrations will not represent the bioavailable fraction, and toxicity values based on the nominal concentration will underestimate the actual toxicity. Similarly, some studies on long-chain aliphatic amines acknowledge that toxicity values should be based on measured concentrations or, where measured toxicity values are not available, should note that the nominal toxicity values are unreliable (ECHA c2007-2018c, c2007-2018d). In addition, toxicity values based on nominal concentrations in a test water with specific conditions (e.g., concentration of organic matter) cannot be extrapolated to waters with different conditions.

It is presumed that the measured concentrations for long-chain aliphatic amines approximate their freely dissolved concentration in test water. This presumption is based on descriptions in study summaries that indicate that less than 100% recovery of nominal aliphatic amines from water and glassware is due to the strong sorption of these substances to organic matter (ECHA c2007-2018d). While this presumption may not be entirely correct, it does provide a more accurate toxicity value than one based on nominal concentrations.

Thus, in this assessment report, when deriving predicted no-effect concentrations (PNECs), toxicity values given as nominal concentrations were adjusted to measured concentrations when possible based on available analytical data. These adjustments assume that the curve for the loss of a tested substance was linear. As this might not be the case, there is uncertainty in the average exposure values calculated. It is noted that in some cases analytical results were highly variable.

To perform these adjustments, average analytical recoveries (i.e., the measured concentrations as percent of the nominal concentrations) were calculated based on the test concentrations at the beginning and end of a study (or end of a renewal period for semi-static tests). Therefore, all average recoveries were calculated as arithmetic means. Recoveries were not available for all nominal concentrations, which may cause additional uncertainty in toxicity values for which the measured concentrations are not monotonic (e.g., no consistent increase as the test concentration increases). For instance, one study provided analytical data for all test concentrations, but the measured concentrations at the start of the test were not dose-dependent, varying from 7% of nominal for the lowest concentration, 83% of nominal for the next lowest concentration, and 23% of nominal for the highest concentration (ECHA c2007-2018d). Although the start-test and end-test recoveries might vary significantly—with the extent of the variation uncertain for most tests—a toxicity value adjustment approach was considered to be more reasonable than the use of the nominal concentrations for PNEC derivations. However, as only some toxicity values could be adjusted due to the lack of analytical measurements, this report contains a summary of both nominal and adjusted toxicity values for fish, invertebrates, and algae (see Table 7-2).

7.1.2.3 Toxicity to aquatic organisms

Toxicity data for a variety of aquatic species (fish, invertebrates and algae) and long-chain aliphatic amines of varying chain lengths (C_8-C_{34}[12]) were identified (see ECCC 2021). Data were quite variable even for the same aliphatic amine and the dataset was predominantly represented by monoalkyl- and dimethyl- monoamines. However, analysis of the dataset demonstrated overlap in the ranges of reported toxicity values for both monoamines and diamines such that it is appropriate to consider both together in the hazard analysis.

In addition, an increase in toxicity with an increase in alkyl-chain length is expected (Rosen and Kunjappu 2012), as observed by Brust (2001) with fish embryos and supported by the general increase in membrane-water partition coefficients as noted in section 3.2.2. However, this was not observed in the dataset. This may be due to the wide variability in data from different studies and/or to the predominant use of toxicity values based on nominal concentrations and different water types that do not take into consideration sorption of the aliphatic amines and their subsequent decrease in bioavailability. Therefore, alkyl-chain length is not considered further in the determination of hazard.

Studies were conducted both on substances in the Aliphatic Amines Group and on other long-chain aliphatic amines. When more than one endpoint was considered in a study, the lowest value was used. In addition, when more than one low- or no-effect level for an endpoint was reported (e.g., no-observed-effect concentration [NOEC], lowest-observed-effect concentration [LOEC], 10% effect concentration [EC_{10}], 20% effect concentration [EC_{20}]), the EC_{10} was preferred over the EC_{20}, which was preferred over the NOEC. The LOEC was the least preferred.

Toxicity to fish

A summary of the available fish toxicity data is presented in Table 7-1. The data show that long-chain aliphatic amines range from being moderately to highly toxic to fish, with most values falling below 1000 µg/L. The dose-response curve for lethality is very steep for long-chain aliphatic amines, often with adjacent test concentrations reporting no mortality and 100% mortality. As a result, LC_{50} values were sometimes determined as the geometric mean of the two test concentrations (e.g., ECHA c2007-2018d). In addition to mortality, some acute studies with fish describe pronounced abnormalities in behaviour, morphology, and physiology at exposure concentrations below the LC_{50} levels. The lowest toxicity value determined was an LC_{50} of 60 µg/L based on measured concentrations.

[12] Long-chain aliphatic amines with two long alkyl-chains were placed in the category corresponding to the sum of their two long alkyl-chains (e.g., a 2xC_8 dialkylamine was considered to with the C_{16} monoamines)

Data from one long-term early life stage test with *Oncorhynchus mykiss* was available. This study determined a NOEC of 78 µg/L nominal for growth rate. The measured NOEC is therefore expected to be lower than this.

Toxicity to aquatic invertebrates

Aquatic invertebrates are more sensitive to long-chain aliphatic amines than fish. Acute 48- or 96-h LC/EC_{50} values for *D. magna* and *Ceriodaphnia dubia* in lab and river water ranged from 11 to 2500 µg/L nominal and from 9 to 822 µg/L adjusted (Table 7-1). One marine species, *Mysidopsis bahia*, was also tested, with a reported 96-h LC_{50} of 74 µg/L nominal, which is within the range observed with *D. magna* (US EPA 2003a). All but four LC_{50} values were less than 1000 µg/L, indicating that long-chain aliphatic amines are highly toxic to invertebrates. Acute and chronic studies with *D. magna* in lab or river water report no- or low-effect values of 5.6 to 1300 µg/L nominal and < 60 µg/L based on measured concentrations (Table 7-1). The highest nominal value (1300 µg/L) is a LOEC value with 20% mortality noted; thus, the NOEC would be lower. Only one other value is greater than 1000 µg/L.

Toxicity to algae

Algal toxicity data, summarized in Table 7-1, were available for a wide variety of long-chain aliphatic amines (ECCC 2021). These data indicate that algae are generally more sensitive to long-chain aliphatic amines than either fish or aquatic invertebrates. No- or low-effect values for algae range from 0.21 to 150 µg/L nominal and from 0.43 to 77 µg/L adjusted, demonstrating the high toxicity of long-chain aliphatic amines to algae.

Table 7-1. Toxicity of long-chain aliphatic amines to aquatic organisms (ECCC 2021)

Test organism	Endpoint	Water type	Nominal toxicity value (µg/L)	Adjusted toxicity value (µg/L)
Fish	96-h LC_{50}	Lab	80 – 25 500	60 (measured)
Fish	96-h LC_{50}	River	256 – 9300	125 – 1 890
Fish (*Oncorhynchus mykiss* early life stage)	96d NOEC growth rate	Lab	78; n = 1	NA
Daphnia magna	EC_{50} immobilization	Lab	11 – 2 500	9 – 83
Daphnia magna	EC_{50} immobilization	River	55.8 – 1 910	24.8 – 823
Daphnia magna	No- or low-effect[a]	Lab	5.6 – 1 300 (immobilization)	< 60
Daphnia magna	No- or low-effect[a]	River	40 – 200 (immobilization) 13 – 738 (reproduction)	NA

Test organism	Endpoint	Water type	Nominal toxicity value (µg/L)	Adjusted toxicity value (µg/L)
Algae	72- or 96-h no- or low-effect[a] biomass or growth	Lab	0.21 – 50	0.431 – 17
Algae	72- or 96-h no- or low-effect[a] biomass or growth	River	0.52 – 150	0.79 – 77

Abbreviations: EC_{10}, concentration causing the effect in 10% of organisms; EC_{50}, median effect concentration; LC_{50}, median lethal (effect) concentration; LOEC, low-observed-effect concentration; n, number of toxicity values; NA, not available; NOEC, no-observed-effect concentration

[a] No- or low-effect values include NOEC, LOEC, EC_0, EC_{10}, and EC_{20} values.

7.1.2.4 Derivation of the aquatic predicted no-effect concentration (PNEC)

Aquatic toxicity data in general indicate similar toxicity across various types of long-chain aliphatic amines; therefore, a single PNEC was derived to describe all long-chain aliphatic amines.

Selection of a critical toxicity value (CTV)

The lowest reliable value in the toxicity dataset comes from a study with the algae *Desmodesmus subspicatus* and hexadecyldimethylamine (CAS RN 112-69-6), which reports an EC_{10} for biomass of 0.43 µg/L (measured) (ECHA c2007-2018c). This value is selected as the CTV for the PNEC derivation.

An assessment factor was applied to the CTV to derive the PNEC. Since the CTV represents a long-term no-effect sub-lethal toxicity value for algae, no further acute-to-chronic extrapolations were needed. The available effects dataset includes more than seven species from three different categories of organisms (primary producers, invertebrates, and vertebrates) so no extrapolation was needed to account for species variation. An additional assessment factor of 2 is used to account for uncertainty in the mode of action of aliphatic amines. Therefore, dividing the CTV of 0.43 µg/L by an assessment factor of 2 results in an aquatic PNEC of 0.22 µg/L (or 220 ng/L). This aquatic PNEC value, which is similar to the PNEC of 260 ng/L derived in the European risk assessment of primary alkyl amines (EC 2008), will be used for the risk characterization of all long-chain aliphatic amines.

The CTV used to derive the PNEC in this assessment is supported by other reliable toxicity studies with measured concentrations. This includes a reliable chronic algal study with an adjusted EC_{10} (biomass) of 0.79 µg/L for decyldimethylamine (ECHA c2007-2018c) and a daphnid acute lethality study with an adjusted EC_{50} of 9 µg/L for cis-9-octadecenylamine (ECHA c2007-2018d). It is also supported by several studies based on nominal concentrations that indicate high toxicity (0.2 to 2.3 µg/L) (ECHA

c2007-2018c; US EPA 2003b) as measured concentrations are expected to be even lower. All would result in similarly low values as the PNEC after applying an assessment factor to adjust for acute to chronic extrapolation (if applicable) and uncertainty in the mode of action.

7.1.3 Effects on sediment organisms

Experimental data on toxicity to sediment-dwelling organisms was found for six long-chain aliphatic amines and for one analogue.[13]

Table 7-2. Key sediment toxicity studies considered in choosing a critical toxicity value for long-chain aliphatic amines

Common name, CAS RN	Test organism	Endpoint	Value (mg/kg dw)
C_{12-14} DMA[a]	Nematode (*Caenorhabditis elegans*)	72-h NOEC reproduction, growth	1620 (nominal)
C_{16-18} (even-numbered) alkylamine acetate, 1273322-45-4[b]	Midge (*Chironomus riparius*)	28-d NOEC emergence, development	188 (measured)[c]
Amines, N-C_{16-18}-alkyl (even numbered) propane -1,3-diamine,133779-11-0[d]	Worm (*Lumbriculus variegatus*)	28-d EC_{10} reproduction	86 (nominal)[c]
N-(Hydrogenated tallow)-1,3-diaminopropane, 68603-64-5[d]	Nematode (*Caenorhabditis elegans*)	96-h NOEC reproduction, growth	1000[e]
N-(Hydrogenated tallow)-1,3-diaminopropane, 68603-64-5[d]	Worm (*Lumbriculus variegatus*)	28-d EC_{10} reproduction	11 (nominal)
1,3-Propanediamine, N-[3-((C_{11-14}, C_{13}-rich)oxy)propyl]- branched acetate, EC 931-295-2[f]	Worm (*Lumbriculus variegatus*)	28-d NOEC reproduction, biomass	134[e]
Amines, N-C_{16-18}-alkyl(even numbered) propane-1,3-diamine, EC 696-364-9[f]	Worm (*Lumbriculus variegatus*)	28-d NOEC reproduction, biomass	68[e]
$C_{20/22}$ ATQ, 68607-24-9[g]	Nematode (*Caenorhabditis elegans*)	96-h NOEC reproduction, growth	250 (nominal)

[13] This substance is a quaternary ammonium compound (QAC) that was considered by the industry consortium as a suitable analogue to the assessed substances (ECHA c2007-2018i, CAS RN 1219010-04-4). Although QACs are permanently charged substances, they are also cationic surfactants, and when the lengths of their aliphatic chains are similar to the long-chain aliphatic amines, QACs are expected to have comparable physical-chemical properties and toxicity.

Common name, CAS RN	Test organism	Endpoint	Value (mg/kg dw)
$C_{20/22}$ ATQ, 68607-24-9[g]	Worm (*Lumbriculus variegatus*)	28-d NOEC reproduction, biomass	62.5 (nominal)[c]
Tallow alkylamine (61790-33-8) [a,b]	Nematode (*Caenorhabditis elegans*)	72-h NOEC reproduction, growth	≥ 2030 (nominal)

[a] ECHA c2007-2018c, CAS RN 112-69-6
[b] ECHA c2007-2018d, CAS RN 124-30-1
[c] Analytical results indicate minor loss (20% or less) over test duration, thus nominal is close to measured
[d] ECHA c2007-2018i, CAS RN 1219010-04-4
[e] Unknown whether value is nominal or measured
[f] ECHA c2007-2018g, EC 931-295-2
[g] Quaternary ammonium compounds used as analogue for hexadecyldimethylamine (CAS RN 112-69-6)

Chronic no-effect sediment toxicity values for long-chain aliphatic amines range from 11 to over 2030 mg/kg dry weight (dw) (ECHA c2007-2018c, c2007-2018d, c2007-2018g, c2007-2018i; Table 7-2). Three tests with *Caenorhabditis elegans* had high NOECs indicating low toxicity. However, two of these studies had a much different artificial sediment composition than the other studies (44% sand, as compared to 70% or greater sand in the other studies), which may explain the different results, as sediment composition can impact sorption and thus bioavailability of the test substance. The other studies (with *C. elegans, Chironomus riparius,* and *L. variegatus*) had lower and more comparable toxicity values (11 to 250 mg/kg dw).

7.1.3.1 Derivation of a predicted no-effect concentration for sediments

The nominal EC_{10} value of 11 mg/kg dw for effects on reproduction and biomass with *L variegatus* exposed to N-(Hydrogenated tallow)-1,3-diaminopropane is the lowest statistically derived toxicity value in the sediment toxicity dataset for long-chain aliphatic amines from a reliable study. Therefore, this value is selected as the CTV.

The CTV represents a long-term, low-effect, and sub-lethal toxicity value; therefore, no assessment factor is needed to account for acute-to-chronic extrapolation. However, since the dataset represents only three species from one category of organisms (invertebrates), an assessment factor of 20 is used to account for species variation. In addition, an assessment factor of 2 is used to account for the uncertainty in the mode of action of these substances. Thus, the overall assessment factor is 40 and the PNEC for the sediment compartment is calculated as follows:

PNEC = 11 mg/kg ÷ (20 × 2) = 0.275 mg/kg dw

The PNEC is based on a nominal toxicity value; however, three studies indicate that measured concentrations were close to nominal (e.g., approximately 80% or greater) (ECHA c2007-2018c, c2007-2018d, c2007-2018i). Thus, it is assumed that a similarly low loss occurs with the other test substances in sediment and that nominal concentrations are a close approximation of actual exposure concentrations.

7.1.4 Effects on soil-dwelling organisms

Data from studies describing the toxicity of long-chain aliphatic amines to earthworms and plants are presented in Table 7-3. All concentrations are given as dry weight nominal concentrations. One test substance is listed only as an abbreviation, C_{12-14} DMA, resulting in uncertainty as to the specific identity of this chemical. Based on an algal study for a different long-chain aliphatic amine (ECHA c2007-2018j), the abbreviation DMA likely refers to dimethyl amines.

Table 7-3. Toxicity of long-chain aliphatic amines to soil organisms

Common name, CAS RN	Test organism	Endpoint	Toxicity value (mg/kg dw nominal)
C_{12-14} DMA[a]	Earthworm (*Eisenia andrei*)	14-d NOEC mortality, biomass, behaviour	≥1000[b]
Hydrogenated tallow alkyl amines, 61788-45-2[c]	Earthworm (*Eisenia fetida*)	56-d NOEC reproduction	200
N-(2-hydroxyethyl)-N,N-dimethyl alkyl-C_{12}-C_{14}-(even numbered)-1-aminium chloride, 1125503-33-4[d]	Earthworm (*Eisenia fetida*)	56-d NOEC reproduction	125
Tallow alkyl amines, 61790-33-8[c]	Earthworm (*Eisenia fetida*)	14-d LC_{10}	> 1000
C_{12-14} DMA[a]	Rapeseed (*Brassica napa*)	21-d EC_{25} shoot height	52
C_{12-14} DMA[a]	Oat (*Avena sativa*)	21-d EC_{25} shoot weight	473
Tallow alkyl amines, 61790-33-8[c]	Oat (*Avena sativa*)	20-d NOEC emergence, biomass	≥ 10[b]
Tallow alkyl amines, 61790-33-8[c]	Radish (*Raphanus sativus*)	20-d NOEC emergence, biomass	≥ 100[b]
Tallow alkyl amines, 61790-33-8[c]	Red clover (*Trifolium pratense*)	20-d NOEC emergence, biomass	≥ 100[b]

[a] DMA = dimethylamine, used as read-across for the tertiary aliphatic amine hexadecyldimethylamine (ECHA c2007-2018c, CAS RN 112-69-6)
[b] Unbounded
[c] Analogue for the primary aliphatic amine octadecanamine (ECHA c2007-2018d, CAS RN 124-30-1)
[d] A quaternary ammonium compound (ECHA c2007-2018k, CAS RN 1125503-33-4) used as an analogue for the tertiary aliphatic amine hexadecyldimethylamine (ECHA c2007-2018c, CAS RN 112-69-6)

In general, long-chain aliphatic amines appear to have low toxicity to earthworms, at least with regard to acute toxicity. For example, both an unbounded NOEC (for mortality, behaviour and biomass) of 1000 mg/kg dw and an LC_{10} of greater than 1000 mg/kg dw were reported for *Eisenia andrei* (ECHA c2007-2018c, c2007-2018d). However, chronic studies indicate that aliphatic amines can significantly impact earthworm reproduction at concentrations lower than 1000 mg/kg dw. For example, two

studies that examined the influence of long-chain aliphatic amines on reproduction with *Eisenia fetida* determined NOEC values of 125 mg/kg and 200 mg/kg dw (Table 7-3). There is some uncertainty in the results of the study with the hydrogenated tallow amines due to reporting errors in the study summary (ECHA c2007-2018d). However, the results are similar to those observed in a long-term earthworm reproduction study using the QAC where a 56-day NOEC of 125 mg/kg was reported. Thus, it appears that QACs and long-chain aliphatic amines have similar toxicity to earthworms. In addition, the study with the QAC had similar results to those seen in the study with C_{12-14} DMA for adult earthworm behaviour, biomass, and survival, as these endpoints were not significantly impacted by the QAC over the 28-day exposure (to adult organisms) up to the nominal concentration of 1000 mg/kg dw.

For terrestrial plants, only results of short-term (20- to 21-day) studies were found (ECHA c2007-2018c, 2007-2018d). One study utilized tallow alkyl amines, but only at concentrations up to 100 mg/kg dw; no significant impact on emergence or plant biomass was noted up to the highest concentration tested (ECHA c2007-2018d). Another study with C_{12-14} DMA reported 21-day EC_{25} values of 52 mg/kg dw for rapeseed (shoot length) and 473 mg/kg dw for oat (shoot, fresh weight) (ECHA c2007-2018c). The EC_{25} value for oat (473 mg/kg dw) is in agreement with the unbounded NOEC of ≥ 100 mg/kg dw for oat with tallow alkyl amine. It is also noted that the no- or low- (i.e., EC_{25}) effect concentrations for plants are similar to the NOECs determined for earthworm reproduction (Table 7-3).

7.1.4.1 Derivation of the soil predicted no-effect concentration

The EC_{25} value of 52 mg/kg dw for rapeseed (shoot length) is the lowest statistically derived toxicity value in the terrestrial toxicity dataset for long-chain aliphatic amines from a reliable study. Therefore, this value was selected as the CTV.

Since the CTV represents an acute (short duration) exposure for plants, a factor of 5 was applied to extrapolate to a long-term (chronic) value. In addition, extrapolation to account for the species variation is required. Since a moderate amount of toxicity data is available, representing six species from two categories of organisms (primary producers and invertebrates), a species-variation factor of 5 was used. In addition, an assessment factor of 2 is used to account for the uncertainty in the mode of action of these substances. Therefore, the PNEC for the soil compartment can be calculated as follows:

$PNEC_{soil}$ = 52 mg/kg ÷ (5 × 5 × 2) = 1 mg/kg dw

This PNEC value was used for the risk characterization of long-chain aliphatic amines to soil organisms since the toxicity data for a variety of long-chain aliphatic amines and analogues, as described above, indicate a similar toxicity for all the long-chain aliphatic amines subject to this assessment.

7.2 Ecological exposure assessment

Long-chain aliphatic amines could potentially be used interchangeably in some industrial processes. Additionally, several long-chain aliphatic amines may be used and released to the same environment from the same site. Therefore, the ecological exposure scenarios consider long-chain aliphatic amines collectively, and the scenarios are based on industrial site capacities for the substances. Scenarios were considered that are expected to have a high potential for release to the environment and for which sufficient information was available for the development of an exposure scenario. These include releases to aquatic and terrestrial systems, with some scenarios addressed quantitatively and others qualitatively. The scenarios covered in this assessment include the production of long-chain aliphatic amines, processing of long-chain aliphatic amines as intermediates to produce other chemicals, polyurethane foam production, release from cleaning products containing unreacted residues, flotation treatment in mineral ore extraction, asphalt emulsions, fertilizer application and formulation, and sludge application to agricultural soils. Each of these scenarios is described in more detail below. There are no monitoring results included in this section, as there are currently no data on environmental concentrations of long-chain aliphatic amines in Canada.

7.2.1 Calculation of PECs and general assumptions

The environmental exposures are estimated and presented in the form of predicted environmental concentrations (PECs), which were typically calculated using the following equation:

$$\mathrm{PEC} = \frac{1000 \text{ x } \mathrm{Q} \text{ x } \mathrm{L} \text{ x } (1 - \mathrm{R})}{\mathrm{D}} \times f_{dissolved}$$

where:
Q = quantity used per site per day (kg/day)
L = losses to wastewater (fraction)
R = wastewater treatment system removal efficiency (fraction)
D = daily dilution volume (L/day)
$f_{\text{dissolved}}$ = fraction freely dissolved

The wastewater treatment system removal efficiency (R) was determined using the results of continuous activated sludge tests utilizing industrial or municipal wastewater and wastewater treatment sludge (Akzo Nobel 1998, 2002a, 2002b), as described in the European Union risk assessment of primary amines (EC 2008). In these tests, the removal of tallow amine or cocoamine from wastewater was determined for wastewater both spiked and not spiked with aliphatic amines. Wastewater removal efficiency was reported to range from 96% to 99.98%. However, one continuous activated sludge test (Akzo Nobel 1998) deviated from the OECD (2001) test guidelines in at least one aspect, as the test unit was much smaller than the guideline recommended test unit. No information was provided by EC (2008) on the size of the test unit used in the other studies (Akzo Nobel 2002a, 2002b), but as the tests appear to be similar and were

conducted by the same company, it can be assumed that all tests used the same test unit apparatus. This increases uncertainty in the removal rates. The studies were unavailable for review by ECCC for this assessment and it is unknown if the tests met data quality guidelines. In addition, the wastewater was spiked with 50 or 57 mg/L tallow amine or cocoamine (Akzo Nobel 1998, 2002a, 2002b). These concentrations are known to be toxic to microorganisms, resulting in greater than 50% inhibition of respiration (Hoechst AG 1989a, 1989b, 1992) and thus may impact wastewater removal. Due to these uncertainties, the lowest reported removal efficiency for all studies, i.e., 96% (or R = 0.96), is chosen as the wastewater removal efficiency for use in this assessment's exposure scenarios for different types of treatments.

Daily dilution volumes are calculated by multiplying the effluent flow of the WWTS or facility discharging to a receiving water body by the dilution factor of the receiving water body. In all cases, aquatic PECs were derived using a dilution factor based on the 10^{th} percentile low flow of the receiving water body and capped at a maximum dilution factor of 10.

The aquatic PEC is calculated as the fraction of long-chain aliphatic amines freely dissolved by incorporating the fraction freely dissolved ($f_{dissolved}$) in the calculation assuming a TOC concentration of 13.05 mg/L (see Table 6-1, Section 6.1). The midpoint value for $f_{dissolved}$ was used to adjust all calculated aquatic PECs to a freely dissolved concentration.

The aquatic PECs represent potential concentrations of the substances in the receiving water body near the discharge point of a WWTS. The soil PEC represents the potential concentration in this medium where biosolids may be applied. The PEC values are presented in each exposure scenario while summarized key assumptions are provided in ECCC (2021). In addition, some PEC values were further adjusted to freely dissolved PECs for each monoamine and diamine alkyl-chain length category for risk characterization. These adjusted PEC values are presented in section 7.3.1. Potential releases via container cleaning and transport, including loading and unloading, are not considered in this assessment.

Given the limited sediment data available, PECs for sediment were not derived for long-chain aliphatic amines. In addition, it is not currently possible to model their distribution and resulting concentrations in sediment due to the unique properties of surfactants. However, there is potential for long-chain aliphatic amines to accumulate in sediment given their high persistence in sediment under anaerobic conditions and their strong sorption affinity (sections 3.2.2 and 6.1). While data on long-chain aliphatic amines are lacking, total concentrations of $C_{16\text{-}22}$ alkyltrimethylammonium compounds, which are analogous to long-chain aliphatic monoamines, were found to increase in concentration in anoxic surficial sediments in Jamaica Bay, New York, from 1998 to 2008, with concentrations ranging from 1600 to 6750 ng/g in 2008 (Lara-Martin et al. 2010).

7.2.2 Exposure scenario 1 – Production

This scenario considered the release of long-chain aliphatic amines from facilities where they are produced. At manufacturing facilities for aliphatic amines, water may be used in the process. Aqueous waste from production processes are fed as wastewater into a central fat separator (EC 2008). For this scenario, it is assumed that the effluent is discharged to a secondary wastewater treatment system (WWTS). Two PECs were developed for this scenario, one for production facilities and one considering sites where production and processing of aliphatic amines to produce other chemicals occur at the same facility.

The aquatic PEC for a representative production facility was calculated using data from different sources. The production batch sizes and duration of production campaigns were provided for one of the manufacturers of aliphatic amines and their derivatives in North America to Environment and Climate Change Canada's New Substances Program. Refer to ECCC (2021) for a summary of assumptions. As no data on Canadian site capacities were available, the manufacturing capacities and batch sizes of a similar site in the United States were used. The unadjusted PEC resulting from the production of aliphatic amines is 0.34 µg/L.

Because aliphatic amines may be further processed at the same site of manufacture, a second aquatic PEC was calculated for this scenario. The exposure assumptions remain the same as the above production scenario except for the emission factor, which included an additional factor for releases from the processing part of the operations. The unadjusted PEC for this scenario is 1.12 µg/L.

7.2.3 Exposure scenario 2 – Processing

This scenario considered long-chain aliphatic amines used as intermediates in the chemical industry for the production of other substances through chemical conversion such as ethoxylates, diamines and amides. No details were available for Canadian long-chain aliphatic amines processing sites. This scenario focuses on the processing of primary aliphatic amine to amine ethoxylate.

Aliphatic amines are almost completely converted into aliphatic amine ethoxylates during the ethoxylation process leaving only small amounts of primary amine in the final product. Although the ethoxylation reaction does not produce wastewater, unreacted aliphatic amines may enter wastewater via reactor cleaning. It is expected that processing reactors are commonly cleaned only once a year for maintenance purposes; however, it has been reported that one of the four amine ethoxylate producing sites analyzed by the European Commission (EC 2008) has more continuous cleaning throughout the year. A worst-case scenario of more continuous cleaning of ethoxylation reactors is assumed. The processing amount of 203 t/yr was based on the scenario in EC (2008). Up to 2.2% is expected to be unreacted in the final product (EC 2008); therefore, 4466 kg/yr is used for the calculation of primary amine releases during the cleaning of processing reactors. An emission factor of 2% is applied to account for

releases from the reactor cleaning (EC 2003). The daily dilution volume distribution for the chemical manufacturing sector was generated and the 10th percentile value was selected as a representative value. A summary of key assumptions are provided in ECCC (2021). The unadjusted PEC for this scenario is 1.30 µg/L.

7.2.4 Exposure scenario 3 – Polyurethane foam production

This scenario considered the production of flexible polyurethane foam. Two aquatic PECs were calculated, one for the formulation of polyol blend (one of the components necessary in the production of polyurethane foam, which may contain from 1% to 5% of amine catalyst) and one for the production of flexible polyurethane foam itself.

Information on one polyurethane chemical blending plant was compiled to calculate the PEC for polyol blend formulation, including site data for known import quantities. A key assumption, the number of release days, was derived using the yearly production capacity of a representative facility and its corresponding number of operation days. This was extrapolated to the yearly production capacity of the polyol blend specifically based on the quantity of aliphatic amines purchased by the facility and the assumption of 1% of amine catalyst in the polyol blend. The quantity used per year was also based on the amount purchased by the facility. The emission factor was estimated using the Technical Guidance Document (TGD) tables (EC 2003).

Information was also available for one polyurethane production facility, including substance use quantities. The formulated amount of polyurethane was estimated based on use quantities, concentration of aliphatic amine in polyol blend and the ratio of polyol blend to other components used in the production of polyurethane (1:2). Key parameters such as the number of processing days per year and the emission factor were derived using TGD tables from the European Commission (EC 2003) based on the estimated amount of polyurethane produced. The daily dilution volume distribution for the polyurethane manufacturing sector was generated and the 10th percentile value was selected as a representative value. Key assumptions are provided in ECCC (2021). The unadjusted PEC for the formulation of polyol blend is 0.55 µg/L, while that for the production of flexible polyurethane foam is 0.0019 µg/L.

7.2.5 Exposure scenario 4 – Down the drain release of amine derivatives

According to information submitted in response to a CEPA section 71 survey, hexadecyldimethylamine (CAS RN 112-69-6) is reported as a residual in amine derivatives that are used for various commercial products and products available to consumers. Use of these products is expected to result in release to wastewater treatment systems. The PEC is estimated using Environment and Climate Change Canada's internal Consumer Release Aquatic Model (CRAM). CRAM is a population-based probabilistic model parameterized for Canada. It is used to estimate environmental exposure resulting from wastewater treatment facility releases of chemicals present in products that are available to consumers and that are released down the drain. The model uses distribution information for dilution factors (derived from

the 10th percentile flow rate of receiving water bodies), WWTS treatment type, and per capita water discharge rates that are relevant to Canada.

Complete data are not available on Canadian quantities of long-chain aliphatic amines present as unreacted residues in products. The available data on quantities of these types of products were data on North American consumption of major surfactants in household detergents. Consumption in the United States and Canada of cationic intermediate alkylmethyl and dimethylamines (ADMA) in household detergents was 45 million kg in 2018 (Bland et al. 2018). It is assumed that consumption of detergents is proportional to the population. Given that in 2018 the U.S. population was 327.2 million and using a Canadian population of 37 million, the total Canadian intermediate ADMA amine consumption per year is estimated as 4.6 million kg. The concentration of unreacted aliphatic amines in the amine derivatives is assumed to be up to 2% based on follow-up communications with a company that imports amine derivatives. Therefore, the mass of unreacted long-chain aliphatic amines in household detergents in Canada is as high as 92 000 kg/yr. The model calculated a distribution of the resulting quantity released to receiving water bodies near the point of discharge. The unadjusted PEC corresponding to the 90th percentile value PEC distribution is 0.12 µg/L.

The applied volume assumption only covers household detergents. Although these products represent the largest general category for the consumption of surfactants, the category excludes all toilet soaps, surfactants for fabric softening, shampoos and related cosmetics. Industrial and institutional cleaners are additional sources of the amine derivatives. Therefore, the PECs are likely underestimating environmental concentrations from this use.

7.2.6 Exposure scenario 5 – Flotation treatment in mineral ore extraction

Long-chain aliphatic amines and their salts may be used as hydrophobic agents in flotation treatment during the extraction of different minerals (e.g., potash, iron, zinc). While this use accounts for the largest direct use of primary long-chain aliphatic amines, other long-chain aliphatic amines (e.g., diamines) and fatty amines (e.g., quaternary compounds) are also used in mining (Roose et al. 2015). According to information submitted in response to a CEPA section 71 survey (Environment Canada 2013), long-chain aliphatic amine products are imported into Canada for mineral flotation.

Iron ore extraction

The use of cationic amine collectors for the flotation process in iron ore mining in Canada is confirmed by information submitted in response to a CEPA section 71 survey (Environment Canada 2013). Therefore, a quantitative scenario was developed for the iron ore mining sector based on a representative site, assuming that the amine collector system is in continuous operation. Characteristics of metal mining sites are usually quite variable and site-specific. A key assumption of the scenario is the adsorption efficiency of the amine collector to silica during iron ore flotation, which was overestimated to be 99%, thus leaving 1% of unbound aliphatic amine present in the siliceous tailing

effluent. Key parameters used in the calculations, including processing capacity, amine collector application rate, and effluent flow at the discharge point, were based on confidential information provided by the company. The unadjusted PEC for iron ore flotation is 0.248 µg/L.

Aquatic aliphatic amine concentrations resulting from this scenario may be significantly higher given that less than 99% adsorption efficiency is expected in the collector, that desorption of aliphatic amines from silica may occur when released to the natural environment, and that effluent flows used in the calculation were on the higher end of the range.

Potash extraction

Long-chain aliphatic amines are used in potash mining (EC 2008; Strathdee et al. 1982; Reid 1984), but since natural evaporation and deep well injection are used for the disposal of potash mining effluents in Saskatchewan (Reid 1984), no PEC was calculated for this scenario. Further information is found in ECCC (2021).

7.2.7 Exposure scenario 6 – Formulation and use of asphalt emulsions

According to information submitted in response to a CEPA section 71 survey and voluntary submissions, one of the main uses of long-chain diamines is as a processing aid for asphalt and paving applications. Specifically, they act as emulsifiers for slow-, medium-, and rapid-setting cationic asphalt emulsions that are used in cold-mix asphalt applications for road paving and repair, as well as for tack and priming coats between layers of hot mixed asphalt. Cationic emulsifiers are used at a low concentration in asphalt emulsion and help increase the adherence of asphalt to the aggregate.

Formulation of asphalt emulsions

Asphalt emulsions are produced in a batch process by mixing hot asphalt and an aqueous solution of emulsifier in a colloid mill. This scenario covers the formulation of the emulsifier solution. Based on information provided for similar substances to Environment and Climate Change Canada's New Substances Program, a key assumption is that 114 kg of the substance can be used per day to formulate the emulsifier solution, based on daily volume of emulsifier solution produced and concentration of aliphatic amine in the solution. It is also assumed that industrial site wastewater effluent is discharged to secondary or tertiary wastewater treatment systems. A summary of key assumptions is provided in ECCC (2021). The unadjusted PEC for this scenario is 0.59 µg/L.

Use of asphalt emulsions

These substances may be used as emulsifying agents for asphalt emulsions used in roadway construction or resurfacing, leading to possible releases of these substances to the environment via the leaching from roadway asphalt. However, quantification of

such releases and resulting environmental concentrations are difficult due to the lack of information on a number of factors (see ECCC 2021). Given these uncertainties, PECs resulting from the use of aliphatic amines in asphalt emulsions were not derived.

7.2.8 Exposure scenario 7 – Formulation and use of fertilizers

Formulation

This scenario considers the use of aliphatic amines as anticaking agents in the formulation of fertilizers. There are different addition methods for the anticaking agent, but for aliphatic amines, they are usually heated to a temperature of about 70°C and evaporated or distilled onto the bulk material at a point in the production process where a thorough mixing is assured (BUA 1994). According to information submitted in response to a CEPA section 71 survey, long-chain aliphatic amines can be used as a component in anticaking agents that are applied to ammonium nitrile prills. Long-chain aliphatic amines, either alone or in oil or glycol dispersion, can also be added to potash crystals at potash mills to reduce potash caking (Strathdee et al. 1982). While there are several different grades of potash produced, only that produced by means of compaction requires amine application.

For a representative site exposure scenario, data from the EU Risk Assessment of Primary Alkyl Amines was used. This data included the processing amount of primary amines at one European inorganic fertilizer production facility (116 000 kg/yr) as well as the concentration of amines in fertilizers (0.004% to 0.01%), yielding an estimated total fertilizer production of 1160 to 2900 megatonnes (Mt) per year. This last value is used to estimate the emission factor and operation days using generic assumptions for this type of industry (EC 2003, TGD Tables A2.1 and B2.1). It is assumed that industrial site wastewater effluent is discharged to secondary or tertiary wastewater treatment systems. A summary of key assumptions are provided in ECCC (2021). The unadjusted PEC for this scenario is 2.01 µg/L.

Use of fertilizers

In addition to being used as anticaking agents in fertilizers, long-chain aliphatic amines may end up in fertilizers during their use as flotation agents in mineral extraction (i.e., potash ore) where they adsorb to the surface of mineral crystals or ore particles. Although the amines are expected to be released to soil in agricultural applications of fertilizers, data were not available to quantify releases from this use and therefore an exposure scenario could not be derived.

7.2.9 Exposure scenario 8 – Biosolids application to land

This scenario considered the application of long-chain aliphatic amines to soil in the form of biosolids. The soil PEC was calculated as an extension of the scenarios described above, recognizing that some of the aliphatic amines that enter a WWTS will be adsorbed onto the sludge, which may then be treated to produce biosolids for

application as an amendment on agricultural soils. As a worst case scenario, the soil PEC was based on the exposure scenario with the highest daily release of aliphatic amines to WWTS, which was exposure scenario 2, processing (section 7.2.3).

The soil PEC after 10 years of biosolids application and considering biodegradation as a loss mechanism, is calculated by iterating the equations below. Concentrations were determined on a yearly basis immediately after application and at the end of the year (after degradation has occurred, but prior to the subsequent application) over a 10-year period.

At the beginning of the year (directly after application):

$$\mathrm{PEC}_{\mathrm{beginning,t}} = \frac{C_s \cdot A}{d \cdot \rho} + \mathrm{PEC}_{\mathrm{end,t-1}}$$

$$(\text{note that } \mathrm{PEC}_{\mathrm{beginning,1}} = \frac{C_s \cdot A}{d \cdot \rho})$$

At the end of the year (after degradation):

$$\mathrm{PEC}_{\mathrm{end,t}} = \mathrm{PEC}_{\mathrm{beginning,t}} \cdot e^{(-0{,}693 \cdot (\frac{365}{\mathrm{Biodeg}}))}$$

where:
$PEC_{beginning}$ = PEC in soil at the beginning of the year after application of biosolid (before degradation) (mg/kg)
PEC_{end} = PEC in soil at the end of the year (after degradation), prior to subsequent application of biosolid (mg/kg)
t = years of biosolids land application (y), varying from 1 to 10 years
BioDeg = biodegradation half-life value in soil (days)
C_s = concentration of the substance in biosolids (mg/kg dry weight)
A = annual biosolids land application rate (kg/m^2-y)
d = soil mixing depth (m)
ρ = dry soil density (kg/m^3)

Half-lives of between 16 and 150 days have been modelled for aliphatic amines (section 6.2.2). In the calculation, a half-life of 150 days was used. Given the half-life, the concentration of aliphatic amine in soil does not accumulate much over the 10-year period, and soil concentrations are maximal after application (decreasing significantly afterwards over the year). The PEC calculated at the start of the 10th year, following biosolids application is 0.46 mg/kg dw. As the PNEC is determined from a nominal concentration (i.e., total concentration), no adjustment of the PEC for sorption is required. A summary of assumptions is provided in ECCC (2021).

7.3 Characterization of ecological risk

The approach taken in this ecological screening assessment was to examine assessment information and develop proposed conclusions using a weight-of-evidence approach and precaution as required under CEPA. Evidence was gathered to determine the potential for long-chain aliphatic amines to cause harm in the Canadian environment. Lines of evidence considered include those that directly support the characterization of ecological risk (e.g., measured endpoints or properties), as well as indirect lines of evidence (e.g., classification of hazard or fate characteristics by other regulatory agencies).

7.3.1 Risk quotient analysis

Risk quotient (RQ) analyses were performed by integrating estimates of exposure (PECs; see section 7.2) with ecological toxicity information (PNECs; see section 7.1) to determine whether there is potential for ecological harm in Canada. In the case of the aquatic PECs, these were adjusted to freely dissolved concentrations. RQs were calculated by dividing the (adjusted) PEC by the PNEC for relevant environmental compartments and associated exposure scenarios. Aquatic RQs for various chain lengths and different release scenarios are presented in Table 7-4 for monoamines and in Table 7-5 for diamines, while more detailed information is provided in Appendix F.

The calculated RQs in Tables 7-4 and 7-5 assume that the total quantity released is only within the alkyl-chain length range under consideration (e.g., the RQ for C_{19}-C_{22} monoamines assumes the total quantity of aliphatic amines released is only monoamines with alkyl chains of C_{19}-C_{22}). This may be the case for some scenarios, but likely not the case for others.

Aquatic RQs for monoamines up to C_{22} and for diamines up to C_{18} were greater than one for many of the exposure scenarios. Monoamines up to C_{24} had at least one exposure scenario with an RQ of 0.5 or greater. Considering the high toxicity of long-chain aliphatic amines, their steep dose-response curve, and the uncertainties in the PECs, these scenarios might still pose a risk to the environment. Therefore, RQs of 0.5 or greater are considered to be of concern. The only aquatic exposure scenario that indicated a low probability of posing a risk for any long-chain aliphatic amines was flexible polyurethane foam production.

For the soil scenario considering biosolids application, an RQ of 0.46 was determined using a PEC of 0.46 mg/kg dw and a PNEC of 1.0 mg/kg dw. It was not possible to calculate a sediment RQ due to lack of data on sediment concentrations.

Table 7-4. Summary of aquatic risk quotients for monoamines[a]

Scenario	RQ (C_8-C_{14})	RQ (C_{15}-C_{18})	RQ (C_{19}-C_{22})	RQ (C_{24})	RQ (C_{26})	RQ (C_{28})	RQ (C_{36})
Production	1.4	1.1	0.47	0.15	0.057	0.022	< 0.001

Scenario	RQ (C_8-C_{14})	RQ (C_{15}-C_{18})	RQ (C_{19}-C_{22})	RQ (C_{24})	RQ (C_{26})	RQ (C_{28})	RQ (C_{36})
Production and processing	4.8	3.5	1.6	0.48	0.19	0.071	0.002
Processing	5.5	4.1	1.8	0.56	0.22	0.083	0.002
Polyurethane foam production (polyol blend)	2.3	1.7	0.77	0.24	0.093	0.035	0.001
Polyurethane foam production (flexible polyurethane foam)	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.001
Down-the-drain release of amine derivatives	0.51	0.38	0.17	0.052	0.020	0.0076	< 0.001
Iron ore extraction	1.1	0.78	0.34	0.11	0.042	0.016	< 0.001
Formulation of asphalt emulsion	2.5	1.8	0.82	0.25	0.10	0.038	0.001
Formulation of fertilizers	8.6	6.3	2.8	0.87	0.34	0.13	0.003

Abbreviations: RQ, risk quotient
[a] For dialkyl amines, the sum of the two alkyl chains are considered for placement in the alkyl-chain length categories (e.g., a 2xC_{12} aliphatic amine is considered in the C_{24} category)

Table 7-5. Summary of aquatic risk quotients for diamines

Scenario	RQ (C_8-C_{14})	RQ (C_{15}-C_{18})	RQ (C_{19}-C_{22})
Production	1.1	0.40	0.079
Production and processing	3.6	1.3	0.26
Processing	4.2	1.5	0.3
Polyurethane foam production (polyol blend)	1.8	0.64	0.13
Polyurethane foam production (flexible polyurethane foam)	< 0.01	< 0.01	< 0.01
Down-the-drain release of amine derivatives	0.39	0.14	0.028
Iron ore extraction	0.80	0.29	0.057
Formulation of asphalt emulsion	1.9	0.69	0.14
Formulation of fertilizers	6.5	2.3	0.47

Abbreviations: RQ: risk quotient

7.3.2 Consideration of the lines of evidence

To characterize the ecological risk of long-chain aliphatic amines, technical information for various lines of evidence was considered (as discussed in the relevant sections of this report) and qualitatively weighted. Weighted lines of key evidence considered to

determine the potential for long-chain aliphatic amines to cause harm in the Canadian environment are provided in section 7.3.3, and are summarized in Appendix G.

7.3.3 Weight of evidence for determining potential to cause harm to the Canadian environment

The subgroup of long-chain aliphatic amines encompasses structures ranging in molecular weight, length and number of alkyl chains, number of amine functional groups, presence or absence of an ether functional group, and degree of saturation. While these properties were not found to impact environmental fate or ecotoxicity across the group according to the American Chemistry Council (ACC) (US EPA 2003c, 2003d), the number of amine groups (e.g., monoamine versus diamine) and the alkyl-chain length were found to impact distribution coefficients derived through models. For this assessment, long-chain aliphatic amines were further categorized according to the number of amines present and alkyl-chain length when considering fate and exposure. However, similar to the conclusion by the ACC, the ecotoxicity of long-chain aliphatic amines were comparable across the entire subgroup, especially for the most sensitive species of algae. Therefore, one PNEC is used to describe the hazard of the entire long-chain aliphatic amine subgroup, and a class conclusion is proposed for long-chain aliphatic amines, which includes CAS RN 112-90-3 and 68955-53-3, that were previously addressed individually.

Analogues used in the ecological portion of this assessment were quaternary ammonium compounds with similar alkyl-chain lengths, which are cationic surfactant substances very similar to long-chain aliphatic amines with the exception that they are permanently charged. There is a high level of confidence for reading across from these analogues to long-chain aliphatic amines for most parameters, although on the basis of preliminary results from a bioaccumulation study, there is uncertainty as to whether quaternary ammonium compounds bioaccumulate in fish in the same manner as aliphatic amines.

Long-chain aliphatic amines are manufactured in or imported into Canada in high tonnages based on data collected for the nine long-chain aliphatic amines in this assessment. Long-chain aliphatic amines are used widely in multiple sectors in Canada, such that there is a high probability that these substances may be released to the Canadian environment, especially to water. In addition, there is potential interchangeability among similar long-chain aliphatic amines identified by different CAS RNs. Due to their widespread and varied use and the UVCB characteristics of many of these substances, there is a high probability that multiple long-chain aliphatic amines are present simultaneously in the receiving environment where they will collectively contribute to the risk. However, no monitoring data were found on concentrations of these substances in the Canadian environment.

Due to their cationic nature, long-chain aliphatic amines can interact both ionically and nonionically with organic and mineral (clay) matter in the environment, sorbing to these

materials. Solids-water, organic carbon-water, and clay distribution coefficients for these cations increase with increasing alkyl-chain length and the number of amines present.

Long-chain aliphatic amines will also partition to cellular membranes via ionic and non-ionic interactions, as described by both modelled and measured membrane-water distribution coefficients. These coefficients increase with increasing alkyl-chain length, with the exception of long-chain dialkyl aliphatic amines, which have lower distribution coefficients than the sum of the alkyl-chain lengths would suggest due to steric effects (Droge et al. 2016; Timmer and Droge 2017).

Once in the environment, the weight-of-evidence indicates that these substances will degrade relatively quickly (days to months) in aerobic media. However, some degradation studies had much lower degradation rates, reducing the confidence in the low persistence of these substances.

The weight-of-evidence indicates that some long-chain monoalkyl amines have high bioaccumulation potential. There is uncertainty as to whether long-chain dialkyl amines have similarly high bioaccumulation potential. Considering the available information and using precaution where data is lacking or uncertain, it is proposed that long-chain aliphatic amines with alkyl chains shorter than C_{14} have low to moderate potential for bioaccumulation in aquatic organisms, and those with alkyl chains of C_{14} and longer have high potential to bioaccumulate. However, due to their propensity to sorb to biological membranes, it is presumed that even those aliphatic amines with low to moderate bioaccumulation potential may result in high, localized concentrations of long-chain aliphatic amines on surface tissues (e.g., gills in fish) that could lead to toxic effects without reaching high total body concentrations.

Organisms with higher surface-to-body weight ratios, such as small invertebrates (e.g., *D. magna*) and single-cell algae, are affected more by sorption to surface tissues, resulting in greater sensitivity to long-chain aliphatic amines as compared to fish, with toxicity observed in the sub-microgram per litre range for invertebrates and algae. Fewer data were available for sediment and soil organisms, although long-chain aliphatic amines are still relatively toxic in these media as well. Due to sorption of long-chain aliphatic amines to organic matter and test vessels during toxicity tests, the amount bioavailable in the test will be less than the nominal concentration added. This is particularly true for static and semi-static test systems. Therefore, toxicity values were adjusted to a measured concentration if needed and if possible, and greater weight was given to measured values.

Sorption will also influence the amount of bioavailable long-chain aliphatic amines in the environment. The aquatic PECs were adjusted to a freely dissolved concentration, thus reflecting the sorption of aliphatic amines to TOC and allowing for a direct comparison between the PNEC and PEC values during the analysis of risk. Because sediment and soil PNECs are based on concentrations in the dry solid matrix and not on pore water concentrations, and because measured concentrations did not differ greatly from

nominal concentrations, no adjustment of these PECs to reflect bioavailability in pore water was required.

Some exposure scenarios assumed shorter durations of release, such as those for manufacturing and processing, which are based on releases per batch, and this assumption may underestimate yearly releases. It is likely that more than one batch may be manufactured or processed simultaneously or consecutively over the year, increasing the total amount released, the duration of exposure, or both.

Moderate-high to high weight is assigned to all aquatic RQs based on confidence in the value and its relevance to the assessment (Appendix G). Freely dissolved PECs of long-chain aliphatic amines in receiving waters are estimated to be higher than PNECs for several aquatic scenarios for both monoamines and diamines. While the magnitude of the RQ decreases as the alkyl-chain length increases, an RQ close to (between 0.5 and 1) or above one is noted in some scenarios for monoamines up to C_{24} and diamines up to C_{18}. According to use information (see section 4.2), monoamines up to C_{18} are used in mineral ore extraction as well as in the formulation of fertilizers, while C_{16} monoamines are used in polyol blend production. Risks to the environment are identified for these alkyl-chain lengths and these scenarios. According to use information, C_{15}-C_{18} diamines are used in mineral ore extraction, and the RQ for this alkyl-chain length category and scenario is 0.29. However, certain parameters used in this scenario lead to an underestimation of the PEC, so the RQ is likely higher. Further information is required to better evaluate the risk of C_{15}-C_{18} diamines in this scenario.

The risk quotients calculated for the down-the-drain release of amine derivatives were generally low. Although the RQ for the C_8-C_{14} monoamines subgroup was calculated as 0.51, this is considered sufficiently high to be indicative of a potential risk for these substances given that the exposure assessment only considered a fraction of the potential releases of amine derivatives. Similarly, given that release quantities and the resulting RQs are underestimated, it is recognized that there may also be concerns for other alkyl-chain lengths, although the degree to which these RQs are underestimated is unknown. Confidence in the RQ values for down-the-drain release is moderate considering there is low confidence in the PEC but high confidence in the PNEC (Appendix G).

Although dialkyl monoamines with longer alkyl chains (e.g., 2xC_{13} and greater, corresponding to the C_{26} and greater alkyl-chain categories) likely pose little risk by themselves, they may be present in the environment with other long-chain aliphatic amines. As a result, they would contribute to the overall risk by contributing to the total amount of long-chain aliphatic amines to which organisms are exposed.

The interchangeability of long-chain aliphatic amines is of concern. For instance, if the uses of monoalkyl monoamines were managed, there may still be environmental impacts if dialkyl monoamines were used as an alternative.

In this assessment, the activities considered mainly result in continuous exposure, thus resulting in long-term exposure and an increased risk in the near field (e.g., near the site of release) despite the biodegradability of these substances in water. Further afield, biodegradation and dilution will decrease the concentration in water, thus decreasing the risk. Therefore, the potential for long-range transport and far-field risk is expected to be low.

The risk quotients determined for each alkyl-chain length category in Tables 7-4 and 7-5 were determined assuming that the total amount released represented only aliphatic amines from one category. In reality, the release of aliphatic amines likely encompasses many alkyl-chain length categories. Therefore, when a proportion of the total concentration of aliphatic amines includes those with longer alkyl chains, the risk may decrease. However, the RQs for the C_8-C_{22} monoamine and C_8-C_{18} diamine categories are sufficiently high that a decrease in the total concentration for a category would likely not negate the risk. It is also unlikely that all the scenarios would consist solely of releases of aliphatic amines with very long alkyl chains (e.g., C_{26} or greater for monoamines or C_{19} or greater for diamines). Therefore, the low risk observed with the use of only higher alkyl-chain aliphatic amines is unlikely to occur for most scenarios. Since it is expected that all long-chain aliphatic amines have a similar toxicity on a freely dissolved basis, a total amount of freely dissolved long-chain aliphatic amines near or above the PNEC would indicate a risk.

In the aquatic environment, long-chain aliphatic amines will partition to dissolved and particulate organic matter and minerals in the water column that will settle to the sediment, as well as sorb to the sediment itself. While long-chain aliphatic amines are expected to degrade fairly quickly in aerobic sediments, they are not expected to do so in anaerobic sediments. Long-chain aliphatic amines are expected to accumulate in anoxic sediments, especially near sites of continuous release. There may also be the potential for these substances to accumulate in aerobic sediments near sites of continuous release, despite higher biodegradation rates, if the rate of addition to sediment is greater than the rate of removal via biodegradation. This might be the case for aliphatic amines with longer alkyl chains that are expected to sorb more strongly to sediments, especially to sediments with higher CEC and organic carbon content. While aliphatic amines with very long alkyl chains may pose a lower risk to the aquatic environment than those with shorter alkyl chains, their accumulation in sediments may increase the risk to sediment organisms. However, at this time there is insufficient data on sediment concentrations to determine the level of risk that long-chain aliphatic amines pose to sediment organisms.

Long-chain aliphatic amines pose a low risk to soil organisms due to the low concentrations added to soils, as calculated for this exposure scenario, and given their degradation.

This information indicates that long-chain aliphatic amines have the potential to cause ecological harm in Canada.

7.3.4 Sensitivity of conclusion to key uncertainties

As cationic surfactants, the long-chain aliphatic amines are difficult substances to test due to their tendency to concentrate at interfaces and sorb to negatively charged surfaces. Many of the aquatic toxicity test reports available for these substances do not provide adequate descriptions of the testing and analytical methods to evaluate the reliability of the results, and in most cases, toxicity data were based on nominal concentrations from static or semi-static (renewal) tests. The studies that did measure concentrations in the test vessels indicated considerable loss of the aliphatic amines over the test period or renewal period in the water. This was assumed to be due to sorption to vessels and organic matter, suggesting that results based on nominal concentrations would significantly underestimate toxicity. Therefore, for the purposes of this assessment, data based on nominal concentrations were adjusted using analytical recoveries when available. tThere is uncertainty in these adjusted values as analytical recoveries for the concentration series were not always linear, but the effect level was calculated assuming linearity (i.e., by adjusting nominal concentrations to average recovery). Although the direction of this uncertainty is not known,due to the steep dose-response curve for these substances, the adjusted estimates are likely within experimental error.

Aquatic toxicity data were not available for all of the long-chain aliphatic amine substances in the Aliphatic Amines Group, nor for all of the aliphatic amines outside of the Aliphatic Amines Group that would also meet the definition of a long-chain aliphatic amine. Toxicity values are available for a wide range of long-chain aliphatic amines (C_8-C_{18} for single alkyl chains, and 2xC_8 to 2xC_{17} for dialkyl chains). Despite high variability between tests, the data indicates that all long-chain aliphatic amines have similar toxicities, especially to the most sensitive taxonomic group, algae. Some types of aliphatic amines are heavily represented in the dataset while others consist of very few data points that may vary widely. While additional data may provide clarity regarding the toxicity of underrepresented aliphatic amines, it is unlikely to change the proposed conclusion.

On the basis of bioaccumulation data for only monoalkyl aliphatic amines, some aliphatic amines were found to be highly bioaccumulative. However, no studies have been conducted on dialkyl aliphatic amines. Studies with dialkyl QACs suggest low bioaccumulation potential for dialkyl aliphatic amines. However, there is uncertainty regarding the extent that QAC bioaccumulation data can be read-across to aliphatic amines, as one preliminary study with only 2 QACs suggests that QACs are accumulated differently than aliphatic amines with similar alkyl-chain lengths.

There is uncertainty regarding the bioavailability of long-chain aliphatic amines in the environment, and the degree to which it is impacted by their sorption to particulate and dissolved organic carbon and to suspended and bottom sediment. Sorption to organic carbon was estimated using the median TOC concentration, and aquatic PECs were adjusted accordingly. However, a similar estimation for sediments could not be done due to the high degree of variability in sediments and associated uncertainties. In some

situations (e.g., sediments with high amounts of clay and organic carbon), sorption to sediments may be high, resulting in lower freely dissolved concentrations in the water, while in other situations (e.g., sandy or gravel sediments with low organic carbon), sorption may be minimal. However, there is also evidence that sorption of aliphatic amines is reversible, and some degree of desorption can also take place. Environmental monitoring data, as well as field studies to examine the sorption and partitioning of long-chain aliphatic amines in environmental compartments, could be helpful in addressing this uncertainty.

The exposure scenarios identified for substances in the Aliphatic Amines Group are developed on the basis of information obtained through CEPA section 71 surveys, follow-up with stakeholders, and data from the literature. Uses for some long-chain aliphatic amines may be missing. In the absence of particular data, realistic assumptions are made in order to estimate PECs. One key uncertainty for several of the exposure scenarios is the degree of removal of aliphatic amines that occurs in WWTSs. A removal rate of 96% is assumed, based on studies with primary aliphatic amines as summarized in EC (2008). However, there are some uncertainties regarding the methods used in these studies. If additional data on removal rates in WWTSs were available, this could result in changes to the PECs and potentially to the risk quotients determined for scenarios that involve wastewater treatment with the impact on risk unknown.

Several exposure scenarios likely underestimated the environmental concentrations of long-chain aliphatic amines. The production scenario (exposure scenario 1) considered the concentration of aliphatic amines in receiving waters, from facilities where they are produced, specifically for the production campaign of one chemical. Releases would be greater if multiple campaigns were running concurrently and/or consecutively in order to produce multiple chemicals., Both the PECs and the overall risk for this scenario are therefore likely underestimated. For the down-the-drain release of amine derivatives scenario (exposure scenario 4), the assumed volume only covers household detergents and excludes all toilet soaps, surfactants for fabric softening, shampoos and related cosmetics, as well as industrial and institutional cleaners. Therefore, both the PECs and the overall risk for this scenario are underestimated. For the flotation treatment in mineral ore extraction scenario (exposure scenario 5), the adsorption efficiency of the amine collector to silica was overestimated as 99%, desorption of aliphatic amines from silica in the natural environment was not taken into account, and the effluent flows used in the calculation were at the higher end of the range. The aquatic aliphatic amine concentrations resulting from this scenario may therefore be significantly higher than the estimated PECs such that the overall risk for this scenario is likely underestimated. Exposure to sediment organisms could not be estimated as it is not currently possible to model the distribution of long-chain aliphatic amines in sediment. Therefore, environmental sampling in sediment is necessary to determine the level of risk quantitatively.

For some uses or potential sources of release, insufficient data or estimation tools were available to develop quantitative exposure scenarios. There is also uncertainty as to

whether fertilizer use is a potential source of release. Use of aliphatic amines as anticaking agents in fertilizers was identified in Europe as a key use, but it is unknown to what extent this use is occurring in Canada. Additional information on these potential sources of release could inform source attribution, but would not result in changes to the proposed conclusion, as there are several other scenarios indicating a risk.

8. Potential to cause harm to human health

8.1 Dimethylbenzylamine

8.1.1 Exposure assessment

Environmental media

Dimethylbenzylamine has a high vapour pressure and high water solubility. No Canadian monitoring data in ambient air or drinking water were identified for dimethylbenzylamine.

The presence of dimethylbenzylamine in indoor air has been associated with its use in polyurethane foam (PUF). In a report prepared for the California Environmental Protection Agency, dimethylbenzylamine was detected as a volatile organic compound emitted from newly installed polyurethane foam carpet cushions, where measurements were taken in a large air chamber following carpet cushion installation (Hodgson 1999). Dimethylbenzylamine was also detected in air concentrations after the application of spray PUF insulation in a crawl space, but was not detected in the living room adjacent to the crawl space 144 hours post application (Havermans and Houtzager 2014). Results of this study were limited as air concentrations of dimethylbenzylamine were not available for time periods immediately after application, or prior to 144 hours post application. Based on the available results and on re-entry procedures associated with professional application of spray PUF (not available to consumers), exposures associated with this use were considered to be transient and minimal as air concentrations are expected to diminish after application of spray PUF.

Maximum dimethylbenzylamine air concentration from the interior of a car was measured to be 6.1 µg/m^3 after 1 hour of sampling (Rampfl et al. 2008). Daily exposure for infants (0-5 months) in cars was estimated to be 4.48 x 10^{-4} mg/kg bw/day, using the maximum one-hour air concentration and assuming 3 hours spent in a car. Details on the approach and parameters used to derive these exposure estimates are found in Appendix H.

The US EPA SCREEN3 modelling tool (SCREEN3 2011) was used to estimate ambient air concentrations of dimethylbenzylamine in Canada, in the absence of measured concentrations in ambient air, based on the highest import volume from the single largest importer of dimethylbenzylamine (Environment Canada 2013). A daily air concentration at a 1000 m distance from the source facility (representing distance to residential areas) was estimated to be 2.68 x 10^{-3} mg/m^3. Using the daily air

concentration estimates, a daily intake estimate of 2.0 x 10^{-4} mg/kg bw/day was estimated for formula-fed 0- to 5 month-olds. Details on parameters and methods used to derive the air concentrations are found in Appendix I.

Concentrations in surface water were estimated with the New Substances Assessment and Control Bureau (NSACB) Environmental Assessment Unit (EAU) Drinking Water Spreadsheets using the industrial release scenario (Health Canada 2015a). Details of model parameters are found in Appendix J. Using total import volumes of dimethylbenzylamine into Canada (Environment Canada reported 2013), the model estimated a maximum 50th percentile surface water concentration of 5.4 x 10^{-3} mg/L among 10 receiving water bodies. This modelled surface water concentration was used to derive a daily intake estimate from drinking water; the highest exposures per unit weight were found for formula-fed 0- to 5 month-olds at 7.1 x 10^{-4} mg /kg bw/day. The use of a modelled surface water concentration using the total import volumes of dimethylbenzylamine to estimate daily intake from drinking water is considered to be conservative.

Products available to consumers

Dimethylbenzylamine was reported in a two-component marine epoxy adhesive product in Canada at a maximum concentration of 10% (SDS 2014d). Inhalation and dermal exposures associated with mixing and applying this product were estimated using ConsExpo Web (ConsExpo Web 2017); the parameters used to estimate exposure are presented in Appendix H. Because equal volumes of the two componentsare mixed, the concentration of dimethylbenzylamine during application is half what is present in the original product. Dermal and inhalation exposures for adults using this product are presented in Table 8-1.

Table 8-1. Estimated intermittent inhalation and dermal exposure to dimethylbenzylamine

Exposure scenario	Maximum concentration[a]	Dermal exposure (mg/kg bw per event)	Inhalation exposure (mg/kg bw per event)	Total exposure (mg/kg bw per event)
Mixing and applying two-component marine epoxy adhesive	10% (mix) 5% (apply)	0.135	0.169	0.304

[a]SDS 2014d

8.1.2 Health effects assessment

Repeated-dose toxicity

Reports of range-finding studies administering dimethylbenzylamine (in corn oil) by gavage for up to 7 days in rats have been identified in a REACH registration dossier (Hazelton UK for BG Chemie 1990, as cited in ECHA 2018a). Although a limited number of doses were tested, the maximum tolerated dose was considered to be in the range of 200 to 250 mg/kg bw/day according to the authors. Higher doses were associated with clinical signs (e.g., tremor, laboured respiration, muscle spasms, reduced activity), general toxicity such as reduced body weights, and mortality.

In a report of a short-term study in the REACH registration dossier, Crl:CD(SD)BR rats (n=5/sex/dose) were administered 0, 6, 30 or 150 mg/kg bw/day dimethylbenzylamine (in corn oil) by gavage for 28 days (BG Chemie 1988, as cited in ECHA 2018a). At the highest dose, absolute and relative testis weights were slightly higher than control (unknown statistical significance), but were not considered adverse due to the lack of correlated histopathological findings. The authors established a NOAEL of 150 mg/kg bw/day (highest tested dose).

In another 28-day study, 0, 50, 100, 200 or 400 mg/kg bw/day dimethylbenzylamine (in corn oil) was administered by gavage to Crl:CD(SD) rats (n=5/sex/dose), followed by a 14-day recovery period for the two highest dose groups (MHLW 1997; ECHA 2018a). At doses equal to or greater than 100 mg/kg bw/day, miosis (pupil dilation) was observed in the animals. At 200 mg/kg bw/day, additional clinical signs were observed (salivation), along with hematological, clinical biochemistry, and organ weight changes. With the exception of increased relative spleen and adrenal weights, none of the aforementioned effects exhibited dose-dependence or were detected during the recovery period. The highest dose was associated with significantly reduced body weight (which normalized during the recovery period) and a high incidence of mortality (80% in males, 100% in females) beginning 2 weeks after treatment. The authors established a NOEL of 50 mg/kg bw/day, based on miosis reported at 100 mg/kg bw/day. However, due to the lack of miosis observed during the recovery period (suggestive of reversibility), a NOAEL of 100 mg/kg bw/day identified on the basis of general toxicity (i.e., salivation, haematological, clinical biochemistry, and organ weight changes) is considered appropriate for risk characterization.

Reports of short-term inhalation studies (5 to 8 days) were identified in the REACH registration dossier, whereby cats, rabbits, guinea pigs, rats, and mice were exposed in whole-body chambers at doses up to 0.989 mg/L dimethylbenzylamine (equivalent to approximately 989 mg/m^3) (Anonymous 1956, as cited in ECHA 2018a; Anonymous 1957, as cited in ECHA 2018a). Clinical signs and mortality were observed. A report of a subchronic inhalation study was also identified, whereby rats exposed to 100 to 200 mg/m^3 dimethylbenzylamine for 2 hours/day over a period of 3 months exhibited signs of local respiratory irritation and systemic toxicity (i.e., effects on the kidneys, liver, spleen, and lung) (Stasenkova et al. 1963, as cited in ECHA 2018a). Exposure to lower doses (i.e., 30 to 40 mg/m^3) for a longer duration (i.e., 6 months) resulted in similar effects. Due to the lack of control groups in these studies however, they were of limited utility for risk characterization.

Developmental and reproductive toxicity

In a prenatal developmental toxicity study conducted in accordance with OECD Testing Guideline (TG) 414, pregnant Sprague-Dawley rats (n=24/dose) were administered 0, 35, 75 or 150 mg/kg bw/day dimethylbenzylamine (in peanut oil) by gavage from gestation day (GD) 5 to 19 (14 days) (Study Submission 2013). At the highest dose of 150 mg/kg bw/day, a marked reduction in body weight gain (-41%) was reported, accompanied by a reduction in food consumption (-13%). No other treatment-related effects on reproduction (fertility index, gestation index) or on the developing fetus (fetal viability, fetal weight, sex ratio, growth, development, external/skeletal/visceral abnormalities, malformations) were reported at doses up to 150 mg/kg bw/day. The NOAEL for maternal toxicity was determined by the authors to be 75 mg/kg bw/day on the basis of general toxicity (reduced body weight). No reproductive or developmental effects were observed up to the highest dose tested (i.e., 150 mg/kg bw/day).

Genotoxicity and carcinogenicity

Dimethylbenzylamine is not expected to be genotoxic on the basis of the information available from bacterial mutagenicity assays, mammalian cell gene mutation assay, and an *in vivo* micronucleus test (ECHA 2018a). With respect to carcinogenicity, there was a lack of tumours observed in a 100-day study of rabbits administered approximately 1060 mg/kg bw/day dimethylbenzylamine in drinking water (Schneider et al. 1977) as well as a lack of cancer-related structural alerts from modelling software (OECD QSAR Toolbox 2017).

8.1.3 Characterization of risk to human health

The prenatal developmental toxicity study (Study Submission 2013) was used for the characterization of risk following intermittent and chronic exposures to dimethylbenzylamine as it demonstrated the most sensitive health effect in the available dataset. The critical effect of dimethylbenzylamine was determined to be general toxicity (i.e., significantly reduced body weight), and a maternal NOAEL of 75 mg/kg bw/day was identified. This effect level is protective of other systemic effects (e.g., miosis) observed in longer term studies available on this substance.

Table 8-2 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for dimethylbenzylamine from products available to consumers (including PUF in car interiors), and environmental media (outdoor air and drinking water).

Table 8-2. Relevant exposure, critical effect levels and margins of exposure for characterization of risk to dimethylbenzylamine

Exposure scenario	Population	Exposure estimate (mg/kg bw/day)	Critical effect level (mg/kg bw/day)[a]	MOE

Two-component marine epoxy adhesive; inhalation and dermal; intermittent	Adult	0.304	75	247
Car interior PUF; inhalation; daily	0-5 months	4.48×10^{-4}	75	167 410
Environmental media; oral and inhalation; chronic	0-5 months	9.1×10^{-4}	75	82 418

[a] NOAEL of 75 mg/kg bw/day identified on the basis of general toxicity (i.e., reduced body weight in dams) observed at the next dose level of 150 mg/kg bw/day, from a prenatal developmental toxicity study in rats.

These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

8.1.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in Table 8-3 below.

Table 8-3. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
There were no dermal studies conducted on dimethylbenzylamine while studies conducted through the inhalation route were considered to be limited. Route-to-route extrapolation from oral studies was applied for the characterization of risk following exposures through these routes. Absorption via the dermal and inhalation routes was considered equivalent to absorption via the oral route.	+/-
Chronic oral toxicity studies were not available for dimethylbenzylamine.	+/-

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

8.2 Ethylenediamine

8.2.1 Exposure assessment

Environmental media

Ethylenediamine has a high vapour pressure and very high water solubility. No information on measured values in the environment in Canada was identified for ethylenediamine. Use of ethylenediamine as a chemical intermediate may result in released emissions to air and wastewater (PubChem 2004-2020).

Estimated concentrations in surface water were derived with the NSACB EAU Drinking Water Spreadsheets using the industrial release scenario (Health Canada 2015a) using total reported import volumes of ethylenediamine into Canada (Environment Canada

2013). The resultingmodelled 50th percentile surface water concentration among the 10 receiving water bodies of 1.7 x 10^{-3} mg/L results in the highest estimated daily intake per unit weight of 6.0 x 10^{-5} mg/kg bw/day in 1 year-olds. Details of model parameters are found in Appendix J. The use of a surface water concentration modelled using the total reported import volume into Canada is considered to be conservative.

The US EPA SCREEN3 modelling tool was used to estimate ambient air concentrations of ethylenediamine in Canada based on the highest import volume from the largest importer of ethylenediamine (Environment Canada 2013). A daily air concentration at 500 m distance from the source facility to residential areas was estimated to be 0.20 mg/m^3. This results in the highest estimated daily intake per unit weight from ambient air of 2.42 x 10^{-2} mg/kg bw/day in one year olds. Details on parameters used to derive air concentrations are found in Appendix I.

Food

Ethylenediamine may be used as an antimicrobial agent in the manufacture of paper used in food packaging applications such as paper/paperboard, and as a component in the manufacture of inks and adhesives used in food packaging materials. However, dietary exposure from these uses is negligible or is not expected, either because the substance is not present, or present in negligible amounts, in the finished packaging material, or the component containing ethylenediamine has no direct contact with food (personal communication, e-mail from the Food Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated January10, 2017; unreferenced).

Ethylenediamine is identified as a formulant in pest control products registered in Canada. The CFIA monitors a variety of chemicals, including pesticide residues and metabolites, in a wide range of agricultural products, as well as some processed foods (CFIA 2019). Ten years of occurrence data collected by the CFIA for ethylenediamine in foods (CFIA 2019) were available for use in the dietary exposure assessment. Positive detection rates (i.e., samples reporting ethylenediamine concentrations above the limit of detection (LOD; range 0.008 to 0.08 µg/g) ranged from 2% to 31%, depending on the food category. Mean ethylenediamine concentrations for each category were estimated, where samples reporting concentrations below their LOD were conservatively set to their respective LODs (Appendix J). These mean concentrations were used to estimate dietary exposure.

The mean ethylenediamine concentrations for a given food category ranged from 0.029 µg/g in nuts to 0.096 µg/g in grain products (Appendix K).

Using the approach outlined in Appendix K, the estimated ‘all persons’ dietary exposures to ethylenediamine are found in Table 8-4. The food category ‘grain products’ contributed most significantly to dietary ethylenediamine exposure. The highest dietary intake per unit weight was identified for 1 year-old infants with a 90th percentile daily intake of 5.9 x 10^{-3} mg/kg bw/day.

Table 8-4. Estimated daily intake to ethylenediamine in foods (mg/kg bw/day)

Age group, males and females (years)	Mean (mg/kg bw/day)	90th percentile (mg/kg bw/day)
1	2.6×10^{-3}	5.9×10^{-3}
2 to 3	2.7×10^{-3}	5.7×10^{-3}
4 to 8	2.0×10^{-3}	4.2×10^{-3}
9 to 13	1.2×10^{-3}	2.6×10^{-3}
14 to 18	8.0×10^{-4}	2.0×10^{-3}
19+	7.0×10^{-4}	1.6×10^{-3}

Products available to consumers

Ethylenediamine has been reported at low concentrations (0.25%) in a shoe polish product (ECCC 2016b), and the resulting dermal exposure associated with use of this product was estimated to be 3.4×10^{-3} mg/kg bw/day for adults. Dermal exposure estimates for this scenario were derived using ConsExpo Web (2017) (see Appendix H). Ethylenediamine has reported uses in other product types (adhesives and sealants, laundry and dishwashing, and paints and coatings). However, follow-up with stakeholders identified that these products were not available to consumers, or that estimated exposures to these products were lower than those of the shoe polish, which was considered a sentinel scenario.

8.2.2 Health effects assessment

Ethylenediamine was reviewed internationally by the OECD in their Screening Information DataSet [SIDS] Initial Assessment Report (SIAR) (OECD 2004) and by the World Health Organization (WHO) in a Concise International Chemical Assessment Document [CICAD] (WHO 1999). The toxicological data from these assessments were taken into consideration for the health effects characterization of ethylenediamine. A literature search was conducted and no health studies, which could impact the health effects assessment (i.e., result in different critical endpoints or lower points of departure than those identified in the OECD SIAR or CICAD) were identified.

In these evaluations, endpoints with limited data were addressed through the use of data from ethylenediamine dihydrochloride as ethylenediamine is expected to be converted to the salt due to the hydrochloric acid naturally present in the stomach (OECD 2004). Yang et al. (1983) also demonstrated that ethylenediamine and its salt exhibited similar oral toxicity through the comparison of effect levels from acute, 7-day, and 90-day studies, when adjusted for molecular weight.

Repeated-dose toxicity

The effects of ethylenediamine following short-term inhalation exposure have been investigated by Pozzani and Carpenter (1954). In this study, Sherman stock rats (n=15/sex/group) were exposed to 0, 59, 132, 225, and 484 ppm ethylenediamine (equivalent to approximately 0, 145, 324, 553, and 1190 mg/m^3, respectively) for 30

days. The animals were subsequently sacrificed and histopathological examinations were performed on the lungs, heart, liver, kidney, adrenal gland, and spleen. At the lowest concentration (145 mg/m^3), no treatment-related, adverse effects were observed. At 324 mg/m^3, no significant tissue damage was observed, but a slight depilatory effect was identified. At higher concentrations, there were findings of treatment-related mortality, “cloudy swelling” of the livers, “cloudy swelling” and degeneration of the renal tubules, congested lungs, and congested adrenal cortices. The authors indicated that 324 mg/m^3 produced no detectable toxic effects on rats, which was considered to be a NOAEC.

The OECD (2004) identified a short-term dietary study, whereby F344 rats and B6C3F1 mice (n=5/sex/group) were administered ethylenediamine dihydrochloride by gavage for approximately 2 weeks (Peters 1982, as cited in OECD 2004). The rats were given the equivalent of 0, 100, 200, 400, 800, or 1600 mg/kg bw/day ethylenediamine (base) while the mice were given the equivalent of 0, 50, 100, 200, 400, or 600 mg/kg bw/day ethylenediamine (base). In the rats, the two highest dose levels were associated with mortality, clinical signs, renal lesions, and lymphoid depletion/necrosis. The OECD (2004) identified the NOAEL to be 100 mg/kg bw/day in rats (no rationale provided). Similar effects were observed in mice.

In a 13-week study, F344 rats (n=10/sex/group) were administered 0, 100, 200, 400, 600 or 800 mg/kg ethylenediamine by gavage (as ethylenediamine dihydrochloride in distilled water) (Peters 1982, as cited in OECD 2004; NTP 1982a, as cited in WHO 1999). At 600 and 800 mg/kg bw/day, clinical signs (gasping, sneezing, and squinting of eyes) were noted. In addition, there were renal tubule lesions, uterine lesions, and decreased body weight gain. For many of the organs examined, relative weights were either unaffected or were related to lower body weights. At all doses, histopathological changes were observed in the eyes. The OECD identified a LOAEL of 100 mg/kg bw/day ethylenediamine.

The OECD also reported results of a similar 13-week study conducted on B6C3F1 mice (n=10/sex/group), whereby 0, 25, 50, 100, 200, or 400 mg/kg bw/day ethylenediamine was administered by gavage (as ethylenediamine dihydrochloride in distilled water) (Peters 1982, as cited in OECD 2004). The highest dose was associated with histopathological changes in the kidneys (mild to moderate degeneration and/or necrosis of the renal tubular epithelium). One high-dose mouse died, while another had a cataract in one eye, which may or may not have been related to treatment. The OECD identified a NOEL of 200 mg/kg bw/day ethylenediamine.

Yang et al. (1983) also conducted a subchronic dietary study, whereby F344 rats (n=10/sex/group) were fed 0, 50, 250 or 1000 mg/kg bw/day ethylenediamine dihydrochloride in the diet for 3 months. This was equivalent to approximately 0, 22.5, 112.5, and 450 mg/kg bw/day ethylenediamine. At the lowest dose, only a slight effect of reduced water consumption was observed in female rats. At the mid-dose level, increased alanine aminotransferase was observed. At the highest dose, body weight gain was significantly reduced throughout the study, which was accompanied by

reduced food/water consumption in females. With regard to clinical chemistry, a significant decrease in serum glucose and increased enzyme levels (alkaline phosphatase, aspartate aminotransferase, and alanine aminotransferase), suggestive of liver damage, was observed in the high-dose animals as well. The most significant histologic changes termed “hepatocellular pleomorphism”, were present in the liver, which consisted of an increase in the size of hepatocytes and hepatocyte nuclei, an increased variation in nuclear size/shape, and an increase in the number of multinucleate hepatocytes. Occasional degenerating hepatocytes were also observed. The OECD (2004) identified a NOAEL of 50 mg/kg bw/day ethylenediamine dihydrochloride (equivalent to approximately 22.5 mg/kg bw/day ethylenediamine), presumably on the basis of increased alanine aminotransferase levels at the next dose level (250 mg/kg bw/day ethylenediamine hydrochloride or 112.5 mg/kg bw/day ethylenediamine).

The effects of ethylenediamine following chronic exposure have been investigated in a study whereby F344 rats (n=100-120/sex/group) were fed 0, 20, 100, and 350 mg/kg bw/day ethylenediamine dihydrochloride for 24 months (Hermansky et al. 1999). This was equivalent to approximately 0, 9, 45, and 158 mg/kg bw/day ethylenediamine. At the highest dose, significantly higher mortality was observed. In addition, there were reductions in body weight gain (up to 23%) and hematological effects such as slightly reduced RBC counts, hemoglobin, hematocrit levels (statistical analyses not performed). Slightly reduced absolute liver and kidney weights were observed in males, but these changes were not evident relative to body weight. In female rats, absolute and relative liver/kidney weights were increased. The principal lesion observed in the animals of the mid- and high-dose groups was hepatocellular pleomorphism. The incidence of inflammatory lesions of the upper respiratory tract was also increased. At the mid-dose, significantly increased mortality was also observed. Increased absolute weights of the liver and kidneys were observed in females, accompanied by hepatocellular pleomorphism. The authors identified the NOEL to be 20 mg/kg bw/day ethylenediamine dihydrochloride (equivalent to 9 mg/kg bw/day ethylenediamine).

Developmental and reproductive toxicity

In a developmental toxicity study in which pregnant rabbits were administered ethylenediamine dihydrochloride by gavage at doses up to 178 mg/kg bw/day (equivalent to 80 mg/kg bw/day ethylenediamine), no treatment-related effects in the dams or fetuses were observed (NTP 1993).

In another developmental toxicity study, pregnant F344 rats (n=20 females/group) were fed 0, 50, 250, and 1000 mg/kg/day ethylenediamine dihydrochloride in the diet from GD 6 to 15 (DePass et al. 1987a). This is equivalent to approximately 0, 27, 140, and 470 mg/kg bw/day ethylenediamine. Dams at the mid-and high-dose groups had significantly decreased weight gain and decreased feed consumption compared to controls. Fetuses in the high-dose group exhibited a significant reduction in fetal weight and crown-rump length. Additional findings included a significantly increased

percentage of litters with resorptions, fetuses with skeletal variations, and fetuses with missing/shortened innominate artery.

To distinguish between the effect of treatment and that of reduced food consumption, a pair-fed experiment was conducted. Pregnant rats were allocated to a treatment group (1000 mg/kg bw/day ethylenediamine dihydrochloride equivalent to 470 mg/kg bw/day ethylenediamine), to an untreated group fed *ad libitum,* or to a pair-fed group fed a comparable quantity of food as the treated animals. Reduced fetal body weight, crown-rump length, and innominate arterial length were observed when compared to both untreated and pair-fed controls. The authors indicated that a shortened innominate artery is not considered a “teratologic effect” since it would not result in a functional deficit and could possibly be reversible. The OECD (2004) identified a NOEL of 50 mg/kg bw/day on the basis of maternal toxicity and a NOEL of 250 mg/kg bw/day for fetal toxicity at the next dose levels. This corresponds to approximately 27 and 140 mg/kg bw/day ethylenediamine, respectively.

No effects were reported in a two-generation reproductive toxicity study, whereby Fischer 344 rats (n=25-26/sex/group) were fed up to 500 mg/kg bw/day ethylenediamine dihydrochloride in the diet (equivalent to approximately 226 mg/kg bw/day ethylenediamine) (Yang et al. 1984).

Genotoxicity and carcinogenicity

Ethylenediamine is not expected to be genotoxic on the basis of the information available from mutagenicity and clastogenicity assays (OECD 2004; Domoradzki 1979, as cited in OECD 2004; Gee et al. 1998; Guzzie and Slesinski 1987; Hedenstedt 1978; Haworth et al. 1983; Leung 1994; Mueller and Dabney 1979; NTP 1983, 1984a, 1984b, 1985, 1986; Slesinski et al. 1983; Zimmering et al. 1985). With respect to carcinogenicity, ethylenediamine is currently assigned a D classification (not classifiable as to human carcinogenicity). In rats, no treatment-related increases in tumour incidence were observed in a chronic study (Hermansky et al. 1999) or in a lifetime skin-painting study (DePass et al. 1984).

Sensitization

Ethylenediamine has been reported to result in respiratory sensitization due to the induction of respiratory symptoms in occupational settings (OECD 2004). Symptoms such as coughing, sneezing, rhinitis, wheezing, dyspnea have been reported in epidemiological studies (Pozzani and Carpenter 1954; Nakazawa and Matsui 1990; Ng et al. 1991; Ng et al. 1995; Villar-Gomez et al. 2009; Lewinsohn and Ott 1991; Hagmar et al. 1982; Aldrich et al. 1987; Lam and Chan-Yeung 1980; Gelfand 1963). The lowest concentration reported to be associated with sensitization was 1 ppm (equivalent to approximately 2.5 mg/m^3), although there is uncertainty associated with this concentration since analytical air concentrations were not provided (Aldrich et al. 1987). On the basis of this information, a reliable point of departure for the purposes of risk assessment could not be derived.

8.2.3 Characterization of risk to human health

Although studies conducted using ethylenediamine were not identified, data from ethylenediamine dihydrochloride was used to inform the assessment for these routes given their similar toxicity profiles and the predicted conversion to the hydrochloride salt under physiological conditions. The 3-month study conducted by Yang et al. (1983) using ethylenediamine dihydrochloride was used for the characterization of risk following intermittent exposures. A NOAEL of 22.5 mg/kg bw/day ethylenediamine was identified on the basis of increased alanine aminotransferase levels at the next dose level (112.5 mg/kg bw/day).

For chronic oral and dermal scenarios, the 2-year dietary study conducted by Hermansky et al. (1999) using ethylenediamine dihydrochloride was used for the characterization of risk. A NOAEL of 9 mg/kg bw/day ethylenediamine was identified on the basis of effects on the liver (hepatocellular pleomorphism), upper respiratory tract (inflammation), and mortality at the next dose level (45 mg/kg bw/day).

For the inhalation route of exposure, the 30-day study conducted by Pozzani and Carpenter (1954) was used for the characterization of risk. A NOAEC of 324 mg/m^3 was identified on the basis of effects of liver, kidneys, lungs, adrenals, and mortality at the next dose level (553 mg/m^3). Table 8-5 provides all relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for ethylenediamine.

Table 8-5. Relevant exposure, critical effect levels and resulting margins of exposure for characterization of risk to ethylenediamine

Exposure scenario	Population	Exposure estimate	Critical effect level	MOE
Shoe polish dermal, intermittent	Adult	3.4 x 10^{-3} mg/kg bw/day	22.5 mg/kg bw/day[a]	6 618
Dietary and drinking water intake, oral, chronic	1 year old	5.96 x 10^{-3} mg/kg bw/day	9 mg/kg bw/day[b]	1 510
Ambient air in vicinity of industrial facility; inhalation chronic	1 year old	0.20 mg/m^3	324 mg/m^3[c]	1 620

[a] NOAEL 22.5 mg/kg bw/day ethylenediamine was identified on the basis of increased alanine aminotransferase levels at the next dose level (112.5 mg/kg bw/day) from a 3-month study dietary study in rats.
[b] NOAEL of 9 mg/kg bw/day ethylenediamine was identified on the basis on the liver (hepatocellular pleomorphism), upper respiratory tract (inflammation), and mortality at the next dose level (45 mg/kg bw/day), from a 2-year dietary study in rats.
[c] NOAEC of 324 mg/m^3 was identified on the basis of effects of liver, kidneys, lungs, adrenals, and mortality at the next dose level (553 mg/m^3), from a 30-day study in rats.

These MOEs are considered adequate to address the uncertainties in the health effects and exposure databases.

Although ethylenediamine is associated with respiratory sensitization (OECD 2004), there is currently no source of inhalation exposure associated with product use or indoor air. The highest inhalation exposure to this substance is from outdoor air (modelled estimate using conservative assumptions) which is more than 10 times lower than the lowest effect level reported to be associated with the elicitation of symptoms (less than 1 ppm, equivalent to 2.5 mg/m^3) (Aldrich et al. 1987). Therefore, respiratory sensitization is not expected to be of concern at current levels of exposure.

8.2.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-6. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
LODs for a given food category were used when samples reported concentrations below their LOD	+
Route-to-route extrapolation from oral studies was applied for the characterization of risk following dermal exposure. Absorption via the dermal route was considered equivalent to absorption via the oral route.	+/-

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

8.3 Diethylenetriamine

8.3.1 Exposure assessment

Environmental media

Diethylenetriamine has a moderate vapour pressure and is “miscible” with water. Canadian data on indoor or outdoor air concentrations of diethylenetriamine were not identified.

Because diethylenetriamine is miscible with water, estimated surface water concentrations were derived using the industrial release scenario (Health Canada 2015a) (details of model parameters are found in Appendix J). The resulting modelled maximum 50th percentile surface water concentration among the 10 receiving water bodies of 5.2 x 10^{-3} mg/L is based on total import information submitted in response to a CEPA section 71 survey (Environment Canada 2013); this corresponds to the highest estimated daily intake (per unit body weight) of 6.8 x 10^{-4} mg/kg bw/day in formula fed 0-5 month olds. The use of a modelled surface water concentration using the total import volumes of diethylenetriamine into Canada to estimate drinking water intake is considered to be conservative.

Food

Diethylenetriamine may be used as a component in the manufacture of food packaging materials as raw material in a retention agent used to manufacture paper food packaging with the potential for direct food contact. Exposure from this use is considered negligible. The substance may also be used as a component in products to be used in the formulation of inks applied on exterior surfaces of materials intended for food packaging applications, and as a component in products to be used in the formulation of adhesives intended to be applied on middle layers of food packaging materials, for which exposure is not expected since there is no food contact (personal communication, e-mail from the Food Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated January 10, 2017; unreferenced).

Products available to consumers

Diethylenetriamine has been identified in two two-component epoxy products, which consist of one epoxy glue and one marine epoxy filler, up to 1% (SDS 2015; 2018b). The two-component epoxy glue is designed to be used on small do-it-yourself (DIY) projects, such as gluing together a broken vase, while the two-component marine epoxy filler is used to fill holes in water-resistant applications, such as repairing holes in a boat. Dermal and inhalation exposure estimates for adults mixing and applying these two products are found in Table 8-7 (details in Appendix H).

Table 8-7. Estimated intermittent inhalation and dermal exposure to diethylenetriamine

Exposure scenario	Maximum concentration	Dermal exposure (mg/kg bw per event)	Inhalation exposure (mg/kg bw per event)	Total exposure (mg/kg bw per event)
Mixing and applying two-component epoxy glue	1%[a] 0.5%[b]	2.0×10^{-2}	0.1	0.13
Mixing and applying two-component marine epoxy filler	1%[c] 0.5%[d]	1.6×10^{-2}	2.0×10^{-4}	1.6×10^{-2}

[a] SDS 2015; concentration reported in one of the two components to be mixed
[b] Concentration after mixing of the two components
[c] SDS 2018b; concentration reported in one of the two components to be mixed
[d] TDS 2018, based on stated mixing ratio of 1:1 by volume

8.3.2 Health effects assessment

The hazard dataset for diethylenetriamine was considered to be limited. However, since diethylenetriamine is expected to be converted to its hydrochloride salt under

physiological conditions, health effects information on diethylenetriamine dihydrochloride was also used to inform the assessment.

Repeated-dose toxicity

In a report of an unpublished, 7-day study, Harlan-Wistar rats (n=5/sex/dose) were fed dietary levels of 240, 620 and 1580 mg/kg bw/day diethylenetriamine in females and 240, 600 and 1350 mg/kg bw/day diethylenetriamine in males. Reduced body weights were observed in mid- and high-dose animals and reduced liver weights were observed in high-dose males (Anonymous, BGC 1994, as cited in HCNL 2005).

A short-term study was also available for the inhalation route, in which Alderly Park specific-pathogen-free rats (n=2/sex/dose) were exposed (whole-body) to 550 mg/m^3 of diethylenetriamine saturated vapour for 6 hours per day for 15 days. No effects were identified with respect to urinalysis, hematological parameters, gross pathology, and histopathological examinations of the lungs, liver, kidneys, spleen, adrenals, heart, jejunum, ileum and thymus (Gage 1970).

In an oral toxicity study conducted under OECD Guideline 409, Fischer 344 rats (n=20-30/sex/dose) were fed 0, 1000, 7500 and 15 000 ppm diethylenetriamine dihydrochloride in the diet for 90 days with an additional 4-week recovery period for 10 additional control and high-dose animals (Leung and van Miller 1997). This is equivalent to approximately 0, 41, 311, 621 mg/kg bw/day diethylenetriamine for males and 0, 47, 363, 709 mg/kg bw/day diethylenetriamine for females. At the mid- and high-doses, statistically significant changes in clinical pathology measurements were observed in males such as an increase in the mean corpuscular volume and mean corpuscular hemoglobin along with a statistically significant decrease in serum glucose concentration in females, both of which persisted after the 4-week recovery period. Additionally, urine pH was significantly increased in females at the end of the treatment but no longer observed following the recovery period. Also at these doses, significant, treatment-related increases in relative kidney, liver and adrenal weights occurred in females, which persisted into the recovery period. At the highest dose, significant increases in relative kidney and testes weights occurred in males, which remained elevated following the recovery period. A NOAEL of 1000 ppm was determined by the authors on the basis of systemic toxicity at higher doses. This level is equivalent to approximately 41 and 47 mg/kg bw/day diethylenetriamine in males and females, respectively.

A chronic dermal study was conducted on groups of Wistar rats (n=5/sex/dose) where 0.4 mL of a diluted diethylenetriamine solution was painted on a 6 cm^2 portion of the back scapula every other day until death. The average daily dose was estimated to be 114 mg/kg for males and 160 mg/kg for females. The average survival time was approximately 407 days in the treated group compared to 581 days in the control group. For all treated animals, histological changes were observed mainly in the kidney and liver, along with pneumonia and lesions in the spleen and adrenal glands (Fujino 1970, as cited in HCNL 2005).

In an unpublished dermal study, diethylenetriamine was applied at doses of 0, 38, or 780 mg/kg bw/day to the shaved dorsal skin of New Zealand White rabbits (n=10 animals/sex/dose) for 4 weeks (Anonymous 1994, as cited in HCNL 2005). Administration of the high-dose level was stopped after 8 days due to severe treatment-related local effects. The low-dose was associated with reduced body weights (9% to 15% lower than controls), increases in alanine aminotransferase (ALAT), aspartate aminotransferase (ASAT) and lactic dehydrogenase (LDH) activities, decreases in the testes/epididymides weights, and skin lesions.

Reproductive and developmental toxicity

In a report of a reproductive/developmental toxicity screening test (conducted in accordance with OECD TG 421), Wistar rats (n=48/sex/dose) were administered 0, 30, 100 or 300 mg/kg bw/day diethylenetriamine (in filtered water, purity of 99.4%) by gavage during a 2-week premating period, during mating, gestation, and up to post-natal day (PND) 4 (Anonymous 1993, as cited in ECHA 2018b). The total duration of treatment was between 29 and 54 days. At 300 mg/kg bw/day, body weight gain was significantly reduced in the parental animals throughout the study. At doses equal to or greater than 100 mg/kg bw/day, maternal reproductive performance was affected as there was an increase in the length of gestation and in the incidence of post-implantation loss, resulting in a decreased litter size. With respect to the offspring, no adverse effects concerning the general health and the body weights of the pups were identified. The REACH registration dossier reported a NOAEL of 100 mg/kg bw/day on the basis of decreased body weight gain and food consumption observed in the parental animals at the next dose level (300 mg/kg bw/day). A NOAEL of 30 mg/kg bw/day was identified for reproductive toxicity on the basis of increased duration of gestation and increased post-implantation loss.

In a prenatal developmental toxicity study conducted in accordance with OECD TG 414, pregnant Sprague-Dawley rats (n=24/dose) were administered 0, 25, 100, 250 mg/kg bw/day diethylenetriamine (in water, purity of 98.9%) by gavage from GD 6 to 19 (Study Submission 2018; Anonymous, as cited in ECHA 2018b). An additional group (n=5) received 250 mg/kg bw/day diethylenetriamine with a copper supplemented diet (150 ppm). The administration of 250 mg/kg bw/day diethylenetriamine (without copper supplementation) was associated with significantly reduced body weight gain (-11%) throughout the study compared with controls. A similar reduction was also observed with copper supplementation, but this was transient and only occurred during the first few days of dosing. No treatment-related effects on gross pathology or pregnancy performance parameters (e.g., corpora lutea, post-implantation loss, resorptions) were observed. With respect to fetal examinations, an increased incidence of unossified bones (metacarpals, sternabrae, phalanges) and reduced body weights (statistical significance was not reported) were observed at the highest dose level (250 mg/kg bw/day), with or without copper supplementation. However, these effects were not associated with any major or minor fetal abnormalities/malformations and occurred in the presence of maternal toxicity. Therefore, they were not considered to be adverse. The REACH registration dossier identified a NOAEL of 250 mg/kg bw/day for

developmental toxicity, representing the highest dose tested. A NOAEL of 100 mg/kg bw/day was also identified for maternal toxicity on the basis of reduced weight gain observed at the next dose level (250 mg/kg bw/day).

Genotoxicity and carcinogenicity

Diethylenetriamine is not expected to be genotoxic on the basis of the information available from mutation and clastogenicity assays (MHLW 2000; Zieger et al. 1987; Leung 1994; Hulla et al. 1981; Gollapudi et al. 1989; Takahashi and Ohno 1993; Hedenstedt 1978; ECHA 2018b; OECD 1994; Slesinski 1984). With respect to carcinogenicity, there was a lack of treatment-related tumours observed in a lifetime skin-painting study (DePass et al. 1987b), as well as a lack of cancer-related structural alerts from modelling software (OECD QSAR Toolbox 2017).

Sensitization

Respiratory sensitization was studied in rats exposed to 300 ppm (1248 mg/m^3) of diethylenetriamine, but no effects were reported (Savitt 1955, as cited in HCNL 2005).

8.3.3 Characterization of risk to human health

The reproductive/developmental toxicity screening test summarized in a REACH registration dossier (Anonymous 1993, as cited in ECHA 2018b) was used for the characterization of risk following intermittent and chronic exposures to diethylenetriamine. A NOAEL of 30 mg/kg bw/day was identified for reproductive toxicity on the basis of increased duration of gestation and post-implantation loss at the next dose level of 100 mg/kg bw/day.

Table 8-8 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for diethylenetriamine.

Table 8-8. Relevant exposure, critical effect levels and resulting margins of exposure for characterization of risk to diethylenetriamine

Exposure scenario	Population	Exposure estimate (mg/kg bw/day)	Critical effect level (mg/kg bw/day)[a]	MOE
Two-component epoxy glue (1%); inhalation and dermal, intermittent	Adult	0.13	30	231
Two-component marine epoxy filler (1%); inhalation and dermal, intermittent	Adult	1.6×10^{-2}	30	1 875
Drinking water; oral, chronic	Infant	6.8×10^{-4}	30	44 118

[a] NOAEL of 30 mg/kg bw/day was identified on the basis of increased duration of gestation and post-implantation loss at the next dose level of 100 mg/kg bw/day, from a reproductive/developmental toxicity screening test in rats.

These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

8.3.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-9. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
Route-to-route extrapolation from oral studies was applied for the characterization of risk following dermal and inhalation exposure. Absorption via the dermal and inhalation routes was considered equivalent to absorption via the oral route	+

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

8.4 Dimethylamine

8.4.1 Exposure assessment

Environmental media

Dimethylamine exists as a gas with a very high vapour pressure and very high water solubility.

According to the National Pollutant Release Inventory (NPRI), dimethylamine is reported to be released to air by one facility in Canada, with 1.6 tonnes reported to be released in 2017 (NPRI 2018). The US EPA SCREEN3 modelling tool (SCREEN3 2011) was used to estimate ambient air concentrations of dimethylamine in Canada based on NPRI reported releases and facility information. At a 3000 m distance (representing distance from the source facility to residential areas), the daily (24 hour) air concentration was 1.11×10^{-3} mg/m^3. Details on the SCREEN3 model and parameters used to derive this concentration are found in Appendix I.

Based on a pKa value of 10.73, dimethylamine is expected to exist in a protonated form in water at environmental pH. Volatilization is not expected from water surfaces (PubChem 2004-2020). A K_{oc} value of 508 indicates that dimethylamine is expected to adsorb to suspended soils and sediment in wastewater (PubChem 2004-2020). There are no measured concentrations of dimethylamine in water in Canada, but there are various sources from the United States and internationally. Wu et al. (2015) measured dimethylamine at a maximum concentration of 25.4 µg/L in finished water from a drinking water treatment plant in Missouri. This value resulted in a daily intake from drinking water of 8.3×10^{-4} mg/kg bw/day in 1 year-olds.

Food

The predominant source of dietary exposure to dimethylamine is expected to result from its natural occurrence in foods. Dimethylamine is naturally occurring in various types of foods, including cheeses, lettuce, kale, corn, and soybean (VCF 2018). Dimethylamine was found to be most prevalent in fish prepared in various forms, such as fresh, smoked, frozen, and canned. It has been detected and measured in 264 food and beverage samples in Germany (Pfundstein et al. 1991).

A summary of the data identified on the presence of dimethylamine in foods from the literature and from the Volatile Compounds in Food (VCF) database (VCF 2018) can be found in Appendix K. The food category contributing most significantly to dietary dimethylamine exposure was “milk”, which included whole, 2%, 1% and skim cow’s milk. This category represented 72% of the total dietary dimethylamine exposure in children 1 to 3 years of age and 35% of total dietary exposure in all age groups combined. Maximum reported concentration values from the VCF database and values from published literature were used to estimate mean and 90th percentile potential exposures to dimethylamine from food for the general population of Canada, resulting in conservative exposure estimates. Intake values for ‘all persons’ are presented in Table 8-10 below. All persons’ exposure estimates are generated by taking the total number of survey respondents into consideration. Children 1-3 years of age had the highest estimated intake per unit weight (0.3 and 0.57 mg/kg bw/day for the mean and 90th percentile daily intake, respectively).

Table 8-10. Estimated daily intake to dimethylamine from natural occurrence in foods

Age group	Mean daily intake (mg/kg bw/day)	90th percentile daily intake (mg/kg bw/day)
1-3 years	0.297	0.569
4-8 years	0.156	0.301
9-13 years	0.088	0.175
14-18 years	0.064	0.124
19-30 years	0.067	0.124
31-50 years	0.063	0.118
51-70 years	0.067	0.129
70+ years	0.062	0.113

Biological monitoring

Two studies have been identified that measure dimethylamine outputs in human urine. Mitchell et al. (2008) measured dimethylamine concentrations in human urine collected from volunteers (n=6) 8 hours following the consumption of 46 different types of foods, including fruits, vegetables, meats, fish, and dairy products. It was found that control urine samples contained an average 8-hr dimethylene output of 6.67 ± 1.75 mg, while

the highest 8-hr dimethylamine output in urine was 48.62 ± 12.61 mg following the consumption of squid (Mitchell et al. 2008). Zhang et al. (1995) collected human urine samples from 102 males and 101 females over 24 hours. The average daily urinary dimethylamine output in urine for all volunteers was 17.43 ± 11.80 mg/day (Zhang et al. 1995). Toxicokinetics for dimethylamine suggests that it is excreted unchanged in human urine.

8.4.2 Health effects assessment

Dimethylamine was included in the Secondary Aliphatic Amines category by the Organisation for Economic Cooperation and Development (OECD) Screening Information Dataset (SIDS) Program, and a SIDS Initial Assessment Profile (SIAP) (OECD 2013) was published. However, the subsequent report was not publicly available. Dimethylamine is expected to be converted to its hydrochloride salt under physiological conditions. Therefore, endpoints with limited data were addressed through the use of data from dimethylamine hydrochloride, where applicable.

Repeated-dose toxicity

Since dimethylamine is a colourless gas, numerous studies through the inhalation route have been conducted. A 90-day subchronic inhalation study found that 9 mg/m^3 dimethylamine resulted in mild inflammatory changes in the lungs of rats, guinea pigs, rabbits, dogs, and monkeys (Coon et al. 1970). However, this study examined a limited number of health outcomes and tissues during histopathology, limiting its utility for risk characterization.

The effects of dimethylamine following chronic inhalation exposure (whole-body) has been investigated in F344 rats and B6C3F1 mice (n=95/sex/group/species) at concentrations of 0, 10, 50 or 175 ppm (equivalent to 0, 18.4, 92 or 322 mg/m^3) for 6 hours/day, 5 days/week, for 12 months (Buckley et al. 1985). In rats, treatment-related lesions in the nasal passages were observed, which increased in severity with higher concentrations. There was focal destruction of the anterior nasoturbinate/nasal septum, local inflammation, and focal squamous metaplasia of the respiratory epithelium, while the olfactory epithelium exhibited loss of sensory cells/olfactory nerves, hypertrophy of Bowman's glands, and distension of the ducts by serocellular debris in proximal regions. Systemic effects manifested at the highest dose (322 mg/m^3), which included significantly decreased body weight gain (approximately 90% of the control) commencing from the third week of treatment. In addition, there were significant hematological changes (decreased platelet count, increased atypical lymphocytes, decreased mean cell volume in females), and clinical biochemistry findings (decreased protein, increased alkaline phosphatase in females). Although similar local and systemic effects were observed in mice, the damage in the olfactory regions were considered to be less extensive compared to rats. A LOAEC of 10 ppm (18.4 mg/m^3) for local effects was identified on the basis of nasal lesions. A systemic NOAEC of 50 ppm (92 mg/m^3) was identified on the basis of decreased body weight observed at the next dose level in rats (175 ppm, equivalent to 322 mg/m^3).

In a similar inhalation study, F344 rats and B6C3F1 mice (n=95/sex/group/species) were exposed to the same concentrations as the previous study, but for a period of 24 months (CIIT 1990). Compared to the previous study, similar effects were observed in both species, which included treatment-related lesions in the nasal passages that increased in severity with higher concentrations and significantly reduced body weights at the highest dose. However, there were also additional organ weight effects. In rats, there were significantly reduced liver weights, reduced kidney weights, and increased relative brain weights at the highest dose. No hematological differences were detected between groups, but serum chemistry results indicated that female rats exposed to the highest dose had significantly increased levels of alkaline phosphatase and aspartate transaminase, suggestive of potential liver damage. In mice, similar effects on the liver, kidney, and brain were observed at the highest dose. There was also a decrease in levels of thrombocytes, albumin, calcium, glucose, and total protein at the highest concentration. Overall, a NOAEC of 92 mg/m^3 was identified on the basis of general toxicity (i.e., decreased body weight, liver and kidney effects) occurring at the next dose level.

Gross et al. (1987) also examined the effects of chronic, inhalation exposure of male F344 rats to dimethylamine for up to 2 years. However, this study tested only one dose (i.e., 175 ppm, equivalent to approximately 332 mg/m^3) and examined only the effects on the nasal cavity, mucosa, mucociliary function, and mucus flow rates. No other potential systemic effects were evaluated.

With respect to the oral route of administration, the hazard dataset was considered to be limited. In a short-term study investigating the toxicity of dimethylamine, Wistar rats (n=30 males/group) were administered 0 or 0.2% dimethylamine in drinking water (equivalent to approximately 0.28 mg/kg bw/day) for a duration of 9 months (Darad et al. 1983). Increased microsomal peroxidation, acid phosphatase, and cathepsin activity were observed in the liver. No other measures of toxicity were evaluated.

Developmental and reproductive toxicity

The potential for dimethylamine to elicit developmental toxicity has been examined in two prenatal developmental toxicity studies (conducted in accordance with OECD TG 414). The first study administered 0, 100, 300, and 1000 mg/kg bw/day dimethylamine hydrochloride (99.6% purity, in water) by gavage to Wistar rats (n=25 females/group) from GD6-19 (Study Submission 2009; BASF 2009, as cited in ECHA 2018c). This was equivalent to approximately 0, 55, 166, and 553 mg/kg bw/day dimethylamine. At the highest dose, food consumption was significantly reduced, and clinical signs such as salivation and yellowish discoloured urine were observed. No treatment-related effects on conception rate, mean number of corpora lutea, implantation sites, post-implantation loss, and resorptions were detected. With respect to fetal data, no treatment-related, adverse effects were observed. The authors identified a NOAEL of 300 mg/kg bw/day (equivalent to 166 mg/kg bw/day dimethylamine) for maternal toxicity on the basis of decreased food consumption and salivation after treatment at the next dose level.

In the second study, New Zealand White rabbits (n=24 females/group) were exposed by whole-body inhalation to 0, 50, 100, and 250 ppm dimethylamine (equivalent to approximately 0, 92, 184, and 461 mg/m^3) for 6 hours per day from GD 7 to 28 (Study Submission 2015; WIL Research 2016, as cited in ECHA 2018c). At the highest dose, adverse clinical signs (rales, clear material around the mouth/nose/eyes), reduced food consumption, and reduced body weight gain were observed in the dams. However, no effects on survival, post-implantation loss, litter size, fetal body weights, and fetal sex ratios were observed. Although external and visceral malformations were observed in the fetuses, they were not statistically significant, did not exhibit dose-dependence, or were within historical control ranges. The REACH registration dossier reported a NOAEC of 184 mg/m^3 on the basis of maternal toxicity (adverse clinical signs, reduced body weight gain, reduced food consumption) at the next concentration (461 mg/m^3). A NOAEC of 461 mg/m^3 was identified for developmental toxicity, representing the highest concentration tested.

Studies specifically examining the potential for dimethylamine to cause reproductive toxicity were not identified in the literature. However, no treatment-related effects on the reproductive organs were identified in any of the repeated-dose toxicity studies that included a full histopathological examination on the gonads in animals exposed to up to 322 mg/m^3 dimethylamine via inhalation (Buckley et al. 1985; CIIT 1990). Furthermore, no treatment-related effects on post-implantation loss, litter size, mean fetal body weights, or fetal sex ratios were reported in developmental toxicity studies of female rats administered up to 1000 mg/kg bw/day dimethylamine by gavage from GD 6 to 19 and female rabbits exposed up to 461 mg/m^3 via inhalation from GD 7 to 28 (BASF 2009, as cited in ECHA 2018c; WIL Research 2016, as cited in ECHA 2018c).

Genotoxicity and carcinogenicity

Dimethylamine is not expected to be genotoxic based on information available from mutagenicity and clastogenicity studies (Zeiger et al. 1987; Green and Savage 1978; Hsie et al. 1987; Ishidate and Odashima 1977; Abe and Sasaki 1977; Martelli et al. 1983; Isakova et al. 1971). With respect to carcinogenicity, there was a lack of treatment-related increases in tumours in chronic inhalation studies (Buckley et al. 1985; CIIT 1990; Gross et al. 1987). Dietary administration of the salt also did not result in tumours (Greenblatt et al. 1971).

8.4.3 Characterization of risk to human health

Studies examining the effects of dimethylamine following chronic exposure were not identified. Therefore, the oral prenatal developmental toxicity study (Study Submission 2009) was used for the characterization of risk following chronic oral exposure to dimethylamine. A NOAEL of 166 mg/kg bw/day was identified on the basis of decreased food consumption and salivation at the next dose level of 553 mg/kg bw/day.

With respect to the inhalation route, the 2-year study conducted by the Chemical Industry Institute of Toxicology (CIIT 1990) was used for the characterization of risk

following chronic inhalation exposure to dimethylamine. A NOAEC of 92 mg/m^3 was identified on the basis of general toxicity (i.e., decreased body weight, liver and kidney effects) at the next dose level (322 mg/m^3).

Table 8-11 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for dimethylamine from environmental media and food.

Table 8-11. Relevant exposure, critical effect levels and margins of exposure for characterization of risk to dimethylamine

Exposure scenario	Population	Exposure estimate	Critical effect level	MOE
Drinking water, food (90th percentile); oral, chronic	1 year-olds	0.57 mg/kg bw/day	166 mg/kg bw/day[a]	291
Outdoor air; inhalation, chronic	All populations	1.1 x 10^{-3} mg/m^3	92 mg/m^{3b}	83 636

[a] NOAEL of 166 mg/kg bw/day was identified from a prenatal developmental toxicity study on the basis of decreased food consumption and salivation at the next dose level of 553 mg/kg bw/day
[b] NOAEC of 92 mg/m^3 was identified on the basis of general toxicity (i.e., decreased body weight, liver and kidney effects) at the next dose level (322 mg/m^3), from a 2-year study.

These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

8.4.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-12. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
Oral studies examining the effects of dimethylamine following chronic exposure were not identified.	+/-

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

8.5 Hexadecyldimethylamine

8.5.1 Exposure assessment

Environmental media

Hexadecyldimethylamine has a low to moderate vapour pressure and moderate solubility in water. There is no existing information of hexadecyldimethylamine measured in ambient or indoor air in Canada. However, hexadecyldimethylamine is a

long-chain aliphatic amine, and because of its size and vapour pressure, exposure to ambient or indoor air is not expected.

A PEC for hexadecyldimethylamine has been estimated to be 0.55 µg/L for the formulation of polyol blend at a polyurethanes chemical blending plant (section 7.2.4) based on the major use of hexadecyldimethylamine in PUF production (Environment Canada 2013). In addition, the PEC estimated for down-the-drain release of amine derivatives, which may include hexadecyldimethylamine, was 0.12 µg/L. These PEC values represent the total PEC before adjustment for dissolved organic carbon to a freely dissolved concentration; the use of the highest PEC to estimate drinking water intake is considered to be conservative. The highest estimated total intake value per unit weight based on the formulation of polyol blend is for formula-fed 0- to 5 month-olds at 7.2×10^{-5} mg/kg bw/day (Appendix J, Table J-2).

Products available to consumers

Hexadecyldimethylamine is found in two rinse-off facial acne cleansers licensed as natural health products in Canada at concentrations of 0.13%. Both of these products are recommended to be used twice daily (personal communication, e-mail from Natural and Non-prescription Health Products Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated December 16, 2016; unreferenced). The highest estimated exposure to these products is 1.4×10^{-3} mg/kg bw/day for 9- to 13 year-olds. According to submissions made under section 71 of CEPA, hexadecyldimethylamine is reported as an impurity in the formulation of products available to consumers, such as cosmetics (Environment Canada 2013). These additional potential use scenarios from cosmetics were considered, but resulted in lower exposure estimates than the exposure estimate for the rinse-off facial cleanser (Table 8-13).

The Danish Environmental Protection Agency (EPA) identified hexadecyldimethylamine in the synthetic outer material of jackets available to children in Denmark (Tønning et al. 2009). This use is in line with the use of hexadecyldimethylamine in fabric, textile, and leather products in Canada (Environment Canada 2013). In this study, hexadecyldimethylamine was detected in one of five jackets tested at a concentration of 96 µg/g in migration fluid (detection limit of <1-10 µg/g). Oral exposures were estimated for a 2- to 3 year-old child mouthing the outer jacket material and dermal exposure from wearing the jacket. Total exposure from both routes is presented in Table 8-13 and details on the method and parameters used to derive these estimates are found in Appendix H.

According to information submitted in a survey issued pursuant to a CEPA section 71 notice (Environment Canada 2013), hexadecyldimethylamine has also been reported to have commercial use in foam seating and bedding. Although consumer use is not identified, it is expected that these products may have potential for consumer use. No data were found on hexadecyldimethylamine in finished polyurethane foam products. In the absence of data, it is assumed that the jacket scenario may be considered to be protective of dermal and oral exposures associated with polyurethane foam. Although

dermal contact and oral mouthing patterns for jacket material and other foam products may be different, an approach using standard assumptions for area of textile mouthed and body surface area contacting surface was used, due to the limited data available. Any potential differences between these two scenarios are not considered to be significant.

Table 8-13. Estimated exposure to hexadecyldimethylamine from the use of products available to consumers

Exposure scenario	Route of exposure	Maximum concentration	Exposure (mg/kg bw/day or per event)
Facial cleanser (9-13 years)	Dermal	0.13%[a]	1.4×10^{-3}
Jacket outer material	Oral and dermal combined	96 µg/g	1.9×10^{-3}

[a] Personal communication, emails dated from Natural and Non-prescription Health Products Directorate, HC, to Existing Substances Risk Assessment Bureau, HC, dated June 6, 2017, unreferenced.

8.5.2 Health effects assessment

The hazard dataset for hexadecyldimethylamine was considered to be limited. To address endpoints with limited data, a read-across approach was applied to inform the assessment and two analogues with relevant health effects data were identified: dodecyldimethylamine (CAS RN 112-18-5) and N,N-dimethyldocosylamine (CAS RN 21542-96-1). These analogues are both tertiary amines substituted by two methyl groups and an alkyl chain, which is structurally similar to the backbone of hexadecyldimethylamine. With respect to the length of the alkyl chain, dodecyldimethylamine contains a C_{12} chain, dimethyldocosylamine contains a C_{22} chain, and hexadecyldimethylamine contains a C_{16}. In addition to being structurally similar, these substances are also expected to exhibit similar reactivity profiles and undergo similar pathways of metabolism (i.e., oxidation of alkyl chain, N-oxidation, N-dealkylation) based on modelling software simulations (OECD QSAR Toolbox 2017).

Repeated-dose toxicity

The hazard data available for hexadecyldimethylamine on repeated-dose toxicity was limited to one short-term, dietary study whereby Sprague-Dawley rats (n=12 males/group) were given 1000 ppm hexadecyldimethylamine (equivalent to approximately 50 mg/kg bw/day) (Svoboda et al. 1977). The average 3-week gain in body weight was significantly reduced, accompanied by significantly reduced feed consumption, absolute epididymal fat weight, and plasma total sterol levels. However, since only one dose was examined, this study was of limited utility for the purposes of risk characterization.

Short-term studies have been conducted on the analogue dodecyldimethylamine. In a 28-day, oral gavage study, Crj:CD(SD)IGS rats (n=6/sex/group) were given 0, 4, 20, and 100 mg/kg bw/day dodecyldimethylamine (in 0.1% Tween80 added to 0.5% CMC-Na) (Mitsubishi Chemical Safety Institute Ltd. 2003). Additional satellite animals (control and high-dose) were monitored for an additional 14 days following treatment to examine recovery. Body weight, food consumption, hematology, biochemistry, organ weights, functional observation battery, urinalysis, and histopathological findings were recorded in accordance with OECD TG 407. At doses greater than or equal to 20 mg/kg bw/day, myocardial degeneration/fibrosis of the heart (slight to moderate in severity) were detected in male animals. At 100 mg/kg bw/day, there were also findings of thickened wall and erosion of the forestomach, which were accompanied by edema, hyperplasia, and inflammatory cell infiltration. The authors established a NOAEL of 4 mg/kg bw/day on the basis of the effects on the heart at the next dose level of 20 mg/kg bw/day.

A study summary for dodecyldimethylamine was also available in a REACH registration dossier. In a 28-day oral gavage study, Sprague-Dawley rats (n=5/sex/group) were given 0, 50, 150, or 300 mg/kg bw/day dodecyldimethylamine (in sesame oil) (Anonymous 1995, as cited in ECHA 2018d). At 150 mg/kg bw/day, there was slight toxicity (rubbing of the snouts in the bedding material), which was transient without any indication of systemic toxicity. At the highest dose, mortality was observed, accompanied by macroscopic findings in the gastric wall/stomach. A NOEL of 50 mg/kg/bw/day was indicated in the REACH registration dossier.

Short-term studies have also been conducted on the analogue N,N-dimethyldocosylamine. In a 14-day range-finding study in which Crl:CD(SD) rats were gavaged with 7.5, 25, 75, or 200 mg/kg bw/day of N,N-dimethyldocoylamine (93% purity, in olive oil), foamy cells were observed in the mesenteric lymph nodes at all dose levels (J-CHECK 2010-). Higher doses were associated with additional effects such as reduced body weight, liver hypertrophy, and foamy cells in other organs (duodenum, jejunum).

In a report of a combined repeated-dose and reproduction/developmental toxicity screening study (OECD TG 422), Sprague-Dawley rats (n=12/sex/dose) were administered 0, 0.5, 5, or 50 mg/kg bw/day N,N-dimethyldocosylamine (in olive oil) via gavage for 42 days in males, or for 42 to 54 days in females (from 14 days before mating to lactation day 4) (CERI Japan 2012; J-CHECK 2010-). Additional satellite animals were administered the control and high-dose treatments and further examined over a 14-day recovery period. At 5 mg/kg bw/day, the authors noted aggregation of foamy cells in the mesenteric lymph nodes in male animals. At 50 mg/kg bw/day (the highest dose), body weight and food consumption were reduced, although statistical analyses were not reported. In males, this dose was also associated with significant increases in levels of aspartate transaminase (AST), alanine transaminase (ALT), albumin, albumin/globin, and a significant decrease in alkaline phosphatase. There was an enlargement and whitening of the mesenteric lymph nodes, accompanied by aggregation of foamy cells, dilatation of lymphatic vessels and medullary sinus, focal necrosis in the mesenteric lymph nodes. Foamy cells were also observed in the ileum

and jejunum. In females, the high-dose was associated with similar findings in the mesenteric lymph nodes along with wall thickening, squamous hyperplasia, and ulceration of the forestomach. With the exception of foamy cells in the mesenteric lymph nodes and jejunum, all other observations were considered to be “recovered” as they were not observed at the end of the recovery period. The authors indicated that the “NOAEL and NOEL were 0.5 mg/kg/day for males and 5 mg/kg/day for females since aggregation of foamy cells in the mesenteric lymph nodes in males given 5 mg/kg or more and in females given 50 mg/kg were observed.” A NOAEL of 0.5 mg/kg bw/day was considered for this screening assessment.

Reproductive and developmental toxicity

Studies examining the reproductive and developmental toxicity of hexadecyldimethylamine were not identified. The hazard data available for the analogues dodecyldimethylamine and N,N-dimethyldocosylamine were taken into consideration, where applicable.

In the aforementioned combined repeated-dose and reproductive/developmental toxicity screening study (CERI Japan 2012; J-CHECK 2010-), Sprague-Dawley rats (n=5/sex/dose) were administered 0, 0.5, 5, or 50 mg/kg bw/day N,N-dimethyldocosylamine by gavage for 42 days in males and 42 to 54 days in females. No treatment-related abnormalities were detected in any of the test parameters (estrous cyclicity, copulation index, conception index, delivery dam index). Furthermore, there were no abnormalities with respect to the external appearance, body weight, viability index, or sex ratio in the developing offspring.

In a reproduction and developmental toxicity screening test, the analogue dodecyldimethylamine (in sesame oil) was administered to Sprague-Dawley rats (n=10/sex/dose) by gavage at doses of 0, 50, 150, 300 or 450 mg/kg bw/day for 28 days in males and 54 days in females (Hoechst AG 1995, as cited in ECHA 2018d). There were no treatment-related effects on pre-coital time, duration of pregnancy, post-implantation loss, viability index, or pup development. At 150 mg/kg bw/day, two dams died before the end of the study, while another two dams were unable to deliver their pups. There was also a significant decrease in the number of pups alive at delivery and in the mean viability index (36.9%), while the number of stillbirths and mean post-implantation loss (50.4%) significantly increased. At higher doses, only one dam delivered a pup. A NOAEL of 50 mg/kg bw/day was identified on the basis of the observed developmental and reproductive effects at the next dose level of 150 mg/kg bw/day. These effects occurred in the presence of maternal toxicity as mortality of the dams was observed at 150 mg/kg bw/day.

Genotoxicity and carcinogenicity

The information available from mutagenicity and clastogenicity studies on hexadecyldimethylamine or its analogues indicates that it is not likely to be a genotoxicant (Szybalski 1958; ECHA 2018d). With respect to carcinogenicity, neoplastic

effects were not reported at a dose of approximately 100 mg/kg bw/day in an 80-week study conducted on the analogue dodecyldimethylamine (Lijinsky and Taylor 1977).

8.5.3 Characterization of risk to human health

Since the hazard dataset for hexadecyldimethylamine was limited, a read-across approach was applied, whereby data from analogues were used to inform the assessment. With respect to intermittent and chronic exposure scenarios, the combined repeated-dose and reproductive/developmental toxicity study on N,N-dimethyldocosylamine (CERI Japan 2012) was determined to be the most relevant for the characterization of risk. A NOAEL of 0.5 mg/kg bw/day was identified on the basis of aggregation of foamy cells in the mesenteric lymph nodes observed at the next dose level (5 mg/kg bw/day).

Table 8-14 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for hexadecyldimethylamine.

Table 8-14. Relevant exposure, critical effect levels and margins of exposure for characterization of risk to hexadecyldimethylamine

Exposure scenario	Population	Exposure estimate (mg/kg bw/day)	Critical effect level (mg/kg bw/day)[a]	MOE
Rinse-off facial cleanser; dermal, chronic	9 to 13 year-olds	1.4×10^{-3}	0.5	357
Drinking water; oral, chronic	0 to 5 month-olds	7.2×10^{-5}	0.5	6 944
Material containing hexadecyldimethyl-amine; oral (mouthing) and dermal; intermittent	2 to 3 year-olds	1.9×10^{-3}	0.5	263

[a] NOAEL of 0.5 mg/kg bw/day was identified on the basis of aggregation of foamy cells in the mesenteric lymph nodes observed at the next dose level (5 mg/kg bw/day), from a combined repeated-dose and reproductive/developmental toxicity study.

These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

8.5.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-15. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
Route-to-route extrapolation from oral studies was applied for the characterization of risk following dermal exposure. Absorption via the dermal route was considered equivalent to absorption via the oral route.	+
No data were found on hexadecyldimethylamine in furnishing products containing polyurethane foam. In the absence of data, it is assumed that the jacket scenario is protective of oral and dermal scenarios involving polyurethane foam containing hexadecyldimethylamine (e.g., furnishings).	+/-
Studies on chronic toxicity through oral or dermal routes were not identified.	+/-

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

8.6 Octadecylamine

8.6.1 Exposure assessment

Environmental media

Octadecylamine has a low vapour pressure and low water solubility. There is no available data on measured concentrations of octadecylamine in indoor or ambient air in Canada. Given its high pKa of 10.6, octadecylamine is expected to exist in the protonated form if released to water at environmental pH; it is not expected to volatilize from water (PubChem 2004-2020).

Data for measured concentrations of octadecylamine in surface waters in Canada have not been identified. A PEC for octadecylamine has been estimated to be 1.3 µg/L for processing primary amine intermediates at a processing site (section 7.2.3) based on the import of octadecylamine as a chemical intermediate (Environment Canada 2013). This PEC value represents the total PEC before adjustment for dissolved organic carbon to a freely dissolved concentration. The use of this PEC to estimate drinking water intake is considered to be conservative. The resulting daily intake value per unit weight for 1 year-olds is 4.0×10^{-5} mg/kg bw/day (Appendix J, Table J-2).

Food

Octadecylamine may be present in foods from its potential use as a component in an incidental additive. Specifically, it is used as a boiler water additive, and therefore may be present in steam that has the potential for direct food contact with a limited number of foods, excluding milk and milk products. Assuming a worst-case scenario, i.e., that 100% of the octadecylamine stays in the foods that can come into contact with the steam, the probable daily intake of octadecylamine estimated from its use as an incidental additive is 1.7×10^{-3} mg/kg bw/day. This estimate is considered to represent

exposure to the general population aged 12 months and older (personal communication, e-mail from the Food Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated March 6, 2019; unreferenced).

Products available to consumers

Cosmetics

Octadecylamine has a reported function as an antistatic agent in cosmetics (EC 2017). Dermal exposure estimates for octadecylamine in the shaving cream is presented in Table 8-16. Details on the method and parameters used to derive estimates of dermal exposure to octadecylamine are available in Appendix H.

The EU RAR identified a dermal absorption value of 60% that may be applied when deriving exposure estimates for primary amines, including octadecylamine and cocoamine (EC 2008). This value is based on a study examining dermal absorption of 1-dodecanamine (C12; radiolabelled) applied to the skin of mice in three different solvents (squalene, castor oil, and triethylcitrate) at four different concentrations (50%, 5%, 0.5%, and 0.05%) (Iwata et al. 1987). This value was applied in calculating the exposure estimates in Table 8-16.

Table 8-16. Estimated dermal exposure to octadecylamine from the use of cosmetics and non-prescription drug products

Exposure scenario	Maximum concentration	Systemic exposure (mg/kg bw per event)[a]
Body shaving product (9 to 13 years)	0.1%[b]	1.4×10^{-3}

[a] Including 60% dermal absorption

[b] Personal communication, emails from Consumer and Hazardous Products Safety Directorate, HC, to Existing Substances Risk Assessment Bureau, HC, dated December 14, 2016; unreferenced.

Other Products

Octadecylamine was identified as an impurity in an automotive lubricant additive product intended for use in automotive transmission fluid, with maximum concentration of the substance in the final transmission fluid expected to be 1.0×10^{-3}% (Personal communication, Aliphatic Amines voluntary data gathering, Existing Substances Risk Assessment Bureau, HC, 2017; unreferenced). Consumer exposure is expected for those who perform their own vehicle maintenance. Systemic exposure resulting from dermal contact, at 60% dermal absorption, is estimated to be 4.5×10^{-4} mg/kg bw/day for adults. Details on the method and parameters used to derive estimates of dermal exposure to octadecylamine are found in Appendix H.

8.6.2 Health effects assessment

Germany drafted a European Union Risk Assessment Report (EC 2008) that examined five primary alkyl amine substances, including octadecylamine (CAS RN 124-30-1),

amines tallow alkyl (CAS RN 61790-33-8), (Z)-octadec-9-enylamine (CAS RN 112-90-3), amines hydrogenated tallow alkyl (CAS RN 61788-45-2), and amines coco alkyl (CAS RN 61788-46-3). These amines were evaluated together in a read-across approach based on (1) the common primary amine group and (2) common predicted metabolic/degradation pathways. A literature search was conducted for octadecylamine and no health studies, which could impact the health effects assessment (i.e., result in different critical endpoints or lower points of departure than those identified by EC), were identified. In addition, a supplemented read-across approach was conducted in accordance with international guidelines (OECD 2014a) and an additional analogue was identified ($C_{16\text{-}22}$-alkyl amines, CAS RN 68037-92-3). The analogues (Z)-octadec-9-enylamine, $C_{16\text{-}22}$-alkyl amines, and amines tallow alkyl were identified to be the most appropriate analogues with data to inform endpoints with limited data. For a comparison of the physical-chemical properties between these analogues, refer to Appendix D.

The lowest NOAEL identified in the hazard dataset for all of the analogues was 3 mg/kg bw/day from a guideline developmental toxicity study in female New Zealand rabbits (n=22/group) (Springborn Laboratories Inc. 1989a, as cited in EC 2008). In this study, animals were administered 0, 3, 10 or 30 mg/kg bw/day (Z)-octadec-9-enylamine (in corn oil) by gavage from GD 6 to 18. Caesarean section occurred on GD 29. At doses greater than 10 mg/kg bw/day, overt clinical signs were observed (e.g., rales, laboured breathing, no feces, emaciation, irritation of the mouth), and two females died at the highest dose. In addition, the animals in these dose groups also exhibited reduced weight gain and food consumption. A NOAEL of 3 mg/kg bw/day is consistent with the lowest effect level identified in the hazard dataset for octadecylamine, which is comprised of subchronic and chronic studies that pre-dated the establishment of internationally accepted testing guidelines (Deichmann et al. 1958; MacDonald et al. 1962; Griffin et al. 1991). In the hazard dataset for octadecylamine, a NOAEL of 3 mg/kg bw/day was identified on the basis of findings in the gastrointestinal tract (mesenteric lymph nodes, small intestine) at the next dose level of 15 mg/kg bw/day, from a 1-year chronic study on dogs (Deichmann et al. 1958).

Studies examining the potential of reproductive and developmental toxicity from exposure to octadecylamine were not identified. However, data available on analogues indicate that reproductive and developmental effects are either not observed or are observed only in the presence of systemic toxicity in the parental animals (EC 2008; ECHA 2018e). On the basis of this information, octadecylamine is not expected to be a reproductive or developmental toxicant.

Octadecylamine is not expected to be genotoxic on the basis of the information available from mutagenicity and clastogenicity studies *in vitro* (Zeiger et al. 1988; Hoechst AG 1988a). With respect to carcinogenicity, there was a lack of cancer effects in chronic 2-year studies (Deichmann et al. 1958; MacDonald et al. 1962).

8.6.3 Characterization of risk to human health

A prenatal developmental study selected by EC (2008) was used for the characterization of risk following both short-term and chronic exposures. In this study, a NOAEL of 3 mg/kg bw/day for an analogue, (Z)-octadec-9-enylamine was identified on the basis of general toxicity (clinical signs, reduced body weight, food consumption) at the next dose level of 10 mg/kg bw/day. This NOAEL is consistent with that identified in a 1-year oral study on octadecylamine conducted by Deichmann et al. (1958) in mongrel dogs, which was determined on the basis of findings in the gastroenteric tract (mesenteric lymph nodes, small intestine) at the next dose level of 15 mg/kg bw/day.

Table 8-17 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for octadecylamine from products available to consumers and environmental media.

Table 8-17. Relevant exposure, critical effect levels, and margins of exposure for characterization of risk to octadecylamine

Exposure scenario	Population	Systemic exposure (mg/kg bw/day)	Critical effect level (mg/kg bw/day)[a]	MOE
Shaving cream (body, 0.1%); dermal, chronic	9 to 13 year-olds	1.4×10^{-3}	3	2 143
Lubricant additive in automotive transmission fluid (0.001%); dermal, intermittent	Adults	4.54×10^{-4}	3	6 608
Drinking water and incidental additive; oral, chronic	1 year-olds	1.7×10^{-3}	3	1 765

[a] NOAEL of 3 mg/kg bw/day was identified on the basis of general toxicity (e.g., clinical signs, reduced body weight, food consumption) at the next dose level of 10 mg/kg bw/day, from a prenatal developmental toxicity study for an analogue, (Z)-octadec-9-enylamine. This NOAEL is consistent with that identified in a 1-year oral study on octadecylamine conducted by Deichmann et al. (1958) in mongrel dogs, which was determined on the basis of findings in the gastroenteric tract (mesenteric lymph nodes, small intestine) at the next dose level of 15 mg/kg bw/day.

These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

8.6.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-18. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
Route-to-route extrapolation from oral studies was applied for the characterization of risk following dermal exposure. A dermal absorption value was applied to estimate systemic exposure.	+/-
There were no studies on reproductive and developmental toxicity. Hazard data from analogues were used to inform the assessment.	+/-

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

8.7 Cocoamine

8.7.1 Exposure assessment

Environmental media

Cocoamine is a liquid with low vapour pressure. A draft European Union Risk Assessment Report (EU RAR) for Primary Alkyl Amines indicates that there is no expected release of cocoamine to air during production and processing. As well, there is negligible volatilization from aqueous media (EC 2008); therefore, exposure to humans from atmospheric sources is not expected.

No data have been identified that measure cocoamine in surface waters in Canada.

A PEC for cocoamine has been estimated to be 1.12 µg/L for the manufacturing and processing of aliphatic amines at an industrial facility (section 7.2.2) based on manufacture and import of cocoamine as a chemical intermediate (Environment Canada 2013). This PEC value represents the total PEC before adjustment for dissolved organic carbon to a freely dissolved concentration. The use of this PEC to estimate drinking water intake is considered to be conservative. This estimation results in the highest intake value per unit weight in formula-fed 0- to 5 month-olds of 1.5×10^{-4} mg/kg bw/day (Appendix J, Table J-2).

Food

Cocoamine may be present in food as an incidental additive from its potential use in cleaners used on food contact surface followed by portable water rinse before use, and in lubricants with incidental contact or no contact. Exposure from these uses is negligible (personal communication, e-mail from the Food Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated January 10, 2017; unreferenced).

Products available to consumers

Cosmetics

Cocoamine has reported cosmetic functions as an emulsifier and as an antistatic agent (EC 2017) and is identified in a limited number of rinse-off hair conditioning products in Canada at a concentration of 0.5% (personal communication, e-mail from the Consumer and Hazardous Products Safety Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated June 6, 2018; unreferenced). A dermal absorption value of 60% (see section 8.6.1) is incorporated into the dermal exposure estimate to derive an estimate of systemic exposure associated with the use of the hair conditioning product. Exposure is highest for 2- to 3 year-olds at 1.04×10^{-2} mg/kg bw/day. Details on the method and parameters used to derive estimates of dermal exposure to cocoamine are available in Appendix H.

8.7.2 Health effects assessment

Repeated-dose toxicity

The short-term effects of cocoamine have been documented in a report of a range-finding study in which rats were administered 0, 10, 40, or 160 mg/kg bw/day cocoamine (100.4% purity) by oral gavage (unknown strain, n=3/sex/dose) for at least 9 days (exact duration not specified in the report) (Exponent 2007). At the highest dose, one male was found dead on day 8 of the study, and the remaining two males were sacrificed due to excessive toxicity on day 9. The animals also had decreased body weight. Necropsy revealed that all lobes of the lungs were spongy and mottled red/dark red, but all other tissues appeared normal. The females in the high-dose group were continued on treatment and mated with untreated males. Two of the females were sacrificed prior to schedule termination on GD 14 due to adverse clinical signs and decreased body weight.

Based on the results of the range-finding study, a combined repeated dose toxicity study with a reproduction/developmental toxicity screening test (OECD TG 422) was conducted, in which Sprague-Dawley (Crl:CD) rats (n=10/sex/dose) were administered 0, 5, 20, 40 and 80 mg/kg bw/day cocoamine (in deionized water/glacial acetic acid) via gavage for 14 days prior to mating until the day before sacrifice. The results of this study were only accessible through the N-Alkyl (C_8-C_{18}) Primary Amines and Acetate Salts (NAPAAS) Inert Ingredients Human Health Risk Assessment (US EPA 2009). In this report, it was noted that male rats received at least 46 days of treatment while females were treated until lactation day 4 (approximately 38 to 42 days of treatment). In addition, five animals/sex/group were tested in a functional observational battery, followed by motor activity testing on the day of scheduled sacrifice. At 20 mg/kg bw/day, microscopic lesions were reported in the stomach (erosions, hyperplasia/ hyperkeratosis, necrosis), jejunum (macrophage infiltration in males), thymus (thymic atrophy in females) and mesenteric lymph nodes (macrophage infiltration in males). In the lymph nodes and liver of the affected animals, the macrophages coalesced to form microgranulomas. At higher doses, the incidence and severity of these lesions increased in a dose-related manner and often affected both sexes. At 40 and 80 mg/kg bw/day, clinical effects were observed, as well as decreased body weight gain and food consumption. The highest dose was also associated with significantly reduced terminal

body weight and reduced absolute/relative weights of the liver, kidney, and heart in males, along with significantly reduced relative weights of the testes, brain, and adrenals. Two of the high-dose male rats were sacrificed due to severe toxicity. A systemic NOAEL of 5 mg/kg bw/day was established by the US EPA on the basis of the observed lesions in the stomach, jejunum, thymus and lymph nodes at the next dose level (20 mg/kg bw/day).

Reproductive and developmental toxicity

In the combined repeated-dose toxicity study with the reproduction/developmental toxicity screening test mentioned above (JITF CST 25 2008, as cited in US EPA 2009), no effects on reproduction or fertility were observed. With respect to developmental toxicity, significant decreases in pup body weights were observed in the 40 and 80 mg/kg bw/day groups, which may be related to maternal toxicity, since reduced food consumption and body weight were observed in the dams at these dose levels. The US EPA (2009) established a NOAEL of 20 mg/kg bw/day for developmental toxicity on the basis of decreased body weight and body weight gain in the offspring at the next dose level (40 mg/kg bw/day).

Genotoxicity and carcinogenicity

Cocoamine is not expected to be genotoxic on the basis of data available from bacterial mutagenicity studies (Hoechst AG 1988b, as cited in EC 2008). With respect to carcinogenicity, no chronic studies on cocoamine were identified. There is a lack of cancer effects observed for the Aliphatic Amines Group in general and a lack of cancer-related structural alerts from modelling software (OECD QSAR Toolbox 2017).

8.7.3 Characterization of risk to human health

The combined repeated-dose study and reproductive/developmental toxicity screening test reported by the US EPA (2009) was used for the characterization of risk following chronic dermal and oral exposure to cocoamine. A NOAEL of 5 mg/kg bw/day was identified on the basis of the histopathological lesions observed in the thymus, stomach, jejunum, and mesenteric lymph nodes at the next dose level (20 mg/kg bw/day). The US EPA also identified the same critical study and endpoint for the NAPAAS Human Health Risk Assessment (US EPA 2009).

Table 8-19 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for cocoamine from rinse-off hair conditioner and environmental media.

Table 8-19. Relevant exposure, critical effect levels and margins of exposure for characterization of risk to cocoamine

Exposure scenario	Population	Exposure estimate (mg/kg bw/day)	Critical effect level (mg/kg bw/day)[a]	MOE
Rinse-off hair conditioner (0.5%); dermal, chronic	2 to 3 year-olds	1.04×10^{-2}	5	481
Drinking water; oral, chronic	Infants	1.5×10^{-4}	5	33 333

[a] NOAEL of 5 mg/kg bw/day was identified on the basis of histopathological findings in the gastrointestinal tract (stomach, intestine, mesenteric lymph nodes), thymus, and liver observed at the next dose level of 20 mg/kg bw/day.

These MOEs are considered adequate to address uncertainties in the health effects and exposure databases.

8.7.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-20. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
There were no dermal studies conducted on cocoamine. Route-to-route extrapolation from oral studies was applied for the characterization of risk following dermal exposure. A dermal absorption value was applied to estimate systemic exposure.	+/-
Chronic studies administering cocoamine were not identified.	+/-

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

8.8 Bis(hydrogenated tallow alkyl) amines (BHTAA)

8.8.1 Exposure assessment

Environmental media

BHTAA is a solid that is insoluble in water. Data quantifying levels in environmental media in Canada for this substance have not been found.

BHTAA (CAS RN 61789-79-5) represents a UVCB substance with carbon-chain lengths ranging from C_{14}-C_{18}, the most predominant being a saturated C_{18} chain (US EPA 2010). BHTAA is also referred to as "N-(C_{16-18})alkyl(C_{16}-C_{18})alkane-1-amine" or "amines, di-C_{16}-C_{18} (even numbered) alkyl" (CAS RN 308062-60-4) in a REACH registration dossier and by the OECD (2014b). N-(C_{16}-C_{18})alkyl(C_{16}-C_{18})alkane-1-amine is a solid with low vapour pressure (2.0×10^{-3} Pa) and is insoluble in water (ECHA 2018f).

A PEC for BHTAA has been estimated to be 1.12 µg/L for the manufacturing and processing of aliphatic amines at an industrial facility (section 7.2.2) based on the manufacture and import of BHTAA as a chemical intermediate. This PEC value represents the total PEC before adjustment for dissolved organic carbon to a freely dissolved concentration. The use of this PEC to estimate drinking water intake is considered to be conservative. This estimation results in an intake value in adults of 2.0 x 10^{-5} mg/kg bw/day (Appendix J, Table J-2).

Food

BHTAA may be used as a stabilizer in the manufacture of polypropylene plastics used to manufacture food packaging materials, with potential for direct food contact. The probable daily intake of BHTAA from its use in food packaging applications is 1.2 x 10^{-3} mg/kg bw/day for the general population aged 12 months and older (personal communication, e-mail from the Food Directorate, HC to the Existing Substances Risk Assessment Burea, HC, dated January 10, 2017; unreferenced).

8.8.2 Health effects assessment

As noted in section 8.8.1, BHTAA is also referred to as "N-(C_{16-18})alkyl(C_{16}-C_{18})alkane-1-amine" or "amines, di-C_{16}-C_{18} (even numbered) alkyl" (CAS RN 308062-60-4) in a REACH registration dossier and by the OECD (2014b). Therefore, hazard information identified for the latter synonyms were also taken into consideration for this screening assessment.

Repeated-dose toxicity

The short-term effects of "amines, di-C_{16}-C_{18} (even numbered) alkyl (CAS RN 308062-60-4)" were examined in a 28-day study, in which Wistar rats (n=5-10/sex/group) were administered 0, 50, 200 or 1000 mg/kg bw/day of test substance (in corn oil) by gavage (Anonymous 2010, as cited in ECHA 2018f). Control and high-dose rats were also subjected to a 14-day recovery period. At doses equal to or greater than 50 mg/kg bw/day, a significant increase in absolute and relative liver weights was observed. Histopathological changes in the mesenteric lymph nodes (granulomatous inflammation) were also noted, which appeared to be irreversible as a thickening of the mesenteric lymph nodes was noted in female animals during the recovery period. At the highest dose (1000 mg/kg bw/day), the effects in the mesenteric lymph nodes increased in severity and persisted during the recovery period. Granulomatous inflammation was also observed in the liver and lungs of the treated animals throughout the study and recovery periods. In addition, spleen weights (absolute/relative) were significantly increased in female animals, accompanied by macrophage aggregation. Other treatment-related effects at this dose level included hematological changes in total and differential leukocyte counts, decreased testis weights, and decreased thymus weights. Since many of the observed effects lasted through the 2-week recovery period and demonstrated dose-dependence (i.e., inflammation of mesenteric lymph nodes), the authors concluded that a NOAEL could not be established. For this assessment, a

LOAEL of 50 mg/kg bw/day was considered on the basis of effects on the mesenteric lymph nodes and liver at this dose level.

In a report of a subchronic study, Wistar rats (n=10/sex/group) were administered 0, 5, 15 or 50 mg/kg/day of "amines, di-C_{16}-$_{18}$ (even-numbered) alkyl" (in corn oil) by gavage for 92 to 93 days (Anonymous 2014, as cited in ECHA 2018f). An additional 5 animals per sex were included in the high dose group and followed during a 42-day recovery period. The main treatment-related effects reported were granulomatous foci in the mesenteric lymph nodes and lymphoid hyperplasia. These effects occurred in all groups and increased in severity with increasing doses, and they persisted after the recovery period in the high dose animals. Other treatment-related effects at the highest dose (i.e., 50 mg/kg bw/day) included significantly increased mean relative neutrophil levels and reduced mean absolute lymphocytes. After the recovery period, there were reduced absolute/relative reticulocyte counts, and a shift in reticulocyte maturity from high-fluorescent to low-fluorescent cells. The report indicated that "granuloma in the mesenteric lymph nodes are generally considered to be non-adverse[…]." However, since effects on the mesenteric lymph nodes have been observed for other aliphatic amines in this group, and can progress to more severe forms of systemic toxicity (e.g., granulomatous foci), a LOAEL of 5 mg/kg bw/day was considered instead for this screening assessment.

Reproductive and developmental toxicity

Studies examining the potential reproductive toxicity of BHTAA were not identified. No effects on the reproductive organs, estrous cyclicity, or spermatogenesis were observed in the subchronic study in Wistar rats administered up to 50 mg/kg bw/day di-C_{16}-$_{18}$ (even numbered) alkyl amines by gavage for 92 to 93 days (Anonymous 2014, as cited in ECHA 2018f). With respect to developmental toxicity, no fetal effects were identified in a report of a prenatal developmental toxicity study, in which pregnant Wistar rats (n=22/dose) were administered up to 1000 mg/kg bw/day "amines, di-C_{16}-C_{18} (even numbered) alkyl" in corn oil by gavage from GD 6 to 20 (Anonymous 2014, as cited in ECHA 2018f).

Genotoxicity and carcinogenicity

BHTAA is not expected to be genotoxic on the basis of the information available from mutagenicity and clastogenicity studies *in vitro* (ECHA 2018f). With respect to carcinogenicity, there is a lack of cancer effects observed for the Aliphatic Amines Group in general and a lack of cancer-related structural alerts from modelling software (OECD QSAR Toolbox 2017).

8.8.3 Characterization of risk to human health

The subchronic study reported in a REACH registration dossier (Anonymous 2014, as cited in ECHA 2018f) was used for the characterization of risk following chronic oral exposure to BHTAA. A LOAEL of 5 mg/kg bw/day was identified on the basis of

histopathological effects in the mesenteric lymph nodes (i.e., granulomatous foci and hyperplasia).

Table 8-21 provides relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for BHTAA from food packaging and drinking water.

Table 8-21. Relevant exposure, critical effect levels, and margins of exposure for the characterization of risk to BHTAA

Exposure scenario	Population	Exposure estimate (mg/kg bw/day)	Critical effect level (mg/kg bw/day)[a]	MOE
Food packaging, drinking water; oral, chronic	Adult	1.35×10^{-3}	5	3 704

[a] LOAEL of 5 mg/kg bw/day was identified on the basis of histopathological effects in the mesenteric lymph nodes (i.e., granulomatous foci and hyperplasia), from a subchronic study in rats.

This MOE is considered adequate to address uncertainties in the health effects and exposure databases.

8.8.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-22. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
Studies on chronic toxicity were not identified for BHTAA or its synonyms.	+/-

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

8.9 1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-, branched (DPDAB)

8.9.1 Exposure assessment

Environmental media

DPDAB is a solid with low vapour pressure and water solubility. DPDAB was not identified or measured in Canadian or international environmental media.

A PEC for DPDAB has been estimated to be 0.248 µg/L for the release from its major use in the flotation of iron ore (section 7.2.6). This PEC value represents the total PEC before adjustment for dissolved organic carbon to a freely dissolved concentration. The use of this PEC to estimate drinking water intake is considered to be conservative. This estimation results in an intake value per unit weight in formula-fed 0- to 5 month-olds of 3.0×10^{-5} mg/kg bw/day (Appendix J, Table J-2).

Products available to consumers

DPDAB has been identified in one two-component marine epoxy adhesive in Canada at a concentration of 5% to 10% (SDS 2018a). The primary route of exposure is dermal due to the low vapour pressure of the substance. Dermal exposures associated with mixing and applying this product were estimated using ConsExpo Web (ConsExpo Web 2017). Details and parameters used to estimate exposure are found in Appendix H. Because the two components of equal volume are mixed, the concentration of DPDAB during application is half what is present in the original product (i.e., 2.5% to 5%). The per-event exposure from mixing and applying the two-component epoxy ranges from 0.07 to 0.14 mg/kg bw/day (for products with 5% to 10%, respectively). The per-event exposure estimate is based on the assumption that dermal absorption is equivalent to absorption following oral intake.

8.9.2 Health effects assessment

The hazard dataset for this substance was considered to be limited and a read-across approach was applied to inform the health effects assessment. 1,3-propanediamine, N-[3-((C_{11-14}, C_{13}-rich)oxy) branched acetate (unknown CAS RN; EC number 931-295-2) was identified as an analogue and it is a UVCB mixture containing DPDAB, its acetate, and other similar constituents with varying carbon-chain lengths (C_{11}-C_{14}) (ECHA 2018g). The representative structures for the analogue and DPDAB are structurally similar, as they are both diamines, possess an ether bond, and contain a carbon chain of approximately 13 carbons. Furthermore, they both share similar physical-chemical properties, such as physical state and boiling points (ECHA 2018g,h). Although toxicokinetic data were not identified, the analogue and DPDAB are predicted to undergo similar metabolic pathways (e.g., addition of alcohol and carboxyl groups, hydrolysis) (OECD QSAR Toolbox 2017).

Repeated-dose toxicity

The short-term effects of the analogue 1,3-propanediamine, N-[3-((C_{11-14}, C_{13}-rich)oxy) branched acetate have been investigated in three studies summarized in a REACH registration dossier, two of which represent range-finding studies with durations of 10 and 14 days (Anonymous 2010, as cited in ECHA 2018g). In the 10-day study, Wistar rats (n=3/sex/dose) were administered 0, 30, 100, and 300 mg/kg bw/day of the substance (in corn oil) by gavage. At the low dose, findings of dyspnea, reduced weight gain, reduced number of lymphocytes (coinciding with thymus weight changes), increased neutrophil/monocyte counts (tissue damage/inflammation), increased platelet counts, reduced albumin (liver damage), reduced bile acids, and increased triglycerides were observed. At higher doses, more severe clinical signs were identified, along with reductions in body weight. In addition, macroscopic findings of stomach mucosa retractions, pancreatic discoloration, reduction in spleen size, and pelvis dilatation were reported. By the end of the study, all animals were either found dead or were sacrificed *in extremis* in the mid- and high-dose groups. A LOAEL of 30 mg/kg bw/day was

determined on the basis of reduced weight gain, effects of the thymus, hematological changes, and clinical chemistry findings.

In a similar study in which Wistar rats (n=3/sex/dose) were administered 0, 3, 10, or 30 mg/kg bw/day of the analogue (in corn oil) by gavage for 14 days, the effects observed at the highest dose (30 mg/kg bw/day) were similar to those observed in the previous study (i.e., clinical signs, reduced body weight, reduced lymphocytes, reduced thymus weight, increased neutrophils/monocytes, decreased albumin, elevated globulins, increased spleen and liver weights) (Anonymous 2010, as cited in ECHA 2018g). Although some of these effects were also observed at lower doses (3 and 10 mg/kg bw/day), the REACH registration dossier indicated that the "NOAEL could be considered to be 10 mg/kg bw/day, as the small changes seen at this level in WBC (elevated in males), liver weights (males) and spleen weights do not show full dose relation…and are also not observed at the higher dose levels in the previous dose range-finding study."

When Wistar rats (n=5/sex/dose) were administered 0, 3, 9, and 25 mg/kg bw/day of the analogue (in corn oil) by gavage for 28 days, similar effects were observed at all dose levels as previous studies (Anonymous 2015, as cited in ECHA 2018g). At the lowest dose, statistically significant effects that exceeded the historical control range included increased reticulocytes, increased absolute/relative neutrophil count, reduced lymphocyte count, increased monocyte count, and reduced albumin in males. In females, there were findings of increased relative neutrophil counts and reduced lymphocyte counts. In addition, some animals had nodular and/or reddish mesenteric lymph nodes accompanied by necrosis and granulomatous inflammation, along with minimal liver granuloma, inflammation and/or submucosal foamy histiocytes in the small intestine. At higher doses, there were also effects on the spleen (extramedullary hemopoiesis), thymus (atrophy, reddish discoloration), lesions in different joints (ankle, tarsal, and/or knee), and reproductive organs (uterus, prostate/seminal weights), accompanied by clinical signs (hunched posture, ruffled fur, dyspnea), reduced food consumption, reduced body weights, and mortality. The histopathological findings in the mesenteric lymph nodes and spleen persisted throughout a 14-day recovery period that was conducted in the high-dose animals. The REACH registration entry indicated that the necrotic and/or inflammatory processes observed in the stomach, small intestine, mesenteric lymph nodes, liver, thymus, heart and joints were considered to be adverse. A LOAEL of 3 mg/kg bw/day was identified.

In a report of a 90-day subchronic study conducted in accordance with OECD TG 408, Wistar rats (n=10/sex/dose) were administered the analogue 1,3-propanediamine, N-[3-(tridecyloxy)propyl]-, branched acetate (in propylene glycol) by gavage at levels of 0, 0.5, 2.2 or 8.8 mg/kg bw/day (Anonymous 2015, as cited in ECHA 2018g). Clinical signs (swelling and hypotonia of the hindlegs, heels, paws, or tail, abnormal gait) and mortality were observed at all doses, with greater frequency at higher doses. At the lowest dose tested, there were statistically significant hematological effects (i.e., increased white blood cells, higher neutrophil count, higher monocyte count, lower hemoglobin, lower hematocrit, lower mean corpuscular volume, lower mean corpuscular

hemoglobin levels) and clinical chemistry changes (decreased albumin, glucose, calcium). At necropsy, lung lesions were observed along with enlarged organs (liver, spleen, mesenteric lymph nodes, iliac lymph nodes), thickened appendages (hindfoot, tail, knee), reduced thigh muscle, and effects on the female reproductive tract (cervix and vagina). These observations were supported by histopathological examinations, which included increased inflammation in the lungs, granulomas in the liver, granulomas in the mesenteric lymph nodes, acinar atrophy of the pancreas, arthritis (tarsal joints, tail vertebra), and myeloid hyperplasia in sternal bone marrow. At higher dose levels, similar effects were observed, but with greater incidence and severity. Furthermore, some of the inflammatory effects extended to additional organs such as the spleen, popliteal lymph nodes, iliac lymph nodes, renal lymph nodes, thymus, and abdominal cavity. These doses were also associated with reduced body weight, food consumption, and mortality. At the highest dose level, some of the animals were sacrificed *in extremis* due to the presence of swollen tarsals/metatarsals, swollen hind legs, and/or abnormal gait. The REACH registration dossier indicated that a NOAEL could not be established, and a LOAEL of 0.5 mg/kg bw/day was therefore identified on the basis of inflammatory effects observed in the small intestine, mesenteric lymph nodes, liver, lungs, spleen, and hind legs.

Developmental and reproductive toxicity

In a report of a prenatal developmental toxicity study conducted in accordance with OECD TG 414, pregnant Wistar rats (n=22 females/dose) were administered 0, 3, 7 or 15 mg/kg bw/day of the analogue 1,3-propanediamine, N-[3-(tridecyloxy)propyl]-, branched acetate (in propylene glycol) by gavage from GD 6 to 20 (15 days) (Anonymous 2015, as cited in ECHA 2018g). At the highest dose, signs of maternal toxicity leading to mortality were observed (lethargy, hunched posture, piloerection, reduced body weight, mortality). Macroscopic effects on the mesenteric lymph nodes (e.g., enlargement) and gastrointestinal tract (e.g., thickened ileum) were observed at all tested dose levels. These effects were accompanied by histopathological findings such as foamy macrophages and granulocytic (necrotizing) inflammation. No treatment-related effects on the number of corpora lutea or implantation sites were identified. In addition, there were no treatment-related effects on the number of viable fetuses, litter size, sex ratio, early or late resorptions or post-implantation loss. At 7 and 15 mg/kg bw/day, there was a trend towards a higher incidence of unossified sternabrae. At the highest dose, a significant decrease in fetal body weights was detected, and a NOAEL of 3 mg/kg bw/day was identified in the REACH registration dossier. These effects occurred in the presence of maternal toxicity.

No reproductive toxicity studies were available for DPDAB or its analogue. No effects on the number of corpora lutea, implantation sites, or post-implantation loss were reported in the aforementioned prenatal developmental toxicity assay (Anonymous 2015, as cited in ECHA 2018g). In the subchronic oral gavage study presented earlier (refer to *Repeated-dose toxicity* section), effects on the female reproductive tract were noted. However, no changes on the estrous cycle were detected. The REACH registration

dossier suggested that these effects were due to the poor health of the animals (Anonymous 2015, as cited in ECHA 2018g).

Genotoxicity and carcinogenicity

DPDAB is not expected to be genotoxic on the basis of the information available from *in vitro* mutagenicity and clastogenicity studies conducted on the analogue (ECHA 2018g). With respect to carcinogenicity, there is a lack of cancer effects observed for the Aliphatic Amines Group in general and a lack of cancer-related structural alerts from modelling software (OECD QSAR Toolbox 2017).

8.9.3 Characterization of risk to human health

Since the hazard dataset for DPDAB was limited, a read-across approach was applied, whereby data from analogues were used to inform the assessment. For both intermittent and chronic exposure scenarios, the subchronic study summarized in a REACH registration dossier for an analogue (Anonymous 2015, as cited in ECHA 2018g) was used for the characterization of risk to DPDAB as it demonstrated the most sensitive health effect in the dataset. A LOAEL of 0.5 mg/kg bw/day was determined based on the inflammatory effects observed at the low-dose level in the small intestine, mesenteric lymph node, liver and lung, in addition to the spleen and hind legs at higher doses.

Table 8-23 provides all relevant exposure estimates, critical effect levels and resulting margins of exposure for characterization of risk to human health for DPDAB from epoxy products available to consumers and environmental media.

Table 8-23. Relevant exposure, critical effect levels and margins of exposure for characterization of risk to DPDAB

Exposure scenario	Population	Exposure estimate (mg/kg bw/day)	Critical effect level (mg/kg bw/day)	MOE
Mixing and applying marine epoxy (5-10%); dermal; per-event	Adult	0.07 to 0.14	0.5[a]	4 to 7
Drinking water intake; oral, chronic	0 to 5 month-olds	3.3×10^{-5}	0.5[a]	15 377

[a] LOAEL of 0.5 mg/kg bw/day was determined from a subchronic study based on the inflammatory effects observed at the low-dose level in small intestine, mesenteric lymph node, liver and lung, in addition to spleen and hind legs at higher doses.

With respect to per-event dermal and inhalation exposure to DPDAB in a marine epoxy product, the MOE of 4 to 7 is considered potentially inadequate to address the uncertainties in the health effects and exposure databases.

With respect to chronic oral exposure to DPDAB from drinking water, the MOE of 15 377 is considered adequate to address uncertainties in the health effects and exposure databases.

8.9.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below.

Table 8-24. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
Dermal and inhalation studies were not identified. Route-to-route extrapolation from oral studies was applied for the characterization of risk following exposures through these routes. Absorption via the dermal and inhalation routes was considered equivalent to absorption via the oral route.	+/-
Studies on chronic toxicity were not identified for any relevant routes of exposure (oral, dermal, inhalation).	+/-

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

9. Conclusion

Considering all available lines of evidence presented in this draft screening assessment, there is risk of harm to the environment from long-chain aliphatic amines. It is proposed to conclude that long-chain aliphatic amines, including the nine long-chain aliphatic amines in this assessment, meet the criteria under paragraph 64(*a*) of CEPA as they are entering or may enter 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. However, it is proposed to conclude that the long-chain aliphatic amines, including the nine long-chain aliphatic amines in this assessment, do not meet the criteria under paragraph 64(*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger to the environment on which life depends.

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to the environment from the four short-chain aliphatic amines (dimethylbenzylamine, diethylenetriamine, dimethylamine, and ethylenediamine). It is proposed to conclude that dimethylbenzylamine, diethylenetriamine, dimethylamine, and ethylenediamine 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 draft screening assessment, it is proposed to conclude that DPDAB meets the criteria under paragraph 64(*c*) of CEPA as it is entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

On the basis of the information presented in this draft screening assessment, it is proposed to conclude that dimethylbenzylamine, ethylenediamine, diethylenetriamine, dimethylamine, hexadecyldimethylamine, octadecylamine, cocoamine, BHTAA, HTAAA, TAAA, TAPDA, TMTADA 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.

It is therefore proposed to conclude that all long-chain aliphatic amines, including hexadecyldimethylamine, octadecylamine, cocoamine, BHTAA, HTAAA, TAAA, TAPDA, DPDAB and TMTADA, meet one or more of the criteria set out in section 64 of CEPA, and that dimethylbenzylamine, ethylenediamine, diethylenetriamine, dimethylamine do not meet any of the criteria set out in section 64 of CEPA.

It is also proposed that long-chain aliphatic amines with C_{14} or greater alkyl chains meet the bioaccumulation criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA, but those with alkyl chains less than C_{14} do not, and that long-chain aliphatic amines do not meet the persistence criteria as set out in the *Persistence and Bioaccumulation Regulations* of CEPA**.**

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Appendix A. Ecological risk classification of organic substances (ERC)

The ecological risks of the four short-chain aliphatic amines (dimethylbenzylamine, ethylenediamine, diethylenetriamine, dimethylamine) in this assessment 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 on the basis of 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 (e.g., median lethal concentration [LC_{50}]) for characterization.

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 scientific literature, from available empirical databases (e.g., OECD QSAR Toolbox 2017), and from responses to surveys under section 71 of CEPA, or they were generated using selected quantitative structure-activity relationship (QSAR) 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 composed of 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 (e.g., 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 (i.e., 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 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 (i.e., mode of toxic action), many of which are predicted values from (Q)SAR models (OECD QSAR Toolbox 2017). However, the impact of this error is mitigated by the fact that overestimation of median lethality will result in a conservative (protective) tissue residue used for critical body residue (CBR) 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 considered to be the current use quantity, and may not reflect future trends.

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

The hazard and exposure classifications for the four short-chain aliphatic amines are summarized in Table A-1.

Table A-1. Ecological risk classification results for the four short-chain aliphatic amines

Substance	ERC hazard classification	ERC exposure classification	ERC risk classification
Dimethylbenzylamine	low	low	low
Ethylenediamine	low	low	low
Diethylenetriamine	low	low	low
Dimethylamine	low	low	low

On the basis of low hazard and low exposure classifications according to information considered under ERC, dimethylbenzylamine, ethylenediamine, diethylenetriamine, dimethylamine 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.

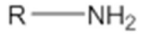
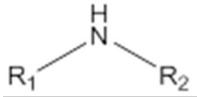
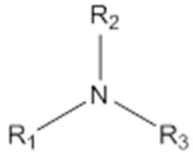
Appendix B. Substance identity information

Aliphatic amines can be defined on the basis of the number of amine functional groups. Monoamines have one amine in the molecule, diamines have two, and triamines have three. Table B-1 describes substances of the Aliphatic Amines Group according to mono-, di- or tri- amines. The aliphatic amines can also be described as primary, secondary or tertiary amines, based on the number of organic substituents associated with the amine, as described in Table B-2. When the organic substituents are alkyl groups, the amine may be described as a mono-, di- or tri- alkyl amine according to the number of alkyl groups (Table B-2). An ether functional group may also be present on the alkyl chain. Substances with this functional group are also known as "ether amines." Some of the aliphatic amines are UVCBs, which have been categorized as primary, secondary or tertiary, based on their representative structures.

Table B-1. Monoamines, diamines and triamines in the Aliphatic Amines Group

Category	Aliphatic amines that fit given category
Monoamines	Dimethylbenzylamine, Hexadecyldimethylamine, Dimethylamine, Octadecylamine, Cocoamine, BHTAA, HTAAA, TAAA
Diamines	Ethylenediamine, TAPDA, DPDAB, TMTADA
Triamines	Diethylenetriamine

Table B-2. Primary, secondary and tertiary aliphatic amines

Category	General structure[a]	Aliphatic amines that fit given category[b]
Primary amine[c]		Ethylenediamine, octadecylamine,cocoamine, HTAAA, TAAA,
Secondary amine[d]		Dimethylamine, BHTAA,
Tertiary amine[e]		Dimethylbenzylamine, hexadecyldimethylamine, TMTADA

[a] R= alkyl chain; an aryl functional group may be attached to the alkyl chain but the aryl group cannot be attached directly to the nitrogen atom
[b] Some diamines and triamines were not included in this column as they fit into more than one category
[c] when R represents an alkyl chain, this may be called a monoalkyl amine
[d] when R represents alkyl chains, this may be called a dialkyl amine
[e] when R represents alkyl chains, this may be called a trialkyl amine

Long-chain aliphatic amines as defined by chemical formulae

$R_1N(R_2)R_3$ (monoamines)
where:
R_1 = H or CH_3
R_2 = H or CH_3 or C_8-C_{22} linear or branched, saturated or unsaturated alkyl chain
R_3 = C_8-C_{22} linear or branched, saturated or unsaturated alkyl chain

OR

$R_1N(R_2)(CH_2)_3OR_4$ (monoamine ethers), or
$R_1N(R_2)(CH_2)_3N(R_3)R_4$ (diamines), or
$R_1N(R2)(CH_2)_3N(R_3)(CH_2)_3OR_4$ (diamine ethers)
where:
R_1, R_2, R_3 = H or CH_3
R_4 = $C_{8\text{-}22}$, linear or branched, saturated or unsaturated alkyl chain

The above description includes aliphatic amines alone or as part of a salt.

Appendix C. Non-exhaustive list of long-chain aliphatic amines

The approach taken in the ecological assessment is to consider all long-chain aliphatic amines that meet the group definition, including but not limited to the nine CAS RNs in the Aliphatic Amines Group. Long-chain aliphatic amines, as captured by the definition of the long-chain aliphatic amine class in the section *Substance identity*, are assessed as a class as they have similar properties, fate and ecological hazard. Long-chain aliphatic amines on the *Domestic Substances List* (DSL), other than those already included in the Aliphatic Amines Group, are listed in Table C-1.

Table C-1. Non-exhaustive list of long-chain aliphatic amines

CAS RN	DSL name
111-86-4	1-Octanamine
112-18-5	1-Dodecanamine, N,N-dimethyl-
112-75-4	1-Tetradecanamine, N,N-dimethyl-
112-90-3	9-Octadecen-1-amine, (Z)-
112-99-2	1-Octadecanamine, N-octadecyl-
124-22-1	1-Dodecanamine
124-28-7	1-Octadecanamine, N,N-dimethyl-
143-27-1	1-Hexadecanamine
929-73-7	1-Dodecanamine, hydrochloride
1120-24-7	1-Decanamine, N,N-dimethyl-
1613-17-8	1-Octadecanamine, N,N-dimethyl-, hydrochloride
1838-08-0	1-Octadecanamine, hydrochloride
1920-05-4	1-Dodecanamine, N,N-dimethyl-, acetate
2016-56-0	1-Dodecanamine, acetate
2016-57-1	1-Decanamine
2190-04-7	1-Octadecanamine, acetate
3007-31-6	1-Dodecanamine, N-dodecyl-
4455-26-9	1-Octanamine, N-methyl-N-octyl-
5538-95-4	1,3-Propanediamine, N-dodecyl-
7173-62-8	1,3-Propanediamine, N-9-octadecenyl-, (Z)-
7378-99-6	1-Octanamine, N,N-dimethyl-
7396-58-9	1-Decanamine, N-decyl-N-methyl-
10460-00-1	9-Octadecen-1-amine, (Z)-, acetate
13281-06-6	1,3-Propanediamine, N-(2-ethylhexyl)-
14676-61-0	1-Propanamine, 3-(tridecyloxy)-
19855-61-9	1-Octadecanamine, N,N-dimethyl-, acetate
22020-14-0	1-Decanamine, N-methyl-N-octyl-
22023-23-0	1,3-Propanediamine, N-[3-(tridecyloxy)propyl]-
24287-35-2	1-Tetradecanamine, N,N-dimethyl-, acetate
25324-14-5	1-Hexadecanamine, N,N-dimethyl-, acetate
28061-69-0	Octadecen-1-amine, N,N-dimethyl-

CAS RN	DSL name
28701-67-9	1-Propanamine, 3-(isodecyloxy)-, acetate
29317-52-0	1-Propanamine, 3-(isononyloxy)-
30113-45-2	1-Propanamine, 3-(isodecyloxy)-
40165-68-2	9-Octadecen-1-amine, N-9-octadecenyl-, (Z,Z)-
50291-24-2	1-Dodecanamine, sulfate
61788-45-2	Amines, hydrogenated tallow alkyl
61788-62-3	Amines, dicoco alkylmethyl
61788-63-4	Amines, bis(hydrogenated tallow alkyl)methyl
61788-91-8	Amines, dimethyl soya alkyl
61788-93-0	Amines, coco alkyldimethyl
61788-95-2	Amines, (hydrogenated tallow alkyl)dimethyl
61789-76-2	Amines, dicoco alkyl
61790-18-9	Amines, soya alkyl
61790-33-8	Amines, tallow alkyl
61790-57-6	Amines, coco alkyl, acetates
65059-85-0	1-Heptadecanamine, N,N-dimethyl-, acetate
67700-98-5	Amines, C_{10-16}-alkyldimethyl
67700-99-6	Amines, di-C_{14-18}-alkylmethyl
68037-91-2	Amines, C_{14-18}-alkyl
68037-92-3	Amines, C_{16-22}-alkyl
68037-95-6	Amines, C_{16-18} and C_{18}-unsatd. alkyl
68037-98-9	Amines, di-C_{14-18}-alkyl
68130-68-7	1,3-Propanediamine, N-[3-(C_{12-18}-alkyloxy)propyl] derivs.
68155-38-4	Amines, C_{14-18} and C_{16-18}-unsatd. alkyl
68439-70-3	Amines, C_{12-16}-alkyldimethyl
68513-50-8	1-Tridecanamine, N-tridecyl-, branched
68603-64-5	Amines, N-(hydrogenated tallow alkyl)trimethylenedi-
68603-65-6	Amines, methylditallow alkyl
68610-26-4	1-Propanamine, 3-(C_{12-15}-alkyloxy) derivs.
68610-68-4	1-Propanamine, 3-(C_{8-10}-alkyloxy) derivs., acetates
68783-23-3	Amines, disoya alkyl
68783-24-4	Amines, ditallow alkyl
68784-38-3	1-Propanamine, 3-(C_{8-10}-alkyloxy) derivs.
68814-69-7	Amines, dimethyltallow alkyl
68855-63-0	Amines, C_{16} and C_{18}-unsatd. alkyl
68909-95-5	1-Propanamine, 3-(tridecyloxy)-, branched and linear
68955-53-3	Amines, C_{12-14}-tert-alkyl
68955-54-4	Amines, C_{16-22}-tert-alkyl
71011-01-3	Amines, bis(hydrogenated tallow alkyl), acetates
71011-03-5	Amines, ditallow alkyl, acetates
75444-69-8	Amines, C_{16-22}-alkyldimethyl
125328-36-1	Amines, C_{20-22}, acetates
125328-37-2	Amines, C_{20-22}-alkyl

CAS RN	DSL name
125328-38-3	Amines, canola-oil alkyl
125328-39-4	Amines, N-canola-oil alkyltrimethylenedi-
125328-41-8	Amines, hydrogenated canola-oil alkyl
125328-42-9	Amines, (hydrogenated canola-oil alkyl)dimethyl
125328-43-0	Amines, hydrogenated rape-oil alkyl
125328-44-1	Amines, hydrogenated rape-oil alkyl, acetates
125328-45-2	Amines, hydrogenated tallow alkyl, distn., residues
125328-46-3	Amines, rape-oil alkyl
1078712-76-1	Amines, (2-ethylhexyl)(hydrogenated tallow alkyl)methyl

Appendix D. Read-across approach for the human health risk assessment

Table D-1. Considerations applied for the identification of relevant analogues for each substance

Substance (CAS RN)	Considerations
Hexadecyldimethylamine (112-69-6)	•Valid CAS RN •Discrete substance •Aliphatic amine: no aromatic rings directly on the nitrogen atom •Structural similarity threshold of at least 60% •Carbon chain length minimum of C8 •Saturated carbon backbone •Lack of alcohol, nitrile, halide functional groups
Octadecylamine (124-30-1)	•Valid CAS RN •Aliphatic amine: no aromatic rings directly on the nitrogen atom •Structural similarity threshold of at least 60% •Saturated or unsaturated carbon backbone •Carbon chain length minimum of C10 •Lack of alcohol, nitrile, halide functional groups
DPDAB (68479-04-9)	•Diamine •Presence of ether bond within carbon chain •Carbon chain length of approximately C13 •Discrete or UVCB substance

Appendix E. Physical-chemical properties of analogues for the human health risk assessment

Table E-1. Physical-chemical property values for hexadecyldimethylamine and its analogues

	Dodecyldimethylamine (CAS 112-18-5)	Hexadecyldimethylamine (CAS 112-69-6)	N,N-dimethyldocosylamine (CAS 21542-96-1)
MW (g/mol)	213.4[a]	269.5[d]	353.7
Physical state	Liquid[b]	Liquid[e]	Solid[i]
Melting point (°C)	-11 to -33[b]	-11[d,e]	41[i]
Boiling point (°C)	237 to >300	> 300[d,f]	>350[i]
Vapour pressure (Pa)	0.009 to 6.4[b]	0.038[f]	0[i]
Water solubility (mg/L)	8.6[c]	5.1 to 18[g,h]	0.001[i]
pKa	9.8[c]	9.9 to10.1[g]	8.8[i]

Abbreviations: MW, molecular weight; NA, not available
References: [a]ChemID 1993-2017; [b]ECHA 2018d (read-across data); [c]Study Submission 2017; [d]ECHA c2007-2018c and ECHA 2018i; [e]SDS 2014a; [f]modelled value; [g]ACD/Percepta c1997-2012
[h]ECHA c2007-2018c (conducted at pH 7.1); [i]ECHA 2018j

Table E-2. Physical-chemical property values for octadecylamine and its analogues

	Amines tallow alkyl (CAS 61790-33-8)	(Z)-octadec-9-enylamine (CAS 112-90-3)	Octadecylamine (CAS 124-30-1)	C16-22-alkyl amines (CAS 68037-92-3)
MW (g/mol)	267	267.5	269.5	283.5
Physical state	Solid[a]	Solid[a]	Solid[b]	Solid[g]
Melting point (°C)	32 to 40[a]	15 to 30[a]	52.9 to 56[c]	38[g]
Boiling point (°C)	200 to 230[a]	128 to 355[a]	346.8 to 348.5[c,d,e]	350[g]
Vapour pressure (Pa)	NA	0.5[a]	0.012[d]	0.022 to 0.036[g]
Density (g/cm^3)	0.79[a]	0.8[a]	0.9	0.95
Water solubility (mg/L)	0.12[a]	0.08[a]	1.6[f]	0.4[g]
pKa	NA	NA	10.6[f]	10.4[g]

Abbreviations: MW, molecular weight; NA, not available
References: [a]EU 2008; [b]SDS 2019; [c]Lide and Frederikse 1996; [d]Modelled for the neutral substance in EPI Suite (c2000-2012) using representative structures for UVCBs; [e]ECHA c2007-2018d; [f]ACD/Percepta c1997-2012; [g]ECHA 2018e

Table E-3. Physical-chemical property values for DPDAB and its analogue

	DPDAB (CAS 68479-04-9)	1,3-propanediamine, N-[3-((C11-14, C13-rich)oxy) branched acetate (Unknown CAS; EC number 931-295-2)
MW (g/mol)	315	Unspecified
Physical state	Liquid[a]	Liquid[e]
Melting point (°C)	-34.4[a]	<-30[e]
Boiling point (°C)	359 to 380[b]	>300[e]
Vapour pressure (Pa)	10^{-3}[b]	0.003 to 0.005[e]
Water solubility (mg/L)	1300 to 19000[c,d]	1300[e]
pKa	NA	7.6[e]

Abbreviations: MW, molecular weight; NA, not available
References: [a]SDS 2017b; [b]Modelled for the neutral substance in EPI Suite (c2000-2012) using representative structures for UVCBs; [c]ECHA c2007-2018g (conducted at pH 7); [d]ACD/Percepta c1997-2012 (modelling done with representative structures at pH 8); [e]ECHA 2018g

Appendix F. Detailed risk quotient summary for long-chain aliphatic amine aquatic exposure scenarios

Table F-1. Summary of aquatic risk quotients for various exposure scenarios for C_8 – C_{14} monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.32	0.22	1.4
Production and processing	1.1	1.1	0.22	4.8
Processing	1.3	1.2	0.22	5.5
Polyurethane foam production (polyol blend)	0.55	0.52	0.22	2.3
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.0018	0.22	0.0081
Down-the-drain release of amine derivatives	0.12	0.11	0.22	0.51
Iron ore flotation	0.25	0.23	0.22	1.1
Formulation of asphalt emulsion	0.59	0.552	0.22	2.5
Formulation of fertilizers	2.0	1.89	0.22	8.6

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-2. Summary of aquatic risk quotients for various exposure scenarios for C_{15} – C_{18} monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.23	0.22	1.1
Production and processing	1.1	0.77	0.22	3.5
Processing	1.3	0.89	0.22	4.1
Polyurethane foam production (polyol blend)	0.55	0.38	0.22	1.7
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.0013	0.22	0.0059

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Down-the-drain release of amine derivatives	0.12	0.08	0.22	0.38
Iron ore flotation	0.25	0.17	0.2	0.78
Formulation of asphalt emulsion	0.59	0.41	0.22	1.8
Formulation of fertilizers	2.0	1.4	0.22	6.3

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-3. Summary of aquatic risk quotients for various exposure scenarios for C_{19} – C_{22} monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.10	0.22	0.47
Production and processing	1.1	0.34	0.22	1.6
Processing	1.3	0.40	0.22	1.8
Polyurethane foam production (polyol blend)	0.55	0.17	0.22	0.77
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.00058	0.22	0.0026
Down-the-drain release of amine derivatives	0.12	0.037	0.22	0.17
Iron ore flotation	0.25	0.076	0.2	0.34
Formulation of asphalt emulsion	0.59	0.18	0.22	0.82
Formulation of fertilizers	2.0	0.62	0.22	2.8

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-4. Summary of aquatic risk quotients for various exposure scenarios for C_{24} (i.e., 2xC_{12}) monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.032	0.22	0.15
Production and processing	1.1	0.11	0.22	0.48

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Processing	1.3	0.12	0.22	0.56
Polyurethane foam production (polyol blend)	0.55	0.052	0.22	0.24
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.00018	0.22	0.00082
Down-the-drain release of amine derivatives	0.12	0.011	0.22	0.052
Iron ore flotation	0.25	0.024	0.2	0.11
Formulation of asphalt emulsion	0.59	0.056	0.22	0.25
Formulation of fertilizers	2.0	0.19	0.22	0.87

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-5. Summary of aquatic risk quotients for various exposure scenarios for C_{26} (i.e., $2xC_{13}$) monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.013	0.22	0.057
Production and processing	1.1	0.041	0.22	0.19
Processing	1.3	0.048	0.22	0.22
Polyurethane foam production (polyol blend)	0.55	0.020	0.22	0.093
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.000070	0.22	0.00032
Down-the-drain release of amine derivatives	0.12	0.0044	0.22	0.020
Iron ore flotation	0.25	0.0092	0.2	0.042
Formulation of asphalt emulsion	0.59	0.022	0.22	0.10
Formulation of fertilizers	2.0	0.074	0.22	0.34

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-6. Summary of aquatic risk quotients for various exposure scenarios for C_{28} (i.e., 2xC_{14}) monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.0048	0.22	0.022
Production and processing	1.1	0.016	0.22	0.071
Processing	1.3	0.018	0.22	0.083
Polyurethane foam production (polyol blend)	0.55	0.0077	0.22	0.035
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.000027	0.22	0.00012
Down-the-drain release of amine derivatives	0.12	0.0017	0.22	0.0076
Iron ore flotation	0.25	0.0035	0.2	0.016
Formulation of asphalt emulsion	0.59	0.0083	0.22	0.038
Formulation of fertilizers	2.0	0.028	0.22	0.13

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-7. Summary of aquatic risk quotients for various exposure scenarios for C_{36} (i.e., 2xC_{18}) monoamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.0001	0.22	< 0.001
Production and processing	1.1	0.0003	0.22	0.002
Processing	1.3	0.0004	0.22	0.002
Polyurethane foam production (polyol blend)	0.55	0.0002	0.22	0.001
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.000001	0.22	< 0.001
Down-the-drain release of amine derivatives	0.12	0.00004	0.22	< 0.001
Iron ore flotation	0.25	0.0001	0.2	< 0.001
Formulation of asphalt emulsion	0.59	0.0002	0.22	0.001

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Formulation of fertilizers	2.0	0.0006	0.22	0.003

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-8. Summary of aquatic risk quotients for various exposure scenarios for C_8 – C_{14} diamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.24	0.22	1.1
Production and processing	1.1	0.79	0.22	3.6
Processing	1.3	0.92	0.22	4.2
Polyurethane foam production (polyol blend)	0.55	0.39	0.22	1.8
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.0013	0.22	0.0061
Down-the-drain release of amine derivatives	0.12	0.085	0.22	0.39
Iron ore flotation	0.25	0.18	0.2	0.80
Formulation of asphalt emulsion	0.59	0.42	0.22	1.9
Formulation of fertilizers	2.0	1.4	0.22	6.5

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-9. Summary of aquatic risk quotients for various exposure scenarios for C_{15} – C_{18} diamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.087	0.22	0.40
Production and processing	1.1	0.29	0.22	1.3
Processing	1.3	0.33	0.22	1.5
Polyurethane foam production (polyol blend)	0.55	0.14	0.22	0.64

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.00049	0.22	0.0022
Down-the-drain release of amine derivatives	0.12	0.031	0.22	0.14
Iron ore flotation	0.25	0.063	0.2	0.29
Formulation of asphalt emulsion	0.59	0.15	0.22	0.69
Formulation of fertilizers	2.0	0.51	0.22	2.3

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Table F-10. Summary of aquatic risk quotients for various exposure scenarios for C_{19} – C_{22} diamines

Scenario	Non-adjusted PECs (µg/L)	Freely dissolved PECs at median TOC (µg/L)	PNEC (µg/L)	RQ (freely dissolved)
Production	0.34	0.017	0.22	0.079
Production and processing	1.1	0.057	0.22	0.26
Processing	1.3	0.066	0.22	0.3
Polyurethane foam production (polyol blend)	0.55	0.028	0.22	0.13
Polyurethane foam production (flexible polyurethane foam)	0.0019	0.00010	0.22	0.00044
Down-the-drain release of amine derivatives	0.12	0.0061	0.22	0.028
Iron ore flotation	0.25	0.013	0.2	0.057
Formulation of asphalt emulsion	0.59	0.030	0.22	0.14
Formulation of fertilizers	2.0	0.10	0.22	0.47

Abbreviations: PNEC, predicted no-effect concentration; PEC, predicted exposure concentration; RQ: risk quotient; TOC, total organic carbon

Appendix G. Summary of weighted lines of evidence

The level of confidence refers to the combined influence of data quality and variability, data gaps, causality, plausibility and any extrapolation required within the line of evidence. The relevance refers to the impact the line of evidence has when determining the potential to cause harm in the Canadian environment. Qualifiers used in the analysis ranged from low to high, with the assigned weight having five possible outcomes.

Table G-1. Weighted lines of key evidence considered to determine the potential for long-chain aliphatic amines to cause harm in the Canadian environment

Line of evidence	Level of confidence[a]	Relevance in assessment[b]	Weight assigned[c]
Similarity in chemical structure for read-across purposes	high	moderate	moderate-high
Environmental fate and behaviour (ionic nature)	moderate	high	moderate-high
Persistence in the environment	moderate	moderate	moderate
Bioaccumulation in aquatic organisms	moderate	moderate	moderate
Mode of action and/or other non-apical data	low	high	moderate
PNEC for aquatic organisms	moderate	high	moderate-high
PNEC for benthic organisms	moderate	low	low-moderate
PNEC for soil organisms	moderate	moderate	moderate
PECs in water- Production	high[d]	high	high
PECs in water- Production and processing	high[d]	high	high
PECs in water- Processing	moderate	high	moderate-high
PECs in water- Polyurethane foam production (polyol blend)	high	high	high
PECs in water- Polyurethane foam production (flexible polyurethane foam)	high	high	high
PECs in water- Down-the-drain release of amine derivatives	low[e]	high	moderate
PECs in water- Iron ore extraction	moderate[d]	high	moderate-high
PECs in water- Formulation of asphalt emulsion	high	high	high
PECs in water- Formulation of fertilizers	moderate	moderate	moderate
PECs in soil	moderate	moderate	moderate
RQ for water- Production	high[d]	high	high
RQ for water- Production and processing	high[d]	high	high
RQ for water- Processing	moderate	high	moderate-high
RQ for water- Polyurethane foam production (polyol blend)	high	high	high
RQ for water- Polyurethane foam production (flexible polyurethane foam)	high	high	high

Line of evidence	Level of confidence[a]	Relevance in assessment[b]	Weight assigned[c]
RQ for water- Down-the-drain release of amine derivatives	moderate[e]	high	moderate-high
RQ for water- Iron ore extraction	moderate[d]	high	moderate-high
RQ for water- Formulation of asphalt emulsion	high	high	high
RQs for water- Formulation of fertilizers	moderate	moderate	moderate
RQ for soil	moderate	moderate	moderate

[a] Level of confidence is determined according to data quality, data variability, data gaps and fitness for purpose.
[b] Relevance refers to the impact of the evidence in the assessment.
[c] Weight is assigned to each line of evidence according to the combined level of confidence and relevance in the assessment.
[d] Although PECs are considered to be underestimates for these scenarios, there is high confidence in the overall outcome since a risk was identified for these scenarios for some alkyl-chain length categories despite the use of non-conservative assumptions. It is recognized that some alkyl-chain categories with low RQs might in reality pose a risk if PECs that are more conservative are used.
[e] The PEC is considered to be an underestimate of the actual environmental concentration and thus RQs are underestimated. Therefore, the actual risk to the environment from down-the-drain releases is higher than calculated here, and some alkyl-chain categories in reality might pose a risk to the environment.

Appendix H. Parameters to estimate exposures to products available to consumers in Canada

Exposure estimates were calculated using default body weights of 74 kg for 19 year-olds and over, 62 kg for 14- to 18 year-olds, 42 kg for 9- to 13 year-olds, 23 kg for 4- to 8-year-olds, 15 kg for 2- to 3 year-olds, 11 kg for 1 year-olds, 9.1 kg for 6 to 11 month-olds, and 6.3 kg for 0- to 5 month-olds (Health Canada 2015b). The estimated inhalation and dermal exposure parameters for cosmetics and other products available to consumers are described in Tables H-1 and H-2, respectively.

Table H-1. Exposure parameter assumptions for inhalation and dermal cosmetic scenarios

Product (substance)	Assumptions[a]
Facial Cleanser (NHP) (Hexadecyldimethyl-amine)	Concentration of hexadecyldimethylamine: 0.13% Frequency of use: twice per day for adults and adolescents as indicated by directions of use[b] Dermal – Direct contact, instant application Product amount: 1.6 g (19 year-olds and over) (Loretz et al. 2008), and 1.2 g (14- to 18 year-olds and 9- to 13 year-olds) (Ficheux et al. 2015) Retention factor: 0.01
Shaving cream – body (Octadecylamine)	Concentration of octadecylamine: 0.1% Retention factor: 0.01 Shaving cream Frequency of Use: 0.29 per day (19 year-olds and over, 14- to 18 year-olds, and 9- to 13 year-olds) (Biesterbos et al. 2013) Dermal Product amount: 12.7 g (19 year-olds and over and 14- to 18 year-olds) (Ficheux et al. 2016), 9.9 g (9- to 13 year-olds) (surface area adjustment)
Rinse-off hair conditioner (Cocoamine)	Concentration of cocoamine: 0.5% Frequency of use: 1.1 per day (19 year-olds and over) (Loretz et al 2008), 0.7 per day for (14- to 18 year-olds and 9- to 13 year-olds), 0.5 per day (4- to 8 year-olds), and 0.45 per day (2- to 3 year-olds) (Wu et al. 2010) Dermal Product amount: 13.1 g (19 year-olds and over) (Loretz et al. 2008), 10 g (14- to 18 year-olds), 7.8 g (9- to 13 year-olds and 4- and 8 year-olds) (Ficheux et al. 2016), and 5.2 g (2- to 3 year-olds) (Garcia-Hidalgo et al. 2017) Retention factor: 0.01

[a] Unless otherwise stated, the retention factor is assumed to be 1

[b] Personal communication, e-mail from Natural and Non-prescription Health Products Directorate, HC to the Existing Substances Risk Assessment Bureau, HC, dated December 16, 2018; unreferenced

Table H-2. Dermal and inhalation exposure parameter assumptions for products available to consumers.

Exposure scenario	Assumptions
Post-application off-gassing of PUF products inside a car (Dimethylbenzylamine)	Total daily exposure: C x ([UF x T x I] ÷ BW) C: Concentration of dimethylbenzylamine in the air: 6.1 x 10^{-3} mg/m^3 (Rampfl et al. 2008)[b] UF: uptake fraction: 1 T: Exposure time per event: 3 hours = 0.125 day I: Inhalation rate of infant: 3.7 m^3/day (US EPA 2011 [modified]) BW: Body weight of infant: 6.3 kg (Health Canada 2015b)
Mixing and application of two-component marine epoxy adhesive (Dimethylbenzylamine; DPDAB)	Concentration of dimethylbenzylamine in one component of product: 10% Concentration of dimethylbenzylamine after mixing two components: 5% Concentration of DPDAB in one component of product: 5-10% Concentration of DPDAB after mixing two components: 2.5-5% Scenario: mixing/loading and application of two-component glue in DIY Fact Sheet (RIVM 2007). <u>Mixing</u> Inhalation – Exposure to vapour, evaporation model (applicable only to dimethylbenzylamine due to the low VP of DPDAB) Exposure duration: 5 minutes Product amount: 20 g Room volume: 1 m^3 Inhalation rate: 15.1 m^3/day (US EPA 2011 [modified]) Ventilation rate: 0.6 change per hour Mass transfer coefficient: 10 m/hr Release area mode: constant Release area: 0.002 m^2 Emission duration: 5 minutes Molecular weight matrix: 3000 g/mol Dermal – direct contact, instant application Exposed area: 2 cm^2 Product amount: 0.05 g <u>Application</u> Inhalation – Exposure to vapour, evaporation model (applicable only to dimethylbenzylamine due to the low VP of DPDAB) Exposure duration: 240 minutes Product amount: 20 g Inhalation rate: 15.1 m^3/ day (US EPA 2011 [modified]) Room volume: 34 m^3 [c] Ventilation rate: 1.5 change per hour [c] Mass transfer coefficient: 10 m/hr Release area mode: increasing Release area: 0.05 m^2 Application duration: 30 minutes

Exposure scenario	Assumptions
	Molecular weight matrix: 3000 g/mol Dermal – direct contact, instant application Exposed area: 43 cm^2 Product amount: 0.1 g
Shoe polish product (Ethylenediamine)	Concentration of ethylenediamine: 0.25% Frequency of use: 26 per year Scenario: application of shoe cream in cleaning products fact sheet (RIVM 2018) Dermal – direct contact, instant application Exposed area: 215 cm^2 Product amount: 0.1g
Mixing and application of two-component glue for small DIY projects (Diethylenetriamine)	Concentration in one component: 1% Concentration after mixing two components: 0.5% Scenario: mixing and application of two-component glue in DIY Fact Sheet (RIVM 2007a). <u>Mixing</u> Inhalation – Exposure to vapour, evaporation model Exposure duration: 5 minutes Product amount: 20 g Room volume: 1 m^3 Ventilation rate: 0.6 change per hour Inhalation rate: 15.1 m^3/day (US EPA 2011 [modified]) Mass transfer coefficient: 10 m/hr Release area mode: constant Release area: 0.002 m^2 Emission duration: 5 minutes Molecular weight matrix: 3000 g/mol Dermal – direct contact, instant application Exposed area: 2 cm^2 Product amount: 0.05 <u>Application</u> Inhalation – Exposure to vapour, evaporation model Exposure duration: 240 minutes Product amount: 20 g Room volume: 20 m^3 Ventilation rate: 0.6 change per hour Inhalation rate: 15.1 m^3/day (US EPA 2011 [modified]) Mass transfer coefficient: 10 m/hr Release area mode: increasing Release area: 0.05 m^2 Application duration: 5 minutes (Gorilla Glue Inc. [modified 2019]) Molecular weight matrix: 3000 g/mol Dermal – direct contact, instant application Exposed area: 43 cm^2 Product amount: 0.1 g

Exposure scenario	Assumptions
Mixing and application of two-component marine epoxy filler (Diethylenetriamine)	Concentration in one component: 1% Concentration after mixing two components: 0.5% Scenario: mixing/loading and application of two-component filler (RIVM 2007). <u>Mixing</u> Inhalation – Exposure to vapour, constant rate Exposure duration: 2 minutes (TDS 2018) Product amount: 113 g (TDS 2018) Room volume: 1 m^3 Ventilation rate: 0.6 change per hour Inhalation rate: 15.1 m^3/day (US EPA 2011 [modified]) Mass transfer coefficient: 10 m/hr Release area mode: increasing Emission duration: 2 minutes (TDS 2018) Molecular weight matrix: 3000 g/mol Dermal – direct contact, instant application Exposed area: 2 cm^2 Product amount: 0.05 g <u>Application</u> Inhalation – Exposure to vapour, evaporation model Exposure duration: 20 minutes (TDS 2018) Product amount: 113 g (TDS 2018) Room volume: 20 m^3 Ventilation rate: 0.6 change per hour Inhalation rate: 15.1 m^3/day (US EPA 2011 [modified]) Mass transfer coefficient: 10 m/hr Release area mode: increasing Release area: 0.005 m^2 Application duration: 20 minutes (TDS 2018) Molecular weight matrix: 3000 g/mol Dermal – direct contact, instant application Exposed area: 22 cm^2 Product amount: 0.2 g
Jacket synthetic outer material (Hexadecyldimethylamine)	Estimated concentration of hexadecyldimethylamine in outer material of jacket: 96 µg/g product (Tønning et al. 2009) Dermal (wearing of jacket): Estimated daily exposure via dermal route = (SA × AW × TPF × C) / BW SA (surface area)[d] = 2770 cm^2 for 2- to 3 year-olds (Health Canada 2018) AW (Area weight of textile) = 1 mg/cm2 (US EPA 2012)[e] TPF (textile penetration factor) = 0.1[f] C (concentration in textile) = 96 µg/g BW (body weight) = 15 kg (Health Canada 2015b)

Exposure scenario	Assumptions
	Oral (mouthing of jacket material): Estimated daily exposure via oral route = (SA x AW x C) / BW SA (surface area; oral: textile object mouthed) = 20 cm^2 (RIVM 2012)
Automotive transmission fluid additive (Octadecylamine)	Product scenario: application of lubricant – motor oil (Versar, Inc. 1986) Dermal Estimated daily exposure via dermal route: (F x D x A x C) / BW C (concentration of octadecylamine) = 0.001% F (film thickness) = 0.0159 cm A (contact area) = 400 cm^2 D (density of product) = 0.88 g/cm^3 BW (body weight) = 74 kg (19 year-olds and over) (Health Canada 2015b)

[a] Based on air concentration from treated crawl space area 144 hours post application
[b] Based on 1-hour air concentration
[c] Room volume and ventilation rate for a standard garage
[d] Total surface area of trunk and arms
[e] The area weight of textiles can vary greatly depending on the type of material. An area weight of 1 mg/cm^2 for synthetic textiles is recommended by the US EPA in Standard Operating Procedures for Residential Pesticide Exposure Assessment.
[f] Driver et al. 2007

Appendix I. SCREEN3: Model and inputs

SCREEN3 is a screening-level Gaussian air dispersion model based on the Industrial Source Complex (ISC) model (for assessing pollutant concentrations from various sources in an industry complex) (SCREEN3 2011). The driver for air dispersion in the SCREEN3 model is wind. The maximum calculated exposure concentration is selected based on a built-in meteorological data matrix of different combinations of meteorological conditions, including wind speed, turbulence and humidity. This model directly predicts concentrations resulting from point, area and volume source releases. SCREEN3 gives the maximum concentrations of a substance at chosen receptor heights and at various distances from a release source in the direction downwind from the prevalent wind one hour after a given release event. During a 24-hour period, for point emission sources, the maximum 1-hour exposure (as assessed by the ISC Version 3) is multiplied by a factor of 0.4 to account for variable wind direction. This gives an estimate of the air concentration over a 24-hour exposure (US EPA 1992; SCREEN3 2011). Similarly, for exposure events happening over the span of a year, it can be expected that the direction of the prevalent winds will be more variable and uncorrelated to the wind direction for a single event; thus, the maximum amortized exposure concentration for 1 year is determined by multiplying the maximum 1-hour exposure by a factor of 0.08 (US EPA 1992; SCREEN3 2011). The parameters used to estimate ambient air concentrations using the SCREEN3 model are presented in Table I-1 below.

Table I-1. Parameters used in SCREEN3 for air releases from industrial facilities

Substance	Dimethylbenzylamine	Ethylenediamine	Dimethylamine
Source type	Area	Area	Area
Effective emission area[a]	500 m x 500 m	100 m x 100 m	100 m x 100 m
Receptor height[b]	1.74 m	1.74 m	1.74 m
Source release height[a]	30 m	5 m	5 m
Adjustment factor[c]	0.4	0.4	0.4
Urban-rural option	Urban	Urban	Urban
Meterology[d]	1 (full meteorology)	1 (full meteorology)	1 (full meteorology)
Minimum and maximum distance	0-3000 m	0-3000 m	0-3000 m
Distance from source facility to residential areas[a]	1000 m	500 m	3000 m

[a] Site specific; based on aerial photograph analysis and professional judgement [b] Average adult height (Curry et al. 1993)
[c] Factor to account for variable wind direction over a 24-hour period (US EPA 1992)
[d] Default value in SCREEN3

Appendix J. Parameters to estimate drinking water exposure

Table J-1. Human exposure parameter inputs and assumptions for releases to wastewater scenarios

Substance	Dimethyl-benzylamine	Ethylenediamine	Diethylenetriamine
Scenario	Industrial release	Industrial release	Industrial release
Wastewater treatment system (WWTS) removal rate (%)[a]	19.4	85	82.7
Number of industrial sites[b]	1	1	1
Release days (per year)[b]	250	250	250
Daily release to wastewater (%)	4[c]	4[c]	4[c]
Receiving water body[b]	Thames River, London ON	Thames River, London ON	Thames River, London ON

[a] ECCC 2016a
[b] NSACB EAU Drinking Water Workbook default
[c] Based on 3% as container residues and 1% as transfer line/process vessel residues for liquid substance

Table J-2. Estimated drinking water exposure (mg/kg bw/day)[a,b] by various age groups within the general population of Canada

Age group	Hexadecyldimethylamine[c]	Octadecyldimethylatmine[d]	Cocoamine[d]	BHTAA[f]	DPDAB[g]
0-5 month (breast fed)[h,i]	N/A	N/A	N/A	N/A	N/A
0- to 5 month-olds (formula fed)[h,j]	7.0×10^{-5}	1.7×10^{-4}	1.5×10^{-4}	1.5×10^{-4}	3.0×10^{-5}
6- to 11 month-olds[k]	5.0×10^{-5}	1.1×10^{-4}	9.0×10^{-5}	9.0×10^{-5}	2.0×10^{-5}
1 year-olds[l]	2.0×10^{-5}	4.0×10^{-5}	4.0×10^{-5}	4.0×10^{-5}	8.12×10^{-6}
2- to 3 year-olds[m]	2.0×10^{-5}	4.0×10^{-5}	3.0×10^{-5}	3.0×10^{-5}	7.11×10^{-6}
4-to 8 year-olds[n]	1.0×10^{-5}	3.0×10^{-5}	3.0×10^{-5}	3.0×10^{-5}	5.71×10^{-6}
9-to 13 year-olds[o]	9.69×10^{-6}	2.0×10^{-5}	2.0×10^{-5}	2.0×10^{-5}	4.37×10^{-6}
14- to 18 year-olds[p]	9.67×10^{-6}	2.0×10^{-5}	2.0×10^{-5}	2.0×10^{-5}	4.36×10^{-6}
19 year-olds and over[q]	1.0×10^{-5}	3.0×10^{-5}	2.0×10^{-5}	2.0×10^{-5}	5.13×10^{-6}

Abbreviations: N/A, not applicable

[a] Based on an estimated surface water concentration as modelled from the EAU Drinking Water Spreadsheet using parameters from Table J-1.
[b] The use of a modelled surface water concentration to estimate drinking water intake may be conservative as water treatment is likely to occur prior to distribution for consumption.
[c] PEC=0.55 µg/L (Section 7.2.4)
[d] PEC=1.3 µg/L (section 7.2.3)
[e] PEC=1.12 µg/L (section 7.2.2)
[f] PEC=1.12 µg/L (section 7.2.2)
[g] PEC=0.248 µg/L (section 7.2.6)
[h] Assumed to weigh 6.3 kg (Health Canada 2015b)
[i] Exclusively for breast milk-fed infants, assumed to consume 0.744 L of breast milk per day (Health Canada 2018), and breast milk is assumed to be the only dietary source
[j] Exclusively for formula-fed infants, assumed to drink 0.826 L of water per day (Health Canada 2018), where water is used to reconstitute formula
[k] Assumed to weigh 9.1 kg (Health Canada 2015b). For breast milk-fed infants, assumed to consume 0.632 L of breast milk per day (Health Canada 2018). For formula-fed infants, assumed to drink 0.764 L of water per day (Health Canada 2018), where water is used to reconstitute formula
[l] Assumed to weigh 11.0 kg (Health Canada 2015b), and to drink 0.36 L of water per day (Health Canada 2017)
[m] Assumed to weigh 15 kg (Health Canada 2015b), and drink 0.43 L of water per day (Health Canada 2017)
[n] Assumed to weigh 23 kg (Health Canada 2015b), and drink 0.53 L of water per day (Health Canada 2017)
[o] Assumed to weigh 42 kg (Health Canada 2015b) and drink 0.74 L of water per day (Health Canada 2017)
[p] Assumed to weigh 62 kg (Health Canada 2015b), and drink 1.09 L of water per day (Health Canada 2017)
[q] Assumed to weigh 74 kg (Health Canada 2015b), and drink 1.53 L of water per day (Health Canada 2017)

Appendix K. Levels of aliphatic amines in food

The dietary exposure to ethylenediamine was estimated by multiplying the mean ethylenediamine concentration for each food category with each mean and 90th percentile single day 'all persons' consumption amounts for each broad food group from the Canadian Community Health Survey (Statistics Canada 2004). All persons' exposure estimates are generated by taking the total number of survey respondents into consideration. The exposure estimates for each food category were then summed to yield an estimate of total dietary exposure for various age groups. As the food categories for which ethylenediamine occurrence data are available are a regular part of the diet of Canadians, all persons consumption figures were considered suitable for use. The summary of ethylenediamine concentrations for food categories included in the dietary exposure assessment are presented in Table K-1 below.

Table K-1. Summary of ethylenediamine concentrations for food categories included in the dietary exposure assessment[a]

Food category	Total number of samples	Number of positive samples (%)	Range[b] (µg/g)	Mean[c] (µg/g)
Fruit	14 775	2513 (17)	0.0049 - 14.1	0.055
Grain products	62	19 (31)	0.040 - 2.1	0.096
Honey	2645	55 (2)	0.019 - 1.1	0.036
Fruit juice	37	2 (5)	0.040 - 0.16	0.043
Nuts	9	1 (11)	0.0080 - 0.065	0.029
Vegetables	13 775	2104 (15)	0.0080 - 12.7	0.058

[a] Canadian Food Inspection Agency. National Chemical Residue Monitoring Program. Surveys 2009-2018.
[b] Minimum value is the lowest reported limit of detection (LOD)
[c] Concentrations calculated where samples reporting EDA concentrations below their LOD were set to their respective LODs (LOD range: 0.0049 to 0.08 µg/g)

Table K-2. Levels of dimethylamine naturally occurring in food

Food category used in dietary exposure assessment	Food type	Maximum DMA concentration (ppm)	Food with the maximum concentration	Reference
Banana	Fruits and vegetables	0.225	Banana	Kataoka et al. 1995
Cabbage	Fruits and vegetables	2.8	Red cabbage	Neurath et al. 1977 [VCF]‡
Cauliflower and broccoli	Fruits and vegetables	14	Cauliflower	Neurath et al. 1977 [VCF]‡
Celery	Fruits and vegetables	5.1	Celery	Neurath et al. 1977 [VCF]‡
Dried mushrooms	Fruits and vegetables	9.99	Dried fungi	Kataoka et al. 1995

Garlic	Fruits and vegetables	4.46	Garlic	Kataoka et al. 1995
Kale	Fruits and vegetables	5.5	Kale	Neurath et al. 1977 [VCF]‡
Beans	Fruits and vegetables	0.6	Beans	Neurath et al. 1977 [VCF]‡
Lettuce (greens)	Fruits and vegetables	7.2	Green salad	Neurath et al.1977 [VCF]‡
Onion	Fruits and vegetables	0.46	Onion	Kataoka et al. 1995
Peas	Fruits and vegetables	2.2	Shelled peas	Neurath et al.1977 [VCF]‡
Radish	Fruits and vegetables	1.1	Radish	Neurath et al.1977 [VCF]‡
Red pepper	Fruits and vegetables	2.04	Red pepper	Kataoka et al. 1995
Tomato	Fruits and vegetables	0.01	Fresh tomato	[VCF]‡
Tomato juice	Fruits and vegetables	0.01	Fresh tomato	[VCF]‡
Beer	Beverages (non-dairy)	3.16	Beer	Kataoka et al. 1995
Coffee	Beverages (non-dairy)	4	Coffee	[VCF]‡
Spirits, liqueurs and coolers	Beverages (non-dairy)	0.1	Spirits and liqueurs	Pfundstein et al. 1991
Tea	Beverages (non-dairy)	0.1	Tea	Pfundstein et al. 1991
Wine	Beverages (non-dairy)	1.2	Wine	Kataoka et al. 1995
Cheese	Dairy	1.47	Cheese	Kataoka et al. 1995
Milk	Dairy	6.93	Cow’s milk	Kataoka et al. 1995
Evaporated milk	Dairy	3.15	Evaporated milk	Singer and Lijinsky 1976. [VCF]‡
Other dairy	Dairy	2.6	Dairy products	Pfundstein 1991
Egg yolk	Egg	5.04	Egg yolk	Kataoka et al. 1995

Eggs whole	Egg	1.66	Egg yolk	Kataoka et al. 1995
Albacore tuna, raw	Meat and seafood	3.6	Albacore, raw	Perez Martin et al. 1987 [VCF]‡
Anchovies, canned	Meat and seafood	173	Anchovies, canned	Lin and Lai 1980
Beef	Meat and seafood	1.21	Beef	Kataoka et al. 1995
Canned tuna	Meat and seafood	23	Canned tuna	Singer and Lijinsky 1976 [VCF]‡
Caviar	Meat and seafood	97	Caviar	Kataoka et al. 1995
Chicken	Meat and seafood	3.6	Chicken	Pfundstein et al. 1991
Cod, cooked	Meat and seafood	19	Cod, cooked	Singer and Lijinsky 1976 [VCF]‡
Cod, dry salted	Meat and seafood	48.6	Cod, salted	Kataoka et al. 1995
Cod, raw	Meat and seafood	92	Cod, raw	Singer and Lijinsky 1976 [VCF]‡
Cured pork bacon	Meat and seafood	0.2	Cured pork bacon	Patterson and Mottram 1974 [VCF]‡
Haddock	Meat and seafood	48.8	Haddock	Fernández-Salguero and Mackie 1987 [VCF]‡
Hake	Meat and seafood	152	hake fillet, cooked	Castell et al. 1971
Ham	Meat and seafood	3.01	Ham steak	Zeisel and DaCosta 1986
Herring (cooked, pickled, salted)	Meat and seafood	7.8	Herring, salted	Neurath et al. 1977 [VCF]‡
Herring, raw	Meat and seafood	5.6	Herring, raw edible	Fernández-Salguero and

				DaCosta 1987 [VCF]‡
Mackerel	Meat and seafood	113.4	Spotted mackerel	Kataoka et al. 1995
Oyster	Meat and seafood	1.86	Oyster	Kataoka et al. 1995
Salmon	Meat and seafood	82	Salmon, raw	Singer and Lijinsky 1976 [VCF]‡
Sardines, canned	Meat and seafood	16.4	Sardines, canned	Lin and Lai 1980
Sausages	Meat and seafood	5.2	Sausages	Pfundstein et al. 1991
Squid	Meat and seafood	38.3	Squid, raw	Perez Martin et al.1987 [VCF]‡
Trout	Meat and seafood	6.75	Trout, raw	Singer and Lijinsky 1976 [VCF]‡
Trout, canned	Meat and seafood	24.1	Trout, canned	Lin and Lai 1980
Barley	Grains and legumes	9.4	Barley	[VCF]‡
Bread	Grains and legumes	5.3	Bread	Pfundstein et al. 1991 [VCF]‡
Maize	Grains and legumes	3.5	Maize grains	Neurath et al. 1977 [VCF]‡
Soybeans	Grains and legumes	0.4	Soybean, raw	[VCF]‡
Almond	Nuts	1.76	Almond	Kataoka et al. 1995
Pickles	Miscellaneous	1.4	Pickled cucumber	Neurath et al. 1977 [VCF]‡
Paprika	Miscellaneous	1	Red paprika	Neurath et al. 1977 [VCF]‡
Confectionary	Miscellaneous	0.7	Confectionary	Pfundstein et al. 1991
Black pepper	Miscellaneous	7.97	Black pepper	Kataoka et al. 1995
Soups	Miscellaneous	4.8	Soup	Pfundstein et al. 1991

Animal fats	Fats and oils	3.4	Animal fats	Pfundstein et al. 1991
Plant fats	Fats and oils	0.1	Plant fats	Pfundstein et al. 1991