Government of Canada Gouvernement du Canada

Canada

Draft Screening Assessment

2H-Azepin-2-one, hexahydro- (Caprolactam)

Chemical Abstracts Service Registry Number 105-60-2

Environment and Climate Change Canada
Health Canada

August 2021

Synopsis

Pursuant to section 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 2H-azepin-2-one, hexahydro-, hereinafter referred to as caprolactam. The Chemical Abstracts Service Registry Number (CAS RN[1]) for caprolactam is 105-60-2. This substance was identified as a priority for assessment as it met categorization criteria under subsection 73(1) of CEPA.

Caprolactam occurs naturally in some plants. Canadian manufacture quantities are not available for caprolactam. The total annual imports of caprolactam into Canada between 2014 and 2018 ranged from 16 639 255 kg (2018) to 21 722 366 kg (2017), according to the Canadian International Merchandise Trade Database.

Caprolactam is primarily used as an intermediate in the production of Nylon 6 polymers, which have a broad range of uses including textiles, carpets, industrial yarns, engineering plastics for industrial and medical applications as well as some products available to consumers such as cosmetics, diapers, and 3D printing filaments. Some residual caprolactam may be present in manufactured articles made with Nylon 6. Caprolactam is also used as a plasticizer, and as a component in the manufacturing of paints and coatings, glue sticks and other adhesives. Caprolactam may also be used as a component in the manufacture of certain food packaging materials and as a food flavouring agent.

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

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to the environment from caprolactam. It is proposed to conclude that caprolactam does not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as it is not entering the environment in a quantity or concentration or under

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

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.

In terms of potential effects on human health, in laboratory studies conducted via the oral route with caprolactam, offspring effects (reduced body weights), and clinical effects were observed. Local larynx effects (keratinization of the metaplastic epithelium) were observed in inhalation studies. Potential exposure of the general population of Canada to caprolactam can occur through environmental media (e.g., indoor air) and in food packaging materials. Potential exposure to caprolactam via food flavouring agents is considered to be negligible. From the use of products available to consumers, the predominant sources of exposure are from glue sticks and from Nylon 6 in carpets, lipsticks, diapers, and 3D printing filaments. On the basis of estimates of exposure compared with critical health effect levels identified from laboratory studies, the margins of exposure are considered to be adequate to address uncertainties in the health effects and exposure data used to characterize risk.

Considering all the information presented in this draft screening assessment, it is proposed to conclude that caprolactam does not meet the criteria under paragraph 64(*c*) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore proposed to conclude that caprolactam does not meet any of the criteria set out in section 64 of CEPA.

Table of Contents

List of Tables

1. Introduction

Pursuant to section 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 2H- azepin-2-one, hexahydro-, hereinafter referred to as caprolactam, to determine whether this substance presents or may present a risk to the environment or to human health. Caprolactam was identified as a priority for assessment as it met categorization criteria under subsection 73(1) of CEPA (ECCC, HC [modified 2017]).

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

Caprolactam has been reviewed internationally through the Organisation for Economic Co-operation and Development (OECD) Cooperative Chemicals Assessment Programme and there is a Screening Information Dataset (SIDS) Initial Assessment Report (SIAR) available (OECD 2001). 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. Caprolactam has also been reviewed by the International Agency for Research on Cancer (IARC) (1999). The OECD SIAR and IARC documents were used to inform the health effects section of this screening assessment. Caprolactam was also reviewed by the US Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS 1988).

This draft screening assessment includes consideration of information on chemical properties, environmental fate, hazards, uses and exposures, including additional information submitted by stakeholders. Relevant human health data were identified up to June 2019 and targeted literature searches were conducted up to October 2019. Empirical data from key studies as well as results from models were used to reach proposed conclusions.

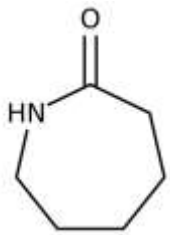
This draft screening assessment was prepared by staff in the CEPA Risk Assessment Program at Health Canada and Environment and Climate Change Canada and incorporates input from other programs within these departments. The ecological portion of this assessment is based on the ERC document (published July 30, 2016), which was subject to an external review as well as a 60-day public comment period.

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.[2] This draft screening assessment presents the critical information and considerations on which the proposed conclusion is based.

2. Substance identity

The Chemical Abstracts Service Registry Number (CAS RN[3]), *Domestic Substances List* (DSL) name, common name and representative structure for caprolactam are presented in Table 2-1.

Table 2-1. Substance identity

CAS RN	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
105-60-2	2H-Azepin-2-one, hexahydro- (caprolactam)	 $C_6H_{11}NO$	113.16

[2] 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.

[3] 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.

3. Physical and chemical properties

A summary of physical and chemical property data of caprolactam is presented in Table 3-1. Additional physical and chemical properties are reported in ECCC (2016b).

Table 3-1. Physical and chemical property values (at standard temperature unless indicated otherwise) for caprolactam

Property	Value[a]
Melting point (°C)	69.2
Vapour pressure (Pa)	0.13 (at 20°C)
Henry's law constant ($Pa \cdot m^3/mol$)	$1.9x10^{-3}$ [b]
Water solubility (mg/L)	$4.6x10^6$ (at 20°C)
Log K_{ow} (dimensionless)	0.12 (at 25°C)
K_{oc} (dimensionless)	57[c]

Abbreviations: K_{ow}, octanol-water partition coefficient; K_{oc}, soil adsorption coefficient
[a] Experimental values obtained from OECD (2001) unless otherwise indicated.
[b] This parameter was modelled using HENRYWIN v3.20 (EPI Suite c2000-2012).
[c] This parameter was modelled using a structure estimation method (Swann et al. 1983 as cited in HSDB 1983-).

4. Sources and uses

Canadian manufacture quantities are not available for caprolactam. This substance was not included in a survey issued pursuant to section 71 of CEPA; however, information was available in the Canadian International Merchandise Trade Database (CIMT). According to the CIMT, the annual total import quantity of caprolactam into Canada from 2014 to 2018 was approximately 19 000 000 kg on average and ranged from 16 639 255 kg (in 2018) to 21 722 366 kg (in 2017) (Statistics Canada [modified 2019]). Caprolactam is imported into Canada for use in the manufacture of polycaprolactam (Nylon 6) along with other unspecified uses (Statistics Canada [modified 2018]).

Caprolactam is primarily used as a monomer in the polymerization process to form Nylon 6 fibres and resins (Fisher et al. 2015). Caprolactam can also be used as a plasticizer (HSDB 1983-), which promotes flexibility to synthetic resins (Godwin 2000). Some residual caprolactam monomer (1% or less) may be present in manufactured articles made with Nylon 6 (Venema et al. 1993 as cited in OEHHA 2013). Nylon 6 fibres are used in the production of textiles, carpets, and industrial yarns (Fisher et al. 2015). Nylon 6 resins are used for plastic film packaging of food, wires, and cables, as well as in engineering plastics with applications in 3D printing, the automotive industry, and medical industry (Fisher et al. 2015; Floyd et al. 2017).

Nylon 6 is used as a bulking agent and opacifying agent in cosmetics (CIR 2013). Nylon 6 has been notified to be present in cosmetics in Canada based upon notifications submitted under the *Cosmetic Regulations* to Health Canada; however, caprolactam as an individual ingredient has not been notified (personal communication, e-mail from the

Consumer and Hazardous Products Safety Directorate (CHPSD), Health Canada (HC) to the Existing Substances Risk Assessment Bureau (ESRAB), HC, dated February 2019 and November 2019; unreferenced).

Caprolactam is also used in liquid and powder paints and coatings with applications on a wide variety of substrates such as textiles, fabrics, furniture, flooring, metal, and plastic materials (Janik et al. 2014).

Caprolactam may be used in the manufacture of certain food packaging materials as a component in resins or can coatings with potential for direct food contact (personal communication, e-mail from the Food Directorate (FD), HC to the ESRAB, HC, dated February 2019; unreferenced). No definitive data is available regarding the potential use of caprolactam as a food flavouring agent in foods sold in Canada. However, since caprolactam is used internationally as a food flavouring agent, it is possible that this substance is present as a flavouring agent in foods sold in Canada (personal communication, e-mail from FD, HC to ESRAB, HC, dated October 15, 2019; unreferenced).

In Canada, caprolactam has been identified in glue sticks and other types of adhesives such as polyamide web adhesives, thermal bonding film, and tape (SDS 2003; SDS 2015; SDS 2019; SDS 2014a). In glue sticks, caprolactam acts as a temporary cross-linking agent between polymer strands of the glue to help form a solid paste (Emsley 2015).

Internationally, caprolactam residue has been identified from the use of Nylon 6 in disposable diapers, 3D printing filaments, the interior materials of car cabins, oven roasting bags, and carpets (Danish EPA 2009; Davis et al. 2019; Danish EPA 2017; Gramshaw et al.1998; Wilke et al. 2004). A possible source of caprolactam in diapers is from nylon threads (VITO 2018) that may be used to form the nonwoven fabric sheets of the inner surface of a diaper. In addition to adhesives, these products may be available to consumers in Canada.

5. Potential to cause ecological harm

5.1 Characterization of ecological risk

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

concentration) for characterization. The following summarizes the approach, which is described in detail in ECCC (2016a).

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

Hazard profiles were based principally on metrics regarding mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity. Exposure profiles were also based on multiple metrics, including potential emission rate, overall persistence, and long-range transport potential. Hazard and exposure profiles were compared to decision criteria in order to classify the hazard and exposure potentials for each organic substance as low, moderate, or high. Additional rules were applied (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 of subsequent risk. The balanced approaches for dealing with uncertainties are described in greater detail in ECCC (2016a). The following describes two of the more substantial areas of uncertainty. Error with empirical or modelled acute toxicity values could result in changes in classification of hazard, particularly metrics relying on tissue residue values (i.e., mode of toxic action), many of which are predicted values from (Q)SAR models (OECD QSAR Toolbox 2014). However, the impact of this error is mitigated by the fact that overestimation of median lethality will result in a conservative (protective) tissue residue value used for critical body residue analysis. Error with underestimation of acute toxicity will be mitigated through the use of other hazard metrics such as structural profiling of mode of action, reactivity and/or estrogen binding affinity. Changes or errors in chemical quantity could result in differences in classification of exposure as the exposure and risk classifications are highly sensitive to emission rate and use quantity. The ERC

classifications thus reflect exposure and risk in Canada on the basis of what is estimated to be the current use quantity, and may not reflect future trends.

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

On the basis of low hazard and low exposure classifications according to information considered under ERC, caprolactam was classified as having a low potential for ecological risk. It is unlikely that this substance is resulting in concerns for the environment in Canada.

6. Potential to cause harm to human health

6.1 Exposure assessment

Potential exposures to caprolactam based on measured and modelled concentrations of caprolactam in environmental media, food, and products available to consumers are presented in this section. Exposure scenarios resulting in the highest exposures were selected to characterize risk.

6.1.1 Environmental media and food

Environmental media

On the basis of its physical and chemical properties, caprolactam is expected to predominantly exist in water when released into the environment (HSDB 1983-). When released to air, caprolactam is expected to exist solely in the vapour phase due to its moderate vapour pressure. When released to surface waters or the terrestrial environment, caprolactam is not expected to adsorb to suspended soils or sediments based on its estimated low K_{oc} value (HSDB 1983-). Volatilization of caprolactam from water and soil surfaces is not expected (OECD 2001).

No measured concentrations of caprolactam in Canadian indoor air, surface water, soil, or dust were identified.

In Canada, caprolactam was detected in ambient air at five different sites within the Lower Fraser Valley region of British Columbia in August 2001 (Cheng et al. 2006). In this study, caprolactam was collected as a fine aerosol on $PM_{2.5}$ filters at forest, tunnel, urban, rural and mixed forest/urban areas with a sampling time of 10 hours. The maximum ambient air concentration detected was 0.070 µg/m^3 (Cheng et al. 2006). There is potential for release of caprolactam from industrial facilities in Canada, where it is used as a monomer in the production of Nylon 6. Daily inhalation exposure from the

evaporative emissions of caprolactam to individuals residing near Nylon 6 manufacturing facilities was considered in this assessment. A maximum caprolactam concentration of 4.631 g/m^3, discharging into the atmosphere through a stack (Ontario Ministry of the Environment 2006), was used to derive the emission rate of 1.991 g/s. The emission rate was used to estimate ambient air concentrations of caprolactam in the vicinity of these manufacturing facilities for which a small portion of the general population residing in the area may be exposed to. The input parameters used to model the releases using the SCREEN3 air dispersion model (SCREEN3 2011) are provided in Table B-1 (Appendix B). The highest ambient air concentration of caprolactam in the vicinity of an industrial facility is estimated to be 338 µg/m^3 at a distance of 100 m from the release source (Appendix B).

Caprolactam was detected in a 27-week indoor air study by Hodgson et al. (2004), which measured caprolactam at a maximum concentration of 30.1 µg/m^3 after 8 weeks of testing. The study was conducted in an elementary school classroom in the US that installed a Nylon 6 broadloom carpet interior finish. There are several chamber emission studies investigating caprolactam emissions from carpets. One study tested 6 carpets made with Nylon 6 fibres; the highest caprolactam emission rate was 840 µg/m^2/hour after 96 hours of chamber emission testing (IWMB 2003). A study done by Wilke et al. (2004) tested 14 carpets and measured caprolactam concentrations ranging from 6 to 97 µg/m^3 following emissions from three polyamide carpets on the 28th day of chamber testing (Wilke et al. 2004). In another chamber study conducted by the Danish EPA (2016), caprolactam was detected during emission testing for 13 out of 21 samples of various types of carpets tested, some made with a nylon surface. The Danish EPA estimated a 28-day average concentration of caprolactam emitted from the carpets made with nylon in a child's bedroom to range from 1 to 20 µg/m^3 (Danish EPA 2016). Due to the decrease in emission rates observed over time in the chamber emission studies of carpets, the long-term studies were considered to be more reflective of long-term exposure to caprolactam via indoor air. The 28-day chamber air study by Wilke et al. (2004) tested a variety of carpets and measured the highest long-term emission concentrations of caprolactam. The maximum chamber air concentration of 97 µg/m^3 (Wilke et al. 2004) was conservatively selected for characterizing exposure of the general population to caprolactam via indoor air (Appendix A). The highest daily intake of caprolactam from indoor air is estimated to be 61.7 µg/kg bw/day in infants 1 year of age (Appendix A).

Estimated concentrations of caprolactam in surface water were derived with the New Substances Assessment Bureau Environmental Assessment Unit Drinking Water Workbook using the industrial release scenario (Health Canada 2015a) based on the 2017 total import quantity of 21 722 366 kg for caprolactam (Statistics Canada [modified 2019]) (see Appendix A for details). The resulting 50th percentile predicted environmental concentration was 471.5 µg/L, which resulted in a conservative daily intake of 61.8 µg/kg bw/day for formula-fed infants aged 0 to 5 months. Internationally, caprolactam has been measured in drinking water, in association with its manufacture and release from facilities that use caprolactam as a raw material in the preparation of fibres and resins (e.g., IARC 1999; US EPA 2000).

Concentrations in soil and dust were modelled using ChemCAN (2003) and based on the highest total import quantities of caprolactam between the years 2014 to 2018 reported in the Canadian International Merchandise Trade Database (Statistics Canada [modified 2019]). Estimated daily intakes of caprolactam via soil and dust resulted in negligible exposure.

Food

Caprolactam may be used in the manufacture of certain food packaging materials as a component in resins or can coatings with potential for direct food contact. Assuming a worst-case scenario (i.e., 100% of the caprolactam migrates into the food), the estimated probable daily intake of caprolactam from food packaging materials is 4.4 µg/kg bw/day for the general population (12 months of age and older) (personal communication, e-mail from FD, HC to ESRAB, HC, dated October 15, 2019; unreferenced).

Caprolactam may also have direct food contact from certain products available to consumers, such as oven roasting bags made with Nylon 6 for use in conventional and microwave ovens. Potential exposure to caprolactam from oven roasting bags was considered in the estimated probable daily intake of caprolactam from food packaging materials (personal communication, e-mail from FD, HC to ESRAB, HC, dated February 21, 2020; unreferenced).

No definitive data were identified on use of caprolactam as a food flavouring agent in foods sold in Canada. The Joint (Food and Agriculture Organization/World Health Organization [FAO/WHO]) Expert Committee on Food Additives (JECFA) estimated the per capita intake of caprolactam as a flavouring agent to be 0.01 µg/day (0.0002 µg/kg bw/day based on a 60-kg person) for the US population based on annual production volumes reported by the food industry in poundage surveys (EFFA 2005; Gavin 2007 as cited in WHO 2009). In the absence of data on the existing use, if any, of caprolactam as a flavouring agent in foods sold in Canada, the JECFA per capita intake estimate for the US population is considered an acceptable estimate of possible Canadian dietary exposure to this substance from this use in food for the general population (12 months of age and older) (personal communication, e-mail from FD, HC to ESRAB, HC, dated October 15, 2019; unreferenced). The exposure potential from the use of caprolactam as a food flavouring agent is considered negligible.

6.1.2 Products available to consumers

Exposure of the general population to caprolactam can result from the use of glue sticks and from residual amounts of caprolactam from use of Nylon 6 in products available to consumers including lipstick, diapers, 3D printing filaments, clothing and other textiles. Estimates for scenarios that result in the highest level of potential oral, dermal, or inhalation exposure (referred to as sentinel scenarios) for relevant age groups are presented in Table 6-1. Details of the parameters used to estimate exposure are presented in Appendix C.

Oral exposures to residual caprolactam were expected from mouthing of textiles (e.g., blankets, textile toys), hand-to-mouth from crawling on carpet, and lipstick. While exposure to caprolactam during use of glue sticks is expected to be primarily via the dermal route, direct oral exposure of younger children due to incidental ingestion is also possible (Health Canada 2011; personal communication, e-mails from Consumer and Hazardous Products Safety Directorate, HC to ESRAB, HC, dated 2016; unreferenced) and is considered a sentinel scenario for oral exposure to caprolactam. Dermal exposures to caprolactam were characterized for certain sentinel products including glue sticks and from residual caprolactam in diapers and baby sleeper textiles, which represent the highest exposures when compared to similar textile products such as adult apparel and carpet.

A possible source of caprolactam in diapers is from nylon threads (VITO 2018) that may be used to form the nonwoven fabric sheets of a diaper. Caprolactam was extracted from the textile inner surface of baby diapers at concentrations ranging from 29 to 590 µg/kg in 10 out of 20 diapers tested (VITO 2018). The maximum concentration was chosen for estimating dermal exposure to diapers. In another study, caprolactam was extracted from the front-printed part of diapers at a concentration of 610 000 µg/kg (Danish EPA 2009); however, this part of the diaper is considered to be associated with minimal dermal contact and thus negligible exposure potential (Rai et al. 2009; Kosemund et al. 2009).

Inhalation exposures to caprolactam were characterized for glue sticks and from residual amounts emitted from Nylon 6 used in 3D printing, which represent the highest exposures when compared to other products such as interior parts of a car cabin. For the 3D printer scenario, inhalation exposure was estimated based on the data from chamber emission studies, while inhalation exposure from glue stick was characterized using ConsExpo Web (2018).

Caprolactam was also detected in several chamber studies that investigated its emission rate from various types of filaments used in desktop 3D printers (Davis et al. 2019; Azimi et al. 2016; Floyd et al. 2017). Azimi et al. (2016) calculated the highest emission rate of 183 µg/min from filaments made with Nylon 6 among nine different filament materials based on the chamber air concentrations measured during the last 45 minutes of 3D printing. When converted to an inhalation exposure level assuming a residential room setting, the exposure concentration of caprolactam is 915 µg/m^3 (see Appendix C for details).

Table 6-1. Estimates of potential oral and dermal exposures to caprolactam from the use of products available to consumers

Product scenario (age groups)[a]	Maximum concentration	Route of exposure	Per event systemic exposure estimate (mg/kg bw)	Daily systemic exposure estimate (mg/kg bw/day)
Textiles (e.g. blankets, textile toys) (0-5 months)	1% [b]	Oral (mouthing)	N/A	0.0000159
Lipstick (2-3 years)	0.3%[c]	Oral	0.0044	0.0044
Glue stick (2-3 years)	1%[d]	Oral (incidental)	0.267	N/A
Textiles - Baby sleeper (0-5 months)	1%[b]	Dermal	N/A	0.00278
Diaper (0-5 months)	0.59 mg/kg[e]	Dermal	0.0022	0.0270
Glue stick (2-3 years)	1%[d]	Dermal	0.053	0.023

Abbreviation: N/A, Not Applicable
[a] 100% absorption is assumed for inhalation and dermal exposures. It is also assumed that 100% of caprolactam is available for absorption.
[b] Based on approximate caprolactam monomer concentration in Nylon 6 (Goldblatt et al. 1954 as cited in CIR 2013; Venema et al. 1993 as cited in OEHHA 2013; SDS 2014b). Considered conservative because textile processing to make final product not considered and assuming textile clothing made of 100% Nylon 6.
[c] Based on approximate caprolactam monomer concentration in Nylon 6 (Goldblatt et al. 1954 as cited in CIR 2013). Nylon 6 present at up to 30% in lip products (personal communication e-mail from CHPSD, HC to ESRAB, HC, dated January 9, 2019) (Possible maximum caprolactam concentration: 0.30 * 0.01 = 0.3%).
[d] SDS 2018
[e] VITO 2018

Table 6-2. Estimates of potential inhalation exposures to caprolactam from the use of products available to consumers

Product scenario (age groups)[a]	Maximum concentration	Route of exposure	Air concentration (mg/m^3)
Glue stick (2-3 years)	1%[b]	Inhalation	0.0126
3D printing filaments	N/A	Inhalation	0.915

Abbreviation: N/A, Not Applicable
[a] 100% absorption is assumed for inhalation and dermal exposures.
[b] SDS 2018

6.2 Health effects assessment

Caprolactam was assessed by the OECD Cooperative Chemicals Assessment Programme in a Screening Information Dataset (SIDS) Initial Assessment Report (SIAR) (OECD 2001). This assessment is used to inform the health effects characterization of caprolactam in this screening assessment. Literature searches were conducted up to April 2019. No health effect studies that would impact the risk characterization (i.e., result in different critical endpoints or lower points of departure than those stated in OECD 2001) were identified.

Caprolactam is absorbed rapidly when dosed orally. It is also rapidly excreted primarily in the urine, with only a small portion of the dose excreted unchanged (OECD 2001).

Repeated-Dose Toxicity

Two 13-week feed studies in rats were identified. Wistar rats (10/sex/dose) were administered caprolactam at doses of 0, 0.1, 0.3, 1.0 or 2.0% (approximately equivalent to 0, 67, 200, 667 or 1333 mg/kg bw/day), while Sprague-Dawley (SD) rats (10/sex/dose) were exposed to 0, 0.05, 0.1, 0.25, 0.5 or 1.0% of caprolactam (approximately equivalent to 0, 33, 67, 167, 333 or 667 mg/kg bw/day). At 67 mg/kg bw/day and above, tubular nephrosis and hyaline-droplet degeneration in kidneys were observed in the male Wistar and SD rats, respectively. At 667mg/kg bw/day and above, decreased body weights and increased liver weights were observed in both sexes andstrains. At this dose, other effects included increased relative kidney weights in male Wistar and SD rats, and the latter also had increased relative testes weight and renal discolouration. Increased relative thyroid and brain weights were only observed in Wistar rats at 1333 mg/kg bw/day (OECD 2001). The tubular nephrosis and hyaline-droplet degeneration are spontaneous nephropathies typically observed in male rats (Peter et al. 1986). OECD (2001) concluded that these effects in male rat kidney were of little or no relevance to humans. OECD (2001) did not identify a point of departure, but in this assessment the dose of 200 mg/kg bw/d is considered to be a no observed adverse effect level (NOAEL) based on decreased body weights observed in both rat strains and sexes at the next dose level of 667 mg/kg bw/day.

In a 13-week oral study, dogs (4/sex/dose) were fed caprolactam at doses of 0, 25, 125, or 250 mg/kg bw/day. The only finding was decreased mean body weight in the high-dose females. No treatment-related effects were noted in clinical chemistry, pathology, ophthalmology or organ weights. A NOAEL of 125 mg/kg bw/day for females and a NOAEL of 250 mg/kg bw/day for males, the highest dose tested, were identified (OECD 2001).

In a 13-week inhalation study, SD rats (10/sex/dose) were exposed by whole body to caprolactam (as an aerosol, average particle size 2.9 µm) at doses of 0, 24, 70 or 243 mg/m^3 (approximately equivalent to 0, 5, 14 or 49 mg/kg bw/day), for 6 hours per day and 5 days per week. In all treated groups, there were transient clinical signs (nasal discharge, laboured breathing), and effects in the upper respiratory tract

(squamous/squamoid metaplasia/hyperplasia of the pseudostratified columnar epithelium covering the ventral seromucous gland in the larynx at all treated doses; hypertrophy/hyperplasia of goblet cells in the respiratory mucosa and intracytoplasmic eosinophilic material in epithelial cells of the olfactory mucosa at 70 mg/m^3 and above) with incomplete recovery at the end of 4-week recovery period (Reinhold et al. 1998 as cited in OECD 2001). These signs/effects were considered adaptive by the OECD. Keratinization of the metaplastic epithelium of the larynx (reversible within 4-week recovery) was observed at 243 mg/m^3 and was considered to be an adverse local effect in the upper respiratory tract by the OECD (Reinhold et al. 1998 as cited in OECD 2001). The no observed adverse effect concentration (NOAEC) for local effects in the upper respiratory tract was considered to be 70 mg/m^3 by the OECD based on keratinization of the metaplastic epithelium in the larynx at 243 mg/m^3 (OECD 2001). The OECD considered the systemic NOAEC as 243 mg/m^3, the highest dose tested.

Carcinogenicity

Caprolactam has been classified as Group 4 (probably not carcinogenic to humans) (IARC 1999) but with the removal of Group 4 has been transferred to Group 3 (not classifiable as to its carcinogenicity to humans) (IARC [modified 2020]).

The US National Toxicology Program (NTP) conducted a carcinogenesis study in rats and mice. Fischer-344 (F344) rats (50/sex/dose) were exposed to caprolactam in a diet at doses of 0, 3750 ppm (188-375 mg/kg bw/day) or 7500 ppm (375-750 mg/kg bw/day) while B6C3F1 mice (50/sex/group) were fed 0, 7500 ppm (1072 mg/kg bw) or 15 000 ppm (2143 mg/kg bw) caprolactam for 103 weeks. Throughout the bioassay, mean body weight gains for dosed rats and mice of either sex were decreased when compared with those of the controls. No other compound-related effects were observed. The NTP concluded that, under the conditions of this bioassay, caprolactam was not carcinogenic for F344 rats or B6C3F1 mice (NTP 1982 as cited in OECD 2001).

Genotoxicity

Caprolactam showed neither mutagenic nor clastogenic potential with respect to most of the different genetic endpoints tested. Positive results from in vitro chromosome aberration tests were shown only with high concentrations, which were much higher than the highest concentration recommended in the OECD test guideline. Several in vitro and in vivo tests showed induction of mitotic recombination. However, the relevance of this effect remains unclear, especially taking into account the negative results in rats and mice carcinogenicity bioassays (OECD 2001).

Reproductive and developmental toxicity

In a three-generation reproductive toxicity study, F344 rats (10 males and 20 females/dose group) were fed caprolactam at doses of 0, 1000, 5000 and 10 000 ppm (approximately equivalent to 0, 83, 417 or 833 mg/kg bw/day) through three successive generations. No exposure related clinical signs, changes in reproductive performance or

gross pathological changes were observed in the parental (P) generations. Slight exposure-related increases in the severity of spontaneous nephropathies, occasionally accompanied by granular casts were observed at the high dose in the first parental (P1) animals. Decreased body weight gains were observed in parental animals (P2 and P3) at 417 mg/kg bw/day and above and significantly decreased body weights and food consumption were observed at 833 mg/kg bw/day. No exposure-related effects with respect to gross appearance, gross pathology, survival, number of pups, and percentage of male pups or kidney weights were observed in offspring. Lower mean body weight in pups of all filial (F1, F2 and F3) generations of both sexes as well as decreased food consumption (F2, F3) were observed at 417 mg/kg bw/day and above, with statistical significance at 833 mg/kg bw/day on postnatal days 1, 7 and 21 (Serota et al. 1988). A NOAEL of 417 mg/kg bw/day based on minor kidney effects observed in P1 animals, an offspring NOAEL of 83 mg/kg bw/day based on decreased pup body weights, and a reproductive NOAEL of 833 mg/kg bw/day at the highest dose tested were identified by OECD (2001).

In a developmental toxicity study, F344 rats (20/group) were administered caprolactam, via gavage, at doses of 0, 100, 500 or 1000 mg/kg bw/day on days 6 to 15 of gestation Increased mortality was observed in dams at 1 000 mg/kg bw/day. Clinical observations such as urine stains, rough hair coat, red discharge from the vagina, bloody crust on eyes, mouth and nose, thin and/or hunched appearance were observed in all treated groups. The mean maternal body weight in the 500 and 1000 mg/kg bw/day groups for gestation days 6-11 and 6-15 were statistically significantly lower than the control group. Decreased mean maternal body weights were also observed in the high dose group on gestation days 15 and 20. The mean food consumption was also significantly lower at 500 mg/kg bw/day groups and above. At these maternally toxic doses, a slight reduction in fetal body weights was observed. Reduced mean implantation efficiencies and increased resorptions were observed in the high-dose group. No increased skeletal variations were observed in treated groups. No skeletal malformations were observed. A NOAEL of 500 mg/kg bw/day for fetotoxicity based on a reduction of mean implantation efficiencies and an increase in resorptions at the highest dose, and a NOAEL of 1000 mg/kg bw/day, the highest dose tested for teratogenic effects were identified. The maternal toxicity NOAEL could not be established based on clinical observations at 100 mg/kg bw/day and above (OECD 2001). The maternal LOAEL of 100 mg/kg bw/day was identified based on decreased body weight, food consumption and clinical observations in dams.

In a developmental toxicity study with New Zealand white rabbits (25/group), animals were administered caprolactam at doses of 0, 50, 150 or 250 mg/kg bw/day, via gavage on days 6 to 28 of gestation, and examined on day 29 of gestation. In the 250 mg/kg bw/day group, four rabbits died during the treatment period with convulsions immediately after treatment, and two additional animals had rapid breathing at 10 minutes post-dosing. Significantly reduced maternal body weights were observed in the mid- and high-dose groups between day 6 and 29 of gestation. No effects on the reproduction parameters (i.e., number of corpora lutea, or sex ratio) were observed. There were no treatment-related indications of embryo- or fetotoxicity (number of live

and dead fetuses, resorptions, pre- or post-implantation losses), except decreased fetal weights at the maternally toxic dose levels of 150 and 250 mg/kg bw/day. No signs of teratogenicity were observed at any dose level (Gad et al. 1984, 1987 as cited in OECD 2001). The OECD concluded that the maternal and fetotoxicity NOAELs were both 50 mg/kg bw/day and the teratogenic NOAEL was 250 mg/kg bw/day, the highest dose tested (OECD 2001).

6.3 Characterization of risk to human health

Table 6-3 provides all relevant exposure and hazard values for caprolactam, as well as resultant margins of exposure (MOEs), for determination of risk.

Table 6-3. Relevant exposure and hazard values for caprolactam, as well as margins of exposure, for determination of risk

Exposure scenario	Systemic exposure	Critical effect level	Critical health effect endpoint	MOE
Daily exposure to drinking water and indoor air (0 to 5 months)[a]	0.112 mg/kg bw/day	NOAEL= 83 mg/kg bw/day	Reduced pup body weights in absence of parental effects at 417 mg/kg bw/day in a reproductive toxicity study in rats	740
Daily exposure to drinking water, indoor air, food and beverages (1 year)[b]	0.0815 mg/kg bw/day	NOAEL= 83 mg/kg bw/day	Reduced pup body weights in absence of parental effects at 417 mg/kg bw/day in a reproductive toxicity study in rats	1000
Daily inhalation exposure via evaporative emissions in the vicinity of a Nylon 6 manufacturing facility	0.34 mg/m^3	NOAEC= 70 mg/m^3	Keratinization of the metaplastic epithelium in the larynx at 243 mg/m^3, in a 13-week inhalation study in rats	210
Daily oral exposure to lipstick (2-3 years)	0.0044 mg/kg bw/day	NOAEL= 83 mg/kg bw/day	Reduced pup body weights in absence of parental effects	19 000

			at 417 mg/kg bw/day in a reproductive toxicity study in rats	
Daily dermal exposure to diapers (0-5 months)	0.0270 mg/kg bw/day	NOAEL= 83 mg/kg bw/day	Reduced pup body weights in absence of parental effects at 417 mg/kg bw/day in a reproductive toxicity study in rats	3000
Daily dermal exposure to glue sticks (2-3 years)	0.023 mg/kg bw/day	NOAEL= 83 mg/kg bw/day	Reduced pup body weights in absence of parental effects at 417 mg/kg bw/day in a reproductive toxicity study in rats	3600
Combined per event oral (incidental ingestion) and per event dermal exposure to glue sticks (2-3 years)	0.32 mg/kg bw	LOAEL= 100 mg/kg bw/day	Clinical observations (such as urine stains, rough hair coat, blood discharge, thin and/or hunched appearance) in dams at 100 mg/kg bw/day and above in a developmental study in rats	310
Per event inhalation exposure to 3D printing filaments (all ages)	0.915 mg/m^3	NOAEC = 243 mg/m^3	No systemic effect up to 243 mg/m^3, the HDT, in a 13-week inhalation study in rats	270

Abbreviations: NOAEC, no observed adverse effect concentration; NOAEL, no observed adverse effect level; LOAEL, lowest observed adverse effect level; HDT, highest dose tested; MOE, margin of exposure

[a] This is the highest daily intake estimate for under 1 year of age.

[b] This is the highest daily intake estimate for the general population 1 year of age and over.

The MOE of 310 for combined per event oral and dermal exposures to glue sticks was derived from comparing a LOAEL of 100 mg/kg bw/day by gavage based on clinical effects observed in pregnant rats from a developmental study to the estimate of exposure level. Considering that the dermal exposure estimate was based on 100% dermal absorption and assuming 100% of caprolactam in the glue stick is available for absorption, this MOE was considered adequate to account for uncertainties in the health effects and exposure data used to characterize risk.

For comparison with daily exposure scenarios, the NOAEL of 83 mg/kg bw/day based on decreased pup body weight in the absence of maternal toxicity in a 3-generation reproductive toxicity study in rats at 417 mg/kg bw/day (Serota et al. 1988) was selected for use rather than a NOAEL of 50 mg/kg bw/day based on decreased fetal and maternal body weights at 150 mg/kg bw/day in a developmental study in rabbits (Gad et al. 1984, 1987 as cited in OECD 2001). Use of the 3-generation reproductive toxicity study was considered more suitable since it is more appropriate in duration for comparison to daily exposures. Given that the NOAEL of 83 mg/kg bw/day is protective of decreased pup body weight at 417 mg/kg bw/day, it may be considered to be protective of the endpoints of concern (decreased fetal and maternal body weights) identified at 150 mg/kg bw/day in the developmental study.

Comparison of critical effect levels and estimates of exposure to caprolactam from environmental media, food and beverages (based on potential use in food packaging materials), glue sticks and caprolactam residue from the use of Nylon 6 in lipsticks, diapers, and 3D printing resulted in MOEs ranging from 210 to 19 000. Daily inhalation exposure to carpets is covered in the risk characterization of environmental media (indoor air) which considers carpet emissions. These calculated MOEs are considered adequate to account for uncertainties in the health effects and exposure data used to characterize risk.

6.4 Uncertainties in evaluation of risk to human health

The key sources of uncertainty are presented in the table below. The achieved MOEs were considered adequate to address these uncertainties.

Table 6-4. Sources of uncertainty in the risk characterization

Key source of uncertainty	Impact
No Canadian environmental media data identified.	+/-
No Canadian manufacturing data for caprolactam.	-
No dermal absorption data for caprolactam. It was considered equivalent to oral absorption.	+
No chronic study available by the dermal or inhalation route.	+/-

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

7. Conclusion

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to the environment from caprolactam. It is proposed to conclude that caprolactam does not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

Considering all the information presented in this draft screening assessment, it is proposed to conclude that caprolactam does not meet the criteria under paragraph 64(*c*) of CEPA as it is not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore proposed to conclude that caprolactam does not meet any of the criteria set out in section 64 of CEPA.

References

[ANSES] Agence nationale de sécurité sanitaire de l'alimentation, de l'environnement et du travail. 2019. Safety of baby diapers: ANSES revised opinion collective expert appraisal report. Paris (FR): ANSES.

Azimi P, Zhao D, Pouzet C, Crain NE, Stephens B. 2016. Emissions of Ultrafine Particles and Volatile Organic Compounds from Commercially Available Desktop Three-Dimensional Printers with Multiple Filaments. Environ Sci Technol. 50(3):1260-1268.

[BfR] Bundesinstitut für Risikobewertung. 2007. Introduction to the problems surrounding garment textiles. Berlin (DE): German Federal Institute for Risk Assessment (BfR). Report No.: BfR Information No. 018/2007, 1 June 2007.

Canada. 1978. *Food and Drug Regulations.* C.R.C., c.870.

Canada. 1999. *Canadian Environmental Protection Act, 1999*. S.C. 1999, c.33. Canada Gazette Part III, vol. 22, no. 3.

ChemCAN [level III fugacity model of 24 regions of Canada]. 2003. Version 6.00. Peterborough (ON): Trent University, Canadian Centre for Environmental Modelling and Chemistry.

Cheng Y, Li SM, Leithead A. 2006. Chemical Characteristics and Origins of Nitrogen-Containing Organic Compounds in $PM_{2.5}$ Aerosols in the Lower Fraser Valley. Environ Sci Technol. 40(19):5846-5852.

[CIMT] Canadian International Merchandise Trade Database. [modified 2019 November 23]. Table 990-0029. Ottawa (ON): Statistics Canada. [accessed 2019 Nov 23].

[CIR] Cosmetic Ingredient Review. 2013. Safety Assessment of Nylon as used in cosmetics. Washington (DC): CIR.

[ConsExpo Web] Consumer Exposure Web Model. 2018. Bilthoven (NL): Rijksinstituut voor Volksgezondheid en Milieu (RIVM) [National Institute for Public Health and the Environment].

Curry P, Kramer G, Newhook R, Sitwell J, Somers D, Tracy B, Oostdam JV. 1993. Reference values for Canadian populations. Ottawa (ON): Health Canada, Environmental Health Directorate Working Group on Reference Values.

[Danish EPA] Danish Environmental Protection Agency. 2009. Survey and Health Assessment of the exposure of 2 year-olds to chemical substances in Consumer Products. Copenhagen (DK): Danish Ministry of the Environment.

[Danish EPA] Danish Environmental Protection Agency. 2016. Survey and risk assessment of chemical substances in rugs for children. Copenhagen (DK): Danish Ministry of the Environment.

[Danish EPA] Danish Environmental Protection Agency. 2017. Risk assessment of hazardous substances in the indoor environment of cars - a pilot study. Copenhagen (DK): Danish Ministry of the Environment.

Davis AY, Zhang Q, Wong JPS, Weber RJ, Black MS. 2019. Characterization of volatile organic compound emissions from consumer level material extrusion 3D printers. Build Environ. 160:106209.

[EC] European Commission. 2016. Guidance document on the application of directive 2009/48/EC on the safety of toys. Brussel (BE): European Commission.

[ECCC] Environment and Climate Change Canada. 2016a. Science approach document: ecological risk classification of organic substances. Ottawa (ON): Government of Canada.

[ECCC] Environment and Climate Change Canada. 2016b. Supporting documentation: data used to create substance-specific hazard and exposure profiles and assign risk classifications. Gatineau (QC): ECCC. Information in support of the science approach document: ecological risk classification of organic substances. Available from: eccc.substances.eccc@canada.ca.

[ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2017 March 12]. Categorization. Ottawa (ON): Government of Canada. [accessed 2019 Sep 26].

[EFFA] European Flavour and Fragrance Association, 2005. European inquiry on volume use. Private communication to the Flavor and Extract Manufacturers Association, Washington, DC, USA, 2005. Submitted to WHO by the International Organization of the Flavor Industry, Brussels, Belgium.

Emsley J. 2015. Chemistry at Home Exploring the ingredients of everyday products. London (UK): Royal Society of Chemistry.

[EPI Suite] Estimation Program Interface Suite for Microsoft Windows [estimation model]. c2000-2012. Ver. 4.11. Washington (DC): US Environmental Protection Agency, Office of Pollution Prevention and Toxics; Syracuse (NY): Syracuse Research Corporation.

Ficheux AS, Chevillotte G, Wesolek N, Morisset T, Dornic N, Bernard A, Bertho A, Romanet A, Leroy L, Mercat AC, et al. 2016. Consumption of cosmetic products by the French population Second Part: Amount data. Food Chem Toxicol. 90:130-141.

Floyd EL, Wang J, Regens L. 2017. Fume emissions from a low-cost 3-D printer with various filament. J Occup Environ Hyg. 14(7):523-533.

Gavin CL, Williams MC, Hallagan JB, 2007. FEMA 2005 poundage and technical effects update survey. Washington (DC): Flavor and Extract Manufacturers Association.

Godwin A. 2000. Plasticizers. In: Craver CD, Carraher CE Jr., editors. Applied Polymer Science: 21st Century. Amsterdam (NL): Elsevier Science. 1088 p.

Goldblatt MW, Farquharson ME, Bennett G, Askew BM. 1954. ε-Caprolactam. Brit J Industr Med. 11(1).

Gramshaw, JW, Soto-Valdez H. (1998). Migration from polyamide 'microwave and roasting bags' into roast chicken. Food Addit Comtam. 15(3):329-335.

Health Canada. [modified 2018 June 14]. Cosmetic Ingredient Hotlist: list of ingredients that are prohibited for use in cosmetic products. Ottawa (ON): Government of Canada. [accessed 2019 Sep 26].

Health Canada. 2011. Children's Product Usage Study: Management Summary. Prepared for Health Canada in September 2011. Unpublished report. Ottawa (ON): Health Canada.

Health Canada. 2015a. Environmental Assessment Unit drinking water spreadsheets. [Excel format]. Ottawa (ON): Government of Canada. [accessed 2019 Sep 26]

Health Canada. 2015b. Food consumption table derived from Statistics Canada, Canadian Community Health Survey, Cycle 2.2, Nutrition (2004), Share file. Ottawa.

[HSDB] Hazardous Substances Data Bank [database]. 1983- . Search results for CAS RN 105-60-2. Bethesda (MD): National Library of Medicine (US). [updated 2005 Jun 24; accessed 2019 Sep 26].

Hodgson AT, Shendell DG, Fisk WJ, Apte MG. 2004. Comparison of predicted and derived measures of volatile organic compounds inside four new relocatable classrooms. Indoor Air. 14(Suppl 8):135-144.

[IARC] International Agency for Research on Cancer. 1999. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Volume 71. Lyon (FR): IARC.

[IARC] International Agency for Research on Cancer. [modified 2020 Feb 12]. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Lyon (FR): IARC. [accessed 2020 Mar 02].

[IWMB] Integrated Waste Management Board. 2003. Building Material Emissions Study. Sacramento (CA): California Environmental Protection Agency.

Janik H, Sienkiewicz M, Kucinska-Lipka J. 2014. Polyurethanes. In: Dodiuk H, Goodman S, editors. Handbook of Thermoset Plastics (Third Edition). Norwich (NY): William Andrew. 800 p.

Joint FAO/WHO Expert Committee on Food Additives. 2009. Evaluation of Certain Food Additives. World Health Organization (WHO) Technical Report Series No. 952. Geneva (CH): WHO.

[OECD] Organisation for Economic Co-operation and Development. 2001. SIDS Initial Assessment Report: Caprolactam CAS No. 105-60-2. SIAM [SIDS Initial Assessment Meeting] 12; 2001 June; Paris (FR). [accessed 2019 Sep 26].

OECD QSAR Toolbox [Read-across tool]. 2014. Version 3.3. Paris (FR): Organization for Economic Co-operation and Development, Laboratory of Mathematical Chemistry.

[OEHHA] Office of Environmental Health Hazard Assessment. 2013. Caprolactam. Sacramento (CA): California OEHHA. [accessed 2021 Jun 3].

Ontario Ministry of the Environment. 2006. Amended Certificate of Approval – Nylene Canada Inc. Toronto (ON): Ontario Ministry of the Environment.

Rai P, Lee B-M, Liu T, Yuhui Q, Krause E, Marsman D, Felter S. 2009. Safety Evaluation of Disposable Baby Diapers Using Principles of Quantitative Risk Assessment. J Toxicol Environ Health A. 72(21-22): 1262-1271.

[RIVM] Rijksinstituut voor Volksgezondheid en Milieu [National Institute for Public Health and the Environment]. 2007. Do-it-yourself products fact sheet: to assess the risks for the consumer. Bilthoven (NL): RIVM. Report No.: 320104007/2007. [accessed 2021 Jun 3].

SCREEN3 [computer model]. 2011. Ver. 3.5.0. Research Triangle Park (NC): US Environmental Protection Agency, Office of Air Quality Planning and Standards, Emissions, Monitoring, and Analysis Division.

[SDS] Safety Data Sheet. 2014a. Loctite Quicktape [PDF]. Rocky Hill (CT): Henkel Corporation. [accessed 2019 Sep 26].

[SDS] Safety Data Sheet. 2014b. Fiberglass/nylon 6 nonwoven [PDF]. Greensboro (NC): BGF Industries. [accessed 2019 Sep 26].

[SDS] Safety Data Sheet. 2015. Stitch Witchery Ultra Light [PDF]. Spartanburg (SC): Prym Consumer USA. [accessed 2019 Sep 26].

[SDS] Safety Data Sheet. 2018. Pritt Glue Stick [PDF]. Mississauga (ON): Henkel Canada Corporation. [accessed 2020 Mar 2].

[SDS] Safety Data Sheet. 2019. 3M Thermal Bonding Film AF42 [PDF]. St. Paul (MN): 3M. [accessed 2019 Sep 26].

Statistics Canada [modified 2019]. Canadian International Merchandise Trade Database Table 990-0029. Ottawa (ON): Government of Canada.

Ulrich H. 2006. Urethane Polymers. Kirk-Othmer Encyclopedia of Chemical Technology. Vol. 25, pp.1-35.

[US EPA] US Environmental Protection Agency. 1992. Screening procedures for estimating the air quality impact of stationary sources, revised. Washington (DC): US EPA. Report No.: EPA-454/R-92-019. [accessed 2021 Jul 28].

[US EPA] US Environmental Protection Agency. 2000. Caprolactam fact sheet. Washington (DC): US EPA, Office of Pollution Prevention and toxics. [accessed 2019 Sep 26].

[US EPA] US Environmental Protection Agency. 2012. Standard operating procedures for residential pesticide exposure assessment. Washington (DC): US Environmental Protection Agency, Office of Pesticide Programs, Health Effects Division.

[VITO] Flemish Institute for Technological Research NV. 2018. Monitoring of the Belgian Market with Regard to Organic Residues in Baby Nappies – Part 2: Target analyses. Mol (BE): VITO.

Venema A, Van de Ven HJFM. 1993. Supercritical Fluid Extraction of Nylon 6: An investigation into the factors affecting the efficiency of extraction of caprolactam and its oligomers. J High Resol Chrom. 16(9):522-524

Wilke O, Jann O, Brödner D. 2004. VOC- and SVOC- emissions from adhesives, floor coverings and complete floor structures. Indoor Air. 14(Suppl 8):98-107.

Zeilmaker MJ, Kroese ED, van Haperen P, van Veen MP, Bremmer HJ, van Kranen HJ, Wouters MFA, Janus J. 1999. Cancer risk assessment of azo dyes and aromatic amines from garment and footwear. Bilthoven (NL): Rijksinstituut voor Volksgezondheid en Milieu (RIVM) [National Institute for Public Health and the Environment].

Appendices

Appendix A. Deterministic estimates of daily human exposure to caprolactam in environmental media and food

Table A-1. Upper-bounding estimates of daily intake (µg/kg-bw per day) of caprolactam

Route of exposure	0 to 5 months [a] (Breast Milk)[b]	0-5 months [a] (Formula Fed)[c]	6 to 11 months[d]	1 year[e]	2 to 3 years[f]	4 to 8 years[g]	9 to 13 years[h]	14 to 18 years[i]	Greater than or equal to 19 years[j]
Indoor air[k]	49.8	49.8	50.4	61.7	52.1	41.0	28.1	21.8	17.3
Drinking water[l]	N/A	61.8	39.6	15.4	13.5	10.9	8.31	8.29	9.75
Food and Beverages[m]	N/A	N/A	N/A	4.4	4.4	4.4	4.4	4.4	4.4
Total intake	**49.8**	**111.6**	**90.0**	**81.5**	**70.0**	**56.2**	**40.8**	**34.5**	**31.5**

Abbreviation: N/A, Not Applicable

[a] Assumed to weigh 6.3 kg (Health Canada 2015b)

[b] 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.

[c] 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. See footnote on drinking water for details

[d] Assumed to weigh 9.1 kg (Health Canada 2015b) and to drink 0 L of water per day (Health Canada 2017). 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 2018a), where water is used to reconstitute formula. See footnote on drinking water for details.

[e] Assumed to weigh 11.0 kg (Health Canada 2015b) and to drink 0.36 L of water per day (Health Canada 2017)

[f] Assumed to weigh 15 kg (Health Canada 2015b) and to drink 0.43 L of water per day (Health Canada 2017).

[g] Assumed to weigh 23 kg (Health Canada 2015b) and to drink 0.53 L of water per day (Health Canada 2017).

[h] Assumed to weigh 42 kg (Health Canada 2015b) and to drink 0.74 L of water per day (Health Canada 2017).

[i] Assumed to weigh 62 kg (Health Canada 2015b) and to drink 1.09 L of water per day (Health Canada 2017).

[j] Assumed to weigh 74 kg (Health Canada 2015b) and to drink 1.53 L of water per day (Health Canada 2017).

[k] A predicted environmental concentration (PEC) of 97 µg/m^3 was selected based on a 28-day chamber emission study done on 14 carpets from which caprolactam was detected in 3 of the polyamide carpets (Wilke et al. 2004). This concentration was used to derive the daily intake estimates of caprolactam from indoor air (Health Canada, in house model unpublished).

[l] No monitoring data of drinking water in Canada were identified. The PEC of 471.5 µg/L was calculated using in-house environmental modelling tool based on the total reported import quantity of caprolactam in 2017 from CIMT (Statistics Canada [modified 2019]). This PEC was selected for deriving daily intake estimates from drinking water (Health Canada, In house model unpublished).

[m] Intakes from food are based on the cumulative probable daily intake of caprolactam from food packaging materials of 4.4 µg/kg bw/day. This intake is based on a bodyweight adjusted intake using a 70 kg bodyweight but which is considered to be sufficiently conservative to represent the entire population 12 months of age and older. (personal communication, e-mail from FD, HC to ESRAB, HC, dated February 2020; unreferenced). The JECFA per capita intake estimate for caprolactam as a food flavouring agent (0.0002 µg/kg bw/day) for the US population was not included in the overall food intake estimate due to negligible exposure potential.

Appendix B. Parameters used to estimate human exposure to caprolactam from industrial facilities

Variable inputs to SCREEN3 for evaporative emissions of caprolactam from a Nylon 6 manufacturing facility and results of modelling are described in Tables B-1 and B-2. Within a specific Canadian facility, Nylene Canada Inc. determined a maximum concentration of 4.631 g/m^3 discharging into the atmosphere through a stack (Ontario Ministry of the Environment 2006). Using SCREEN3 modelling, the variations in caprolactam concentration with changes in distance from the centre of the facility are given in Table B-2. The evaporative emissions scenario was considered for individuals living in the vicinity of manufacturing facilities that use caprolactam as a raw material. The highest daily ambient air concentration of caprolactam was found at approximately 100 m from the centre of the manufacturing facility. Photomap analysis also indicates that residences may be located as close as 100 m from the manufacturing facilities, and thus values estimated at this distance are selected as caprolactam exposure estimates for the general population.

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 one year is determined by multiplying the maximum 1-hour exposure by a factor of 0.08 (US EPA 1992; SCREEN3 2011). Such scaling factors are not used for non-point source emissions. However, to prevent overestimation of the exposures originating from area sources, a scaling factor of 0.2 was used to obtain the yearly amortized concentration from the value of the maximum 1-hour exposure concentration determined by SCREEN3 (SCREEN3 2011).

Table B-1. Variable inputs to SCREEN3 for evaporative emission of caprolactam in the vicinity of Nylon 6 manufacturing facilities.

Variables	Input variables
Source type	Area
Effective emission area[a]	120 × 180 m^2

Emission rate of caprolactam[b]	1.991 g/s
Receptor height[c]	1.74 m (average adult height)
Source release height[d]	3.35 m
Adjustment factor[e]	0.4 (variable wind direction during 24-hr period);
	0.2 (average wind direction during 1-yr period)
Urban–rural option	Urban
Meteorology[f]	1 (full meteorology)
Minimum and maximum distance	0–1900 m

[a] Professional judgement based on the photomap analysis.
[b] Converted 4.631 g/m^3 of caprolactam discharging into atmosphere to g/s using PR-93 system volumetric flow rate of 0.43 m^3/s (4.631 g/m^3 * 0.43 m^3/s) (Ontario Ministry of the Environment 2006).
[c] Curry et al. (1993).
[d] Based on reported height of the stack above grade (Ontario Ministry of the Environment 2006).
[e] US EPA (1992).
[f] Default value in SCREEN3.

Table B-2. Ambient air concentrations of caprolactam in the vicinity of a Nylon 6 manufacturing facility for the range of emission rates using SCREEN3

Distance (m)	Maximum 1 hour conc. (µg/m^3)	Maximum daily exposure conc. (µg/m^3)
1	1075	215
100	**1688**	**337.6[a]**
200	1021	204.2
300	637.5	127.5
400	452.2	90.44
500	338.3	67.66
600	263.1	52.62
700	211.3	42.26
800	174.3	34.86
900	146.9	29.38
1000	126.1	25.22
1100	109.9	21.98
1200	96.9	19.38
1300	86.41	17.282
1400	77.76	15.552
1500	70.48	14.096
1600	64.36	12.872
1700	59.15	11.83
1800	54.65	10.93
1900	50.7	10.14

[a] This distance is representative of the likely location of a residence relative to a Nylon 6 manufacturing facility according to the photomap analysis. Values indicated in bold were selected for exposure characterization.

Appendix C. Parameters used to estimate human exposure to caprolactam from use of products available to consumers

Exposure estimates were calculated based on default body weights (BW) of 74 kg, 62 kg, 42 kg, 23 kg, 15 kg, 11 kg, 9.1 kg, 6.3 kg for adults (19 years and older), teens (14 to 18 years old), children (9 to 13 years), younger children (4 to 8 years old), toddlers (2 to 3 years), toddlers (1 years old), infants (6 to 11 months old), and infants (0-5 months old) respectively (Health Canada 2015b). Dermal absorption of 100% was assumed for daily systemic exposures in the absence of dermal absorption data. 100% absorption from the inhalation route was also assumed. The parameters used in the estimation of oral, dermal and inhalation exposure are summarized in Table B-1.

Table C-1. Parameters and assumptions used to estimate oral, dermal, and inhalation exposures to caprolactam from use of products available to consumers.

Product scenario	Model parameters and assumptions
3D printing filaments (inhalation)	The estimated exposure concentration of a target emission for a particular room model was derived based on a steady state mass balance model using the equation below (Davis et al. 2019): $C = ER * (A/V_m) * (1/N_m)$ C: Estimated exposure concentration (µg/m^3) of a target emission ER: Emission rate of target substance= 183 µg/min (Azimi et al. 2016) A: Number of printers in the modelled room= 1 (Davis et al. 2019) V_m: Volume of modelled room (m^3)= 20 m^3 (ConsExpo Web; default for unspecified room) N_m: Air exchange rate of the modelled room (per hour)= 0.6/hour (ConsExpo Web 2018) Assumption: emissions were well-mixed within the modelled room.
Glue stick	Concentration of caprolactam: 1% (SDS 2018) Oral: Product amount= 0.4 g (EC 2016) External event dose= (product amount * concentration)/BW Dermal: Product amount= 0.08 g (RIVM 2007) External event dose= (product amount * concentration)/BW

	Inhalation: Scenario from ConsExpo Web: universal glue in a tube (RIVM 2007) Exposure to vapour, evaporation model Exposure duration: 240 minutes Product amount: 9 g Room volume: 20 m^3 (default for unspecified room) Ventilation rate: 0.6/hour Inhalation rate: 9.2 m^3/day (Health Canada 2015b) Mass Transfer Coefficient: 10 m/hour Release area: 0.02 m^2 Application duration: 10 minutes
Textiles (i.e. blankets, textile toys) (mouthing)	Estimated Daily exposure= C*SA*AW*M*F/BW C : Concentration= 1% (SDS 2014b) SA: Total surface area= 20 cm^2 (Zeilmaker et al. 1999) AW: Area weight of textile= 1 mg/cm^2 (all synthetic textiles, US EPA 2012) M: Migration fraction= 0.0005 (BfR 2007)[b] F: Frequency = 1/day
Textiles – baby sleeper (dermal)	Estimated daily exposure= C*SA*AW*SCF*M*F*DA/BW C:Concentration= 1% (SDS 2014b) SA: total surface area= 3 020 cm^2 (Health Canada 2018) AW: Area weight of textile= 1 mg/cm^2 (all synthetic textiles, US EPA 2012) M: Migration fraction= 0.0005 (BfR 2007)[b] F: Frequency= 1/day DA: dermal absorption= 100%
Diaper (dermal)	Approach obtained from ANSES 2019: DED = ($C_{shredded\ material}$ * W * F * T * Abs)/ BW DED: daily exposure dose $C_{shredded\ material}$: concentration of the chemical extracted with a solvent from shredded whole diapers and diaper parts (mg/kg of diaper)= 0.59 mg/kg (VITO 2018) W: average weight of a diaper or diaper part (kg)=0.024 kg (Krause et al 2006 and Rai et al 2009) F: frequency of use (#/day)= 12/day (Ishii et al. 2015 as cited in ANSES 2019) T: transfer to skin (%)= 100% (ANSES 2019) Abs: fraction absorbed by the skin (%)= 100% (ANSM 2010 as cited in ANSES 2019)

Lipstick (oral)	Scenario from ConsExpo Web: lipstick Direct product contact – Direct oral intake Concentration: 0.3%[c] Frequency: 1/day Amount applied/ingested: 0.022 g (Ficheux et al. 2016)

[a] Transfer coefficient = (1800 cm^2/hr * 4500 cm^2)/ 5300 cm^2 = 1528 cm^2/hr

[b] The "Textiles" Working Group (BfR 2007) uses a peak initial migration of 0.5% to estimate exposure to dyes from newly bought unwashed garments. The migration rate after 28 hours of simulated wash and wear cycles was observed to be less than one-tenth of the value measured for the first migration. The migration fraction of 0.0005 which is one-tenth of the peak initial migration (0.5%) is used to reflect exposure after the initial washes. It is assumed that the sweat migration rate is similar to the salivary migration rate; this is consistent with observations of leaching behaviours of dyes from textiles reported by Zeilmaker et al. (1999). This value is considered conservative because caprolactam is not used as a dye in the material, it is part of the fibres that make up the textile.

[c] Based on approximate caprolactam monomer concentration of 1% in Nylon 6 (Goldblatt et al. 1954 as cited in CIR 2013). Nylon 6 present at up to 30% in lip products (maximum caprolactam concentration: 0.30 * 0.01 = 0.3%)