Draft Screening Assessment

Aliphatic Diesters Group

Hexanedioic Acid, Diisodecyl Ester

Chemical Abstracts Service Registry Number 27178-16-1

Environment and Climate Change Canada
Health Canada

January 2018

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 one of two substances originally referred to collectively under the Chemicals Management Plan as the aliphatic diesters group. The substance in question, hexanedioic acid, diisodecyl ester (Chemical Abstracts Service Registry Number (CAS RN[1]) 27178-16-1), hereinafter referred to as DIDA, was identified as a priority for assessment as it met categorization criteria under subsection 73(1) of CEPA. The other substance was subsequently determined to be of low concern through another approach, and the proposed decision for this substance is provided in a separate report.[2] Accordingly, this screening assessment addresses DIDA.

According to information submitted under section 71 of CEPA, there were no reports of manufacture of DIDA above the reporting threshold of 100 kg in Canada in 2011. DIDA was reported to be imported into Canada in 2011 in the range of 1 000 000 to 10 000 000 kg for use as a plasticizer in electrical cables, as processing aids and as an ingredient in lubricants and greases. Lubricant-type products available to consumers in Canada containing DIDA were identified as motor oils, power steering fluids, aerosol lubricants and lubricant products designed to stop oil leaks. Additionally, DIDA is present as a non-medicinal ingredient in natural health products.

The ecological risks of DIDA 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. The ERC identified DIDA as having low potential to cause ecological harm.

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from DIDA. It is proposed to conclude that DIDA 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

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[2] A proposed conclusion for CAS RN 103-24-2 is provided in the Substances Identified as Being of Low Concern based on the Ecological Risk Classification of Organic Substances and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Draft Screening Assessment.

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.

With respect to human health, a read-across approach was used to characterize potential health effects of DIDA. Specifically, developmental toxicity was identified as the critical effect for risk characterization purposes using data available from the analogue di-(2-ethylhexl) adipate (DEHA, CAS RN 103-23-1). On the basis of a comparison of exposure estimates and critical effect levels identified in health effects studies, the margins of exposure were considered to be adequate to address uncertainties in the exposure and human health effects databases.

On the basis of the information presented in this draft screening assessment, it is proposed to conclude that DIDA 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.

Therefore, it is proposed to conclude that DIDA does not meet any of the criteria set out in section 64 of CEPA.

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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 one of two substances (hexanedioic acid, diisodecyl ester, Chemical Abstracts Service Registry Number [CAS RN[2]] 27178-16-1, hereinafter referred to as DIDA) originally referred to collectively under the Chemicals Management Plan as the aliphatic diesters group, to determine whether it presents or may present a risk to the environment or to human health. This substance was identified as a priority for assessment as it met categorization criteria under subsection 73(1) of CEPA (ECCC, HC [modified 2007]).

The other substance (nonanedioic acid, bis(2-ethylhexyl) ester, CAS RN 103-24-2) was considered in the Ecological Risk Classification of Organic Substances (ERC) and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances science approach documents (ECCC 2016a; Health Canada 2016) and was identified as being of low concern to both human health and the environment. As such, it is not addressed in this report. Proposed conclusions for this substance are provided in the Substances Identified as Being of Low Concern based on the Ecological Risk Classification of Organic Substances and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Draft Screening Assessment (ECCC, HC 2017).

The ecological risk of DIDA was characterized using the ERC approach (ECCC 2016a). The ERC describes the hazard of a substance using key metrics, including mode of action, chemical reactivity, food-web derived internal toxicity threshold, bioavailability, and chemical and biological activity, and it considers the possible exposure of organisms in the aquatic and terrestrial environments on the basis of factors including 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.

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 February 2017. Empirical data from key studies as well as some results from models were used to reach proposed conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

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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, which was subject to an external peer-review and a 60-day public comment period. The human health portion of this assessment has undergone external review and/or consultation. Comments on the technical portions relevant to human health were received from Lynne Haber, Department of Environmental Health, College of Medicine, University of Cincinnati, Michael Jayjock, Jayjock & Associates, and Chris Bevan, CJB Consulting. 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 DIDA meets the criteria as set out in section 64 of CEPA, by examining scientific information and incorporating a weight-of-evidence approach and precaution.[3] This draft screening assessment presents the critical information and considerations on which the proposed conclusion is based.

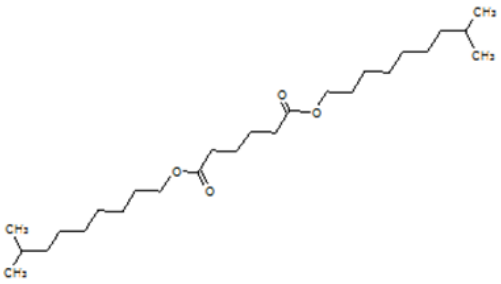
2. Identity of Substance

The Chemical Abstracts Service Registry Number (CAS RN), *Domestic Substances List* (DSL) name, common name and acronym for DIDA are presented in Table 2-1.

Table 2-1. Substance identity

CAS RN (acronym)	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)

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

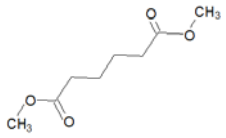
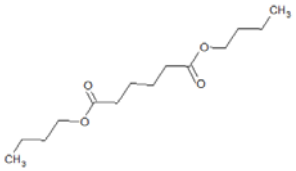
CAS RN (acronym)	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
27178-16-1 (DIDA)	Hexanedioic acid, diisodecyl ester (diisodecyl adipate)	 $C_{26}H_{50}O_4$	426.68

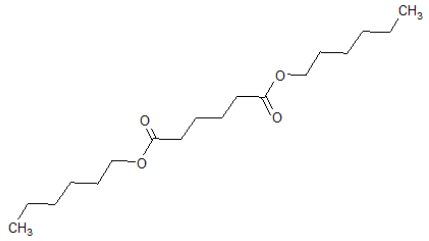
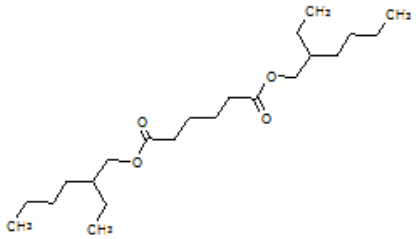
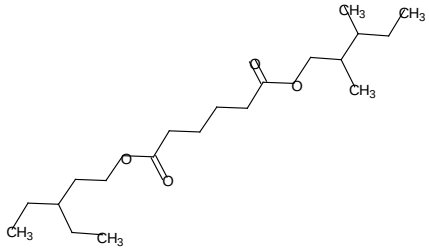
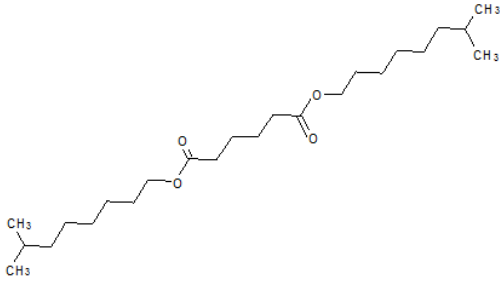
Abbreviations: DIDA, diisodecyl adipate

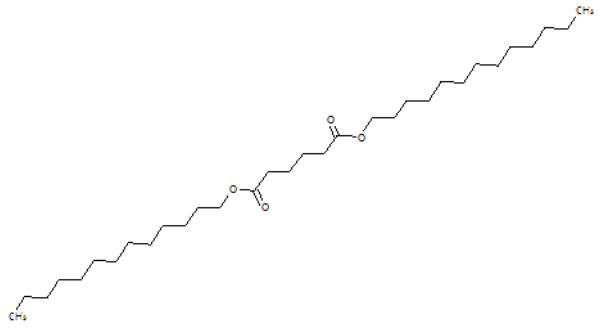
2.1 Selection of Analogues

A read-across approach using data from analogues has been applied to inform the human health assessment. Analogues were selected that were structurally and/or functionally similar to DIDA (e.g., with respect to physical-chemical properties, toxicokinetics, and reactivity) and that had relevant empirical data that could be used to inform the characterization of potential health effects for DIDA. Appendix A describes the considerations applied to identify relevant analogues. A list of the various analogues used to inform this assessment is presented in Table 2-2. For further information on the physical-chemical properties of the analogues, please refer to Appendix B. Details of the application of the read-across approach used to inform the human health assessment of DIDA are further discussed in the relevant sections of this report.

Table 2-2. Analogue Identities

CAS RN	Common name (acronym)	Chemical structure, molecular formula, and molecular weight (g/mol)
627-93-0	Adipic acid, dimethyl ester	 $C_8H_{14}O_4$, 174.95 g/mol
105-99-7	Hexanedioic acid, 1,6-dibutyl ester	 $C_{14}H_{26}O_4$, 258.36 g/mol

110-33-8	Hexanedioic acid, dihexyl ester	 $C_{18}H_{34}O_4$, 314.46 g/mol
103-23-1	Hexanedioic acid, 1,6-bis(2-ethylhexyl) ester (DEHA)	 $C_{22}H_{42}O_4$, 370.57 g/mol
68515-75-3	Hexanedioic acid, di-c7-c9 branched and linear alkyl esters	 (Representative structure)[1] UVCB, 356.54-413 g/mol
33703-08-1	Hexanedioic acid, diisononyl ester (DINA)	 $C_{24}H_{46}O_4$, 398.62 g/mol

16958-92-2	Hexanedioic acid, ditridecyl ester	 $C_{32}H_{62}O_4$, 510.84 g/mol

[1] Reference: US EPA 2008

3. Physical and Chemical Properties

A summary of physical and chemical properties of DIDA are presented in Table 3-1. When experimental information was limited or not available, cited results from estimation programs were used as predicted values for the substance. Additional physical and chemical properties are presented in ECCC (2016b).

Table 3-1. Experimental physical and chemical property values (at standard temperature) for DIDA

Property	Range	Type of value	Key reference(s)
Physical state	Liquid	N/A	US EPA 2008
Boiling point (°C)	426	Modelled	US EPA 2008
Vapour pressure (mm Hg @ 20°C)	1.15×10^{-7}	Experimental	Anonymous 2010, as cited in ECHA, c2007-2016a
Henry's law constant ($Pa \cdot m^3/mol$)	8.6	Modelled	US EPA 2008
Water solubility (mg/L @ 25°C)	4.4×10^{-5}	Experimental	Letinski et al. 2002
log K_{ow} (dimensionless)	10.1	Modelled	US EPA 2008

Abbreviations: N/A, not applicable; K_{ow}, octanol–water partition coefficient.

4. Sources and Uses

DIDA was included in a survey issued pursuant to section 71 of CEPA (Canada 2012). DIDA was not manufactured in Canada above the reporting threshold of 100 kg in 2011. Table 4-1 presents a summary of the total reported import quantities for DIDA in 2011.

Table 4-1. Summary of information on Canadian imports of DIDA submitted pursuant to a section 71 survey of CEPA

Common name	Total imports[a] (kg)	Reporting year	Survey reference
DIDA	1 000 000–10 000 000	2011	Canada 2012

[a] Values reflect quantities reported in response to the survey conducted under section 71 of CEPA (Environment Canada 2013). See survey for specific inclusions and exclusions (schedules 2 and 3).

In Canada, the reported uses of DIDA were as a plasticizer in low temperature electrical cables, as a processing aid, and as a lubricant and lubricant additive. DIDA is noted to have lower volatility and lower compatibility with the polymer relative to other specialty low-temperature plasticizers (Hallstar c2017).

In Canada, most reported uses of DIDA in lubricants and greases were associated with commercial uses; however, a limited number of products are available to consumers, specifically motor oils, power steering fluids, aerosol lubricants and a lubricant product designed to stop oil leaks (ECCC 2016c; SDS 2015; SDS 2012).

No notifications for cosmetics containing DIDA were identified in Canada (personal communication, email from the Consumer Product Safety Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated September 21, 2016; unreferenced). DIDA was not found on the List of Prohibited and Restricted Cosmetic Ingredients (more commonly referred to as the Cosmetic Ingredient Hotlist or simply the Hotlist), an administrative tool that Health Canada uses to communicate to manufacturers and others that certain substances may contravene the general prohibition found in section 16 of the *Food and Drugs Act*, or may contravene one or more provisions of the *Cosmetic Regulations* (Health Canada 2015).

DIDA is listed in the Natural Health Products Ingredients Database with a non-medicinal role for topical use (only) as a plasticizer, skin-conditioning agent – emollient, or solvent in natural health products (NHPID [modified 2017]). It is listed in the Licensed Natural Health Products Database as being present as a non-medicinal ingredient in currently licensed natural health products (such as an acne treatment sulphur wash) (LNHPD [modified 2016]). DIDA is not permitted for use in Canada as a food additive nor has it been identified for use in food packaging (personal communication, email from the Health Products Food Branch, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated September 22, 2016; unreferenced). The United States Food and Drug Administration identify DIDA as permitted for use in indirect food additives as a component of adhesives and coatings and as a component of rubber articles intended for repeated use (US CFR 2016a, 2016b).

In Canada, DIDA was not found to be a non-medicinal ingredient in drug products (personal communication, email from the Therapeutic Products Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated January 19, 2017; unreferenced).

DIDA was reported to be used as a formulant in one registered pesticide product in Canada (personal communication, email from the Pest Management Regulatory Agency, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated October 6, 2016; unreferenced).

Globally, this substance is used in products such as washing and cleaning products, metal surface treatment products, textile treatment products and dyes, polymers and polishes and waxes. It may be used for the manufacture of plastic products, chemicals and rubber products (ECHA, c2007-2016a). There is limited evidence for the use of DIDA as a plasticizer in toys, but one migration study noted the presence of DIDA in three toys on the market in Europe (Fiala and Steiner 2005). A limited number of uses of DIDA in products available to consumers, including a sunscreen product, have been found from sources in the United States (Hallstar c2017; DailyMed c2001-2017).

5. Potential to Cause Ecological Harm

5.1 Characterization of Ecological Risk

The ecological risk of DIDA was characterized using the ecological risk classification of organic substances (ERC) (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., LC_{50}) 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, 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), 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 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, 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 in empirical or modeled 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 QSAR models. The impact of this error is mitigated, however, by the fact that overestimation of median lethality will result in a conservative (protective) tissue residue used for critical body residue (CBR) analysis. Error in 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 based on what is believed to be the current use quantity, and may not reflect future trends.

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

DIDA was classified under ERC as having a moderate hazard potential based on mode of toxic action above baseline (i.e., above narcosis) and a moderate hazard assessment factor (HAF). The exposure potential was classified as high because of its high overall persistence and large use volume. Given its classification as having a moderate potential for ecological risk, it is unlikely that this substance results in concerns for organisms or the broader integrity of the environment in Canada considering current use patterns. As DIDA is currently being used in very high quantities in Canada, fluctuations in use patterns are unlikely to result in a significant increase in risk to the environment.

6. Potential to Cause Harm to Human Health

6.1 Exposure Assessment

Environmental media and food

DIDA is of low water solubility and low vapour pressure. There is no Canadian data for DIDA in dust, soil, food, indoor or outdoor air, or drinking water. A screening assessment done by the Swedish Environmental Research Institute for the Swedish Environmental Protection Agency, reported that DIDA was not detected in air, water, sediment, sludge or biota (Remberger et al. 2005). This substance was noted to be below the detection limit (20 µg/L) in 40 samples of breast milk in Sweden (Remberger et al. 2005). Given this data, DIDA exposure associated with presence in breast milk is anticipated to be minimal.

Environmental distribution of DIDA was examined using ChemCAN (2003). Drinking water concentration estimates were based on environmental concentrations for surface water derived from ChemCAN simulations. Ambient air estimates were also derived from ChemCAN simulations. Indoor air concentrations of DIDA were not found; however, Bui et al. (2016) noted that plasticizers such as DIDA, with relatively high octanol-water partition coefficients (K_{ow}) and air-water partition coefficients (K_{aw}) were not likely to partition significantly to indoor air. In the estimate of total daily intake, the ambient air concentration was used to represent the indoor air concentration. As no soil or dust data for DIDA were available, concentrations were based on environmental concentrations for soil derived from ChemCAN simulations. The amount of indoor dust ingested each day is based on Wilson et al. (2013).

The highest total daily intake was estimated to be 1.2×10^{-4} mg/kg bw/day for formula-fed infants (0 to 6 months). Total daily intake for various age groups from sources including air, drinking water and soil are presented in Table C-2 of Appendix C.

Products available to consumers

DIDA was identified as being present in motor oil products in concentrations up to 15% (wt %) (SDS 2015); the motor oil scenario was considered to address other similar exposure scenarios, such as a power steering fluid and stop leak product containing up to 3% DIDA (SDS 2012).

DIDA was identified at a concentration of 14.2% (wt%) in an aerosol lubricant available to consumers (ECCC 2016c).

DIDA was identified to be present as a non-medicinal ingredient in currently licensed natural health products (such as an acne treatment sulphur wash), at a concentration of 1% to 5% (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated September 19, 2016; unreferenced). Dermal exposure estimates were derived for teens and adults using this product.

No dermal absorption data was found for DIDA. However, its physical-chemical properties, such as its high log K_{ow} (i.e., >8) and its molecular weight of 427 g/mol, are considered to be an indication of lower potential for dermal absorption (EC 2004).

As noted in sections 2.1 and 6.2, DEHA is one of the analogues considered in a read-across approach for DIDA. This substance was assessed under the Chemicals Management Plan (CMP) (Environment Canada, Health Canada 2011a). In the Challenge screening assessment, the dermal absorption of DEHA was expected to be low given its physical and chemical properties (low water solubility and high log K_{ow}) and also given preliminary results of an in vitro study demonstrating low amounts in receptor fluid. However, uncertainty associated with the skin-bound portion in the in vitro study resulted in a dermal absorption estimate of 10% being applied in the DEHA screening assessment.

Final results of the DEHA in vitro study published in 2013 (Zhou et al. 2013), after the publication of the DEHA screening assessment, do not contraindicate the use of a 10% dermal absorption for DEHA.

Another analogue identified in the read-across approach was hexanedioic acid, ditridecyl ester. No studies specifically designed to measure dermal absorption of this substance were identified. However, a study summary report for a dermal toxicity study in which rats were treated with 0, 800 or 2000 mg/kg bw/day 5 days a week for 13 weeks noted that dermal absorption was 10%, as measured using the ^{14}C-radiolabeled substance in a separate group of rats (EPA 2008).

On the basis of available information, a dermal absorption value of 10% was considered appropriate for DIDA and was applied to estimate systemic exposure from dermal uses.

DIDA is also used as a plasticizer in products that may be available to consumers (i.e., electrical cables). However, exposure via the oral (i.e., children mouthing) and dermal routes associated with contact with electrical cables is expected to be minimal. A study conducted in Austria in 2003 noted the presence of DIDA in the migration solutions of 3 toys on examination of 11 toy samples (Fiala and Steiner 2005). The highest mean migration value for DIDA was 180 µg/100 mL water based on a 10 cm^2 piece of toy immersed in 100 mL pure water and rotated for 3 hours. Although this substance was not demonstrated to be present in toys on the market in Canada, on the basis of conservative assumptions, oral exposure to infants and children from mouthing of toys is considered to be less than other scenarios presented in this section. Details of assumptions for this potential source of exposure are provided in Appendix C.

Exposure estimates for scenarios associated with the use of products available to consumers containing DIDA are presented in Tables 6-1. Parameters used in the calculations are presented in Appendix C, Table C-1.

Table 6-1. Estimates of exposure to DIDA from the use of products available to consumers

Product scenario	Product concen-tration (%)	Frequency of exposure	Dermal exposure (mg/kg bw/day)[a]	Inhalation exposure (air concentra-tion) and dose (mg/kg bw)	Oral exposure (mg/kg bw)
Acne treatment sulphur wash (teen)	5%	Daily	0.004	N/A	N/A
Motor oil (adult)	15%	Intermittent	0.04	N/A	N/A
Aerosol spray lubricant (adult)	14.2%	Intermittent	0.06	17 mg/m^3 (per event) 0.35 mg/m^3 (mean concentration on day of exposure) Dose: 0.1 mg/kg bw	0.02[c]

Abbreviations: NA, not available; N/A, not applicable
[a] Dermal exposure estimates incorporate a dermal absorption factor of 10%
[b] Toddler: 0.5 to 4 years
[c] Includes oral intake of non-respirable particles

6.2 Health Effects Assessment

There are no hazard classifications for DIDA by the International Agency for Research on Cancer (IARC), the European Chemicals Agency (ECHA), or the United States Environmental Protection Agency (US EPA).

Toxicokinetics

There is no primary literature on the absorption, distribution, metabolism and elimination of DIDA. However, given its low water solubility (4.4×10^{-5} mg/L) and high lipophilicity (log K_{ow} ~ 10.1), uptake and absorption through the dermal route of exposure is expected to be low. DIDA is also considered to have low volatility (i.e., low vapour pressure of 1.15×10^{-7} mm Hg) and a high boiling point (426°C). Therefore, it is unlikely to be available as a vapour for inhalation. As a result of its high lipophilicity and low water solubility, however, any DIDA reaching the respiratory epithelium may be potentially absorbed via micellular solubilization. Once absorbed, the distribution of

DIDA is expected to be limited by its water solubility and may concentrate in adipose tissue because of its lipophilicity (anonymous 2010, as cited in ECHA c2007-2016a).

The chemical structure of DIDA can be characterized by a C6 backbone (hexanedioic acid) and two isodecyl alkyl chains. Metabolism is expected to occur initially through enzymatic hydrolysis, resulting in the release of the C6 dicarboxylic acid, along with the corresponding alcohols (Fiume et al. 2012). However, enzyme hydrolysis may be incomplete, resulting in the production of monoesters that could be further metabolized to the dicarboxylic acid and respective alcohol. Such metabolites for DIDA (i.e., hexanedioic acid monoisodecyl ester, hexanedioic acid, isodecyl alcohol) have been predicted using rat liver metabolism simulators (OECD QSAR Toolbox 2013; TIMES 2014). The hydrolysis products may then be further metabolized or undergo conjugation reactions to polar compounds that are excreted (ACC 2003). Alternatively, they may be conjugated, excreted in the bile and potentially undergo enterohepatic recycling (anonymous 2010, as cited in ECHA c2007-2016a).

Repeated-dose toxicity

The short-term effects of DIDA have been investigated in a 14-day oral study in which rats were administered 1000 mg/kg bw/day of DIDA (n=7/sex/group) (anonymous 1970, as cited in ECHA c2007-2016a). Clinical signs, hematological parameters, urinalysis, gross pathology, and histopathology were examined in the study. No treatment-related adverse effects were identified. The study results were summarized in a registration dossier (ECHA c2007-2016a), but only limited details on study design and outcome were provided.

With respect to subchronic toxicity, the data from the analogue hexanedioic acid, diisononyl ester (DINA, CAS 33703-08-1) were considered. DINA is considered to be a suitable analogue because of its high structural similarity to DIDA, differing in only one carbon atom on each of the two alkyl chains (i.e., C9 vs C10). DINA and DIDA also share similar physical-chemical properties, similar reactivity profiles, and similar degradation products as determined using metabolism simulators (OECD QSAR Toolbox 2013; TIMES 2014).

Two 13-week subchronic dietary studies on DINA have reported effects in rats and beagle dogs at the highest doses tested. In the rat study, a no-observed-adverse-effect level (NOAEL) of 500 mg/kg bw/day (highest dose tested) was determined by the authors on the basis of a statistically significant increase in the ratio of kidney weight to body weight, although absolute kidney weights remained unchanged (unpublished information 1971a, as cited in ACC 2003). In the dog study, a NOAEL of 1% (~274 mg/kg bw/day) was determined by the authors on the basis of the presence of adverse effects in the high-dose group (decreased body weight, food consumption, increased liver weight, elevated enzyme levels, liver and kidney discoloration, and histopathological changes in the liver and kidneys) (unpublished information 1971b, as cited in ACC 2003).

Chronic toxicity/carcinogenicity

No studies on the effects of DIDA from long-term/chronic exposure were identified. Di-(2-ethylhexyl) adipate (DEHA, CAS RN 103-23-1) was found to be the closest analogue to DIDA for which data on chronic toxicity/carcinogenicity was identified. DEHA contains a 6-carbon (C6) diacid backbone with two branched alkyl chains and shares the same structural alerts as DIDA (OECD QSAR Toolbox 2013). For example, both DEHA and DIDA have a structural alert for in vivo mutagenicity since their structures have the potential to interact with DNA and protein through non-covalent binding. They are also associated with a structural alert for carcinogenicity through a non-genotoxic mode of action. In addition, both DIDA and DEHA may be metabolized to hexanedioic acid, although other metabolites may differ (e.g., alcohols and monoesters). With respect to physical-chemical properties, both DIDA and DEHA have relatively similar molecular weights (427 vs. 370 g/mol, respectively), low vapour pressures (1.15×10^{-7} vs. 8.5×10^{-7} mm Hg, respectively), and high log K_{ow} values (10.1 vs >6.1, respectively). However, the two substances differ in water solubility by orders of magnitude (4.4×10^{-5} vs. 0.0032 to 0.78 mg/L, respectively).

The Government of Canada has published a screening assessment report (SAR) for DEHA (Environment Canada, Health Canada 2011a). The health effects characterization of DEHA from this assessment was used to inform the health effects characterization of DIDA, where applicable. A literature search was conducted from one year prior to the DEHA SAR (i.e., September 2011) to June 2016. No health effects studies, which could impact the health effects assessment (i.e., result in different critical endpoints or lower points of departure than those stated in the SAR) were identified. DEHA is classified by the IARC as a Group 3 substance (not classifiable as to its carcinogenicity to humans) (IARC 2000). The US EPA has classified DEHA as a Class C substance (possible human carcinogen) because of the absence of human data and the increased incidence of liver tumours in female mice (US EPA 1994).

As indicated in the DEHA SAR (Environment Canada, Health Canada 2011a), no histopathological changes other than liver tumours were observed in an oral, chronic toxicity/carcinogenicity study in Fischer 344 rats and B6C3F1 mice administered DEHA at doses of up to 25 000 ppm (NTP 1982; US EPA 1984b; Kluwe et al. 1985). Furthermore, no treatment-related increases in tumour incidence was observed in a 2-year dietary study in rats administered up to 2.5% DEHA (equivalent to 1286 mg/kg bw/day) or a 1-year dietary study in dogs administered 0.2% DEHA (equivalent to 50 mg/kg bw/day) (Hodge et al. 1966).

With regard to the dermal route of exposure, no gross or histopathological changes in the skin and no treatment-related increases in tumour incidence were noted in C3H mice administered 0, 0.1, and 10 mg DEHA (equivalent to 0, 3.3, and 333 mg/kg bw) in 0.2 mL acetone on the scapular region over a period of the animal's lifetime (Hodge et al. 1966). However, this study only examined a small number of endpoints (i.e., average cage weights, gross autopsies).

The hepato-carcinogenic effects of DEHA are proposed to be mediated through peroxisome proliferation (Reddy et al. 1980). For a comprehensive analysis of these effects, please refer to the SAR for DEHA (Environment Canada, Health Canada 2011a). Some of the metabolites for DEHA (e.g., 2-ethylhexanol and 2-ethylhexanoic acid) have been implicated in the induction of peroxisome proliferation (Keith et al. 1992), suggesting that the 2-ethylhexyl moiety of the chemical structure may play a role in peroxisome proliferation. Such effects have been observed with other chemicals containing the 2-ethylhexyl moiety (Moody and Reddy 1978; Kawashima et al. 1983a; Kawashima et al. 1983b; Kluwe et al. 1985).

The Government of Canada concluded that the effects reported in short-term and subchronic studies and subsequent tumours found in chronic studies related to peroxisome proliferation after exposure to DEHA would not be relevant for risk characterization to human health (Environment Canada, Health Canada 2011a). This conclusion was based on the available evidence indicating that liver carcinogenesis induced by peroxisome proliferation is not likely to occur in humans. Accordingly, carcinogenicity is not considered a relevant endpoint in the characterization of risk to human health from exposure to DIDA.

Further support that carcinogenicity is likely not a relevant endpoint for DIDA is provided by the following lines of evidence: (1) DIDA does not contain the 2-ethylhexyl moiety in its chemical structure; (2) DIDA has not been predicted to be biotransformed to metabolites that harbour the 2-ethylhexyl moiety (OECD QSAR Toolbox 2013; TIMES 2014); (3) The anticipated metabolites for DIDA (e.g., adipic acid, isodecanol) have not been identified to be carcinogenic or result in peroxisome proliferation (Moody and Reddy 1978; OECD 2004; OECD 2006); and (4) DIDA has not been determined to be "active" in PPARα assays in the ToxCast/Tox21^{TM} High Throughput Screening Program (iCSS ToxCast Dashboard 2015).

Genotoxicity

The genotoxicity data for DIDA is currently limited to in vitro studies. In a bacterial reverse mutation assay, genotoxicity was negative in the following strains of *Salmonella typhimurium* with and without metabolic activation: TA1535, TA1537, TA98, TA100, and TA102 (Anonymous 2002, as cited in ECHA c2007-2016b). In a gene mutation assay using mouse lymphoma L5178Y cells, a general increase in mutant frequency was observed in the absence of metabolic activation, although these increases did not meet the evaluation criteria of a reproducible two-fold increase in the mutant frequency relative to the controls (Anonymous 2002, as cited in ECHA c2007-2016b). Increases in mutant frequency were not observed in the presence of metabolic activation. It was concluded that without metabolic activation, an ambiguous increase in mutant frequency was observed. In a chromosome aberration test using human lymphocytes, DIDA was observed to induce chromosome aberrations (Anonymous 2002, as cited in ECHA c2007-2016b). However, these results only occurred following long-term treatment without metabolic activation and at doses that also elicited cytotoxicity. Furthermore, there were no findings of chromosome aberrations in the presence of metabolic

activation. Overall, these results suggest that DIDA is not likely to be genotoxic in in vitro systems.

Reproductive and developmental toxicity

Developmental toxicity was identified as a critical effect for the analogue DEHA, but no reproductive and developmental toxicity studies were identified for DIDA. Therefore, data from multiple analogues, namely DEHA (CAS RN 103-23-1), hexanedioic acid, di-C7-C9 branched and linear alkyl esters (CAS RN 68515-75-3), and hexanedioic acid, ditridecyl ester (CAS RN 16958-92-2), were taken into consideration for characterization of these endpoints. Information on the physical-chemical properties of the analogues is available in Appendix B.

A more detailed assessment of the effects of DEHA on reproductive and developmental toxicity can be found in the DEHA SAR (Environment Canada, Health Canada 2011a). Pertinent findings for the assessment of DIDA are summarized in the following paragraphs.

In a subacute oral toxicity study in which DEHA was orally administered to rats by gavage, disturbance of the estrous cycle and increased ovarian follicle atresia were detected at the highest dose tested (1000 mg/kg bw/day) (Miyata et al. 2006). No abnormalities were detected in the male rats. In another study, an increase in atresia of large follicle, decrease in formed corpus luteum and follicular cyst, a significant increase in mean estrous cycle and post-implantation loss rate were observed in animals administered ≥ 1000 mg/kg bw/day, which were accompanied by histopathological changes in the ovaries (Wato et al. 2009). The lowest lowest-observed-adverse-effect level (LOAEL) reported for reproductive toxicity (800 mg/kg bw/day) was identified in a study in female Wistar rats administered DEHA at doses of 0 to 800 mg/kg bw/day by oral gavage from gestation day (GD) 7 to postnatal day (PND) 17 (Dalgaard et al. 2003). At 800 mg/kg bw/day, effects of prolonged gestation period and decreased maternal body weight gain were observed.

In the developmental study conducted by Dalgaard et al. (2003), pregnant rats were administered 0, 200, 400, or 800 mg/kg bw/day of DEHA via oral gavage. Dose-dependent post-natal death was observed in the study, which was statistically significant at doses ≥400 mg/kg bw/day. The NOAEL for development effects was determined to be 200 mg/kg bw/day. This is based on the observations of post-natal death at the next dose levels. The mechanism of these effects is not currently understood.

No reproductive toxicity studies were available for the analogue hexanedioic acid, di-c7-c9 branched and linear alkyl esters (CAS RN 68515-75-3). However, no treatment-related adverse effects to male or female reproductive organs were observed in rats administered up to 2.5% in the diet (approximately 1500 mg/kg bw/day for males and 1950 mg/kg \-bw/day for females) for 90 days (Solutia Inc 1972, as cited in ACC 2003; US EPA 2008).

In terms of developmental toxicity, hexanedioic acid, di-c7-c9 branched and linear alkyl esters was investigated in a prenatal developmental toxicity study in female rats administered 0, 1000, 4000, or 7000 mg/kg bw/day by oral gavage during GD 6 to 19 (Solutia Inc 1981, as cited in ACC 2003). Clinical signs and body weights were recorded on GD 0, 6, 15, and 20. Animals were sacrificed on GD 20 and the uteri were removed and weighed. The numbers of implantations, live fetuses, resorptions and corpora lutea were determined with no statistically significant effects observed. Fetuses were weighed and examined for external, skeletal, and soft tissue defects. At the highest dose (7000 mg/kg bw/day), maternal body weights were significantly decreased. At the same dose, there were also observations of lower fetal body weights (although not statistically significant) and an increased incidence of rudimentary structures (unilateral/bilateral and adjacent to the last thoracic or first lumbar vertebral transverse process, unknown significance). Treatment-related, adverse effects on fetal development were not reported in the absence of maternal toxicity. No dermal or inhalation studies investigating developmental toxicity have been identified for hexanedioic acid, di-C7-C9 branched and linear alkyl esters.

No reproductive toxicity studies were available for the analogue hexanedioic acid, ditridecyl ester (CAS RN 16958-92-2). However, no treatment-related adverse effects were seen in sperm morphology, uterus or epididymides weights, or histopathology in rats, at doses up to 2000 mg/kg bw/day dermally, 5 days a week for 13 weeks (unpublished information 1988a, as cited in ACC 2003; US EPA 2008).

In terms of developmental toxicity, hexanedioic acid, ditridecyl ester was investigated in a prenatal developmental toxicity screen administering 0, 800, or 2000 mg/kg bw/day dermally to female rats during GD 0 to 19 (unpublished information 1988a, as cited in ACC 2003). Clinical signs were examined throughout the gestation period. On GD 20, the animals were sacrificed and uteri were removed, weighed, and examined for the number of corpora lutea, number of implantation sites and number/location of fetuses/resorptions. Fetuses were inspected on total number, sex, weight, length, and external, visceral and skeletal defects. No adverse effects were reported in the dams. In fetuses, however, visceral anomalies (increased incidence of levocardia) were detected at 2000 mg/kg bw/day, resulting in a NOAEL of 800 mg/kg bw/day, as reported by US EPA (2008). However, a subsequent prenatal developmental toxicity study in a larger group of dams did not result in any maternal or developmental effects in animals treated with doses up to 2000 mg/kg bw/day (unpublished information 1988b, as cited in ACC 2003; US EPA 2008). The NOAEL for developmental toxicity for this study was reported to be 2000 mg/kg bw/day by the US EPA (2008). No oral or inhalation studies on developmental toxicity have been identified for hexanedioic acid, ditridecyl ester.

Overall, data on DEHA provided the most appropriate point of departure (i.e., the lowest NOAEL) and was selected as the analogue for the reproductive and developmental toxicity endpoints for read-across purposes. This approach is consistent with the US EPA's Screening Level Hazard Characterization for the Diesters Category (2008). Registration dossiers submitted to the ECHA have also presented DEHA studies in weight-of-evidence approaches in determining the hazard for the following substances:

hexanedioic acid, 1,6-dibutyl ester (CAS RN 105-99-7) (ECHA c2007-2016c), hexanedioic acid, dihexyl ester (CAS RN 110-33-8) (ECHA c2007-2016d), hexanedioic acid, ditridecyl ester (CAS RN 16958-92-2) (ECHA c2007-2016e), and DINA (CAS RN 33703-08-1) (ECHA c2007-2016f). These substances have also been identified as analogues of DIDA (Table 2-2).

6.3 Characterization of Risk to Human Health

On the basis of the available information on DIDA and the analogues, DIDA is not considered to be genotoxic or carcinogenic. A NOAEL of 200 mg/kg bw/day based on post-natal death observed at the next dose level (400 mg/kg bw/day) from a developmental toxicity study in rats conducted with DEHA, an analogue of DIDA, was identified as the critical effect level for characterization of risk for intermittent and chronic exposure to DIDA. This critical effect level is consistent with that identified in the DEHA SAR generated by the Government of Canada (Environment Canada, Health Canada 2011a). The lowest NOAEL associated with the analogue DINA (highest similarity in chemical structure, metabolism, reactivity, and physical-chemical properties) was 274 mg/kg bw/day and was also taken into consideration for intermittent exposure scenarios. However, the analogue DEHA provided a more conservative point of departure (i.e., 200 mg/kg bw/day) and was based on a critical effect (developmental toxicity) that has not been investigated for DINA.

The maximum estimated exposure to DIDA through environmental media was 1.21 x 10^{-4} mg/kg bw/day (based on the subpopulation with the highest estimates, i.e., formula fed infants 0 to 6 months old). Using the NOAEL of 200 mg/kg bw/day results in MOEs greater than 1 000 000.

Comparison of the NOAEL of 200 mg/kg bw/day based on DEHA to the estimate of exposure to DIDA from intermittent use of motor oil or aerosol lubricant products resulted in margins of exposure (MOEs) of 5000 and 1111, respectively. Comparison of this NOAEL to the estimate of exposure from the chronic use of the acne treatment sulphur wash resulted in an MOE of 45 700. These MOEs are considered adequate to address uncertainties in the health effects and exposure databases for these scenarios.

Table 6-2 provides all relevant exposure and hazard values for DIDA, as well as resultant MOEs for determination of risk.

Table 6-2. Relevant exposure, critical effect level and resulting MOEs for DIDA

Exposure scenario	Systemic exposure (mg/kg bw/day)	Critical effect level (NOAEL, mg/kg bw/day)	Critical health effect endpoint	MOE

Environmental media	1.21 x 10^{-4}	200	Dose-related increase in post-natal deaths.	>1 000 000
Acne treatment sulphur wash (chronic dermal)	0.004	200	Dose-related increase in post-natal deaths.	45 700
Motor oil (intermittent dermal)	0.04	200	Dose-related increase in post-natal deaths.	5 000
Aerosol lubricant (intermittent all routes)	0.18	200	Dose-related increase in post-natal deaths.	1 111

While exposure of the general population to DIDA is not of concern at current levels, this substance is considered to have a health effect of concern given its potential to elicit developmental toxicity (based on read-across from the analogue DEHA). Therefore, there may be a concern for human health if exposures were to increase.

6.4 Uncertainties in Evaluation of Risk to Human Health

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

Table 6-3. Sources of uncertainty in the risk characterization

Key source of uncertainty	**Impact**
Exposure	
Dermal absorption data is not available for DIDA; the dermal absorption value is based on available information, including considering physical-chemical properties (including modelled values, e.g., log K_{ow}) and dermal absorption potential of analogues. Given these factors, the dermal absorption factor is considered conservative.	+
Inhalation was identified as a potential route of exposure associated with the aerosol product; however, there are no route-specific inhalation toxicity studies. Characterization of risk from inhalation exposure to DIDA is based on route-to-route extrapolation.	+/-
Hazard	
There is inherent uncertainty in the use of a read-across approach and in the extrapolation of data from analogues to DIDA.	+/-

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

7. Conclusion

Considering all available lines of evidence presented in this draft screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from DIDA. It is proposed to conclude that DIDA 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.

On the basis of the information presented in this draft screening assessment, it is proposed to conclude that DIDA 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.

Therefore, it is proposed to conclude that DIDA does not meet any of the criteria set out in section 64 of CEPA.

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Appendices

Appendix A. Considerations applied for the identification of relevant analogues

Table A-1. Considerations applied for the identification of relevant analogues

Consideration	Rationale
1) Diacid backbone. Emphasis was placed on chemical structures with a C6 (hexanedioic acid) backbone.	Aliphatic diesters are expected to be metabolized to the parent reaction products, namely the dicarboxylic acids and the corresponding monoalcohols. Analogues that breakdown to metabolic products similar to those predicted for DIDA are expected to contribute valuable information regarding toxicity.
2) Alkyl chains (branched or unbranched). Emphasis was placed on chemical structures with branched chains. However, linear chains were also considered for trend analysis purposes.	
3) Similar metabolites (predicted or observed).	
4) Common structural alerts (e.g., *in vivo* genotoxicity, carcinogenicity, etc.).	Analogues with similar structural alerts are expected to share greater similarity in terms of toxicity.
5) Similar physical-chemical properties. Emphasis was placed on chemical structures with similar molecular weight, water solubility, and log $K_{o/w}$. However, chemical structures with different physical chemical properties were also considered if they met the other selection considerations.	Analogues with similar physical chemical properties may potentially share similar toxicological profiles.

Appendix B. Physical-chemical property values for DIDA and its analogues

Table B-1. Physical-chemical property values for DIDA and its analogues

	Dimethyl adipate, CAS RN 627-93-0[a]	Dibutyl adipate, CAS RN 105-99-7[b]	Dihexyl adipate, CAS RN 110-33-8[a]	DEHA, CAS RN 103-23-1[c]	Hexanedioic acid, di-c7-c9 branched and linear alkyl esters, CAS RN 68515-75-3[b]	DINA, CAS RN 33703-08-1[b]	DIDA, CAS RN 27178-16-1	Hexanedioic acid, ditridecyl ester, CAS RN 16958-92-2[b]
MW (g/mol)	175	258	314	371	356-413	399	427	511
Physical state	Liquid	Liquid	Liquid	Oily liquid	Viscous liquid or solid	Liquid	Liquid	Solid
Vapour pressure (mm Hg)	$0.073^{\dagger}$ (25°C)	$0.003^{\dagger}$ (25°C)	$4 \times 10^{-5\dagger}$ (25°C)	$8.5 \times 10^{-7\ddagger}$	$9.75^{\ddagger}$ (224°C) $0.09^{\dagger}$ (25°C)	$0.9^{\ddagger}$ (200°C) $2.2 \times 10^{-5\dagger}$ (25°C)	$1.2 \times 10^{-7\ddagger}$	$1.4 \times 10^{-7\dagger}$ (25°C)
Henry's law constant ($atm \cdot m^3/mol$)	$2.3 \times 10^{-6\dagger e}$	$9.3 \times 10^{-7\dagger}$	1.7×10^{-5e}	$4.3 \times 10^{-7\ddagger}$	$1.8 \times 10^{-5\dagger}$	$2.9 \times 10^{-5\dagger}$	$8.5 \times 10^{-5\dagger}$	$4.7 \times 10^{-4\dagger}$
Water solubility (mg/L)	$14^{\dagger}$ (25°C)	$4.2^{\dagger}$ (25°C)	$0.0082^{\dagger}$ (25°C)	$0.0032^{\ddagger}$ (20°C) – $0.78^{\ddagger}$ (22°C)	$<0.048^{\ddagger}$ (25°C)	$0.00022^{\ddagger}$ (20°C)	$4.4 \times 10^{-5\ddagger}$ (25°C)	$3.4 \times 10^{-9\dagger}$ (25°C)
log $K_{o/w}$ (unitless)	$0.95^{\dagger}$	$4.33^{\dagger}$	$6.0^{\dagger}$	$>6.1^{\ddagger}$	$>6.48^{\ddagger}$	$9.24^{\dagger}$	$10.1^{\dagger}$	13.7^{d}

Abbreviations: MW, molecular weight
References: [a] Fiume et al. 2012; [b] US EPA 2008, unless specified otherwise; [C] Environment Canada, Health Canada 2011a; [d] ACC 2003; [e] ChemIDplus 1993
[†] estimated; [‡] measured

Appendix C. Parameters used to estimate exposure to DIDA

Exposures were based on the assumed weight and use behaviours of adults and teens, with body weights of 70.9 kg and 59.4 kg, respectively. Exposures for aerosol lubricant were estimated using ConsExpo Web (ConsExpo 2016) using specific inputs for penetrating spray lubricant (RIVM 2009) and DIY spray input parameters (RIVM 2007). A dermal absorption value of 10% was incorporated into dermal exposure estimates. An inhalation rate of 21 m^3/day was assumed for adults (Health Canada 1998).

Table C-1: Dermal and inhalation exposure parameter assumptions

Exposure scenario	Assumptions
Motor oil	Skin surface area exposed: 12 cm^2 (based on fingertip area found RIVM 2007) Film thickness on skin: 0.01588 cm (Versar 1986) Density of product: 0.88 g/cm^3 (Versar 1986) Concentration of diisodecyl adipate: 15% (SDS 2015)
Aerosol lubricant (inhalation)	Model: ConsExpo aerosol spray (all parameters are from ConsExpo (2006) unless otherwise stated) Median particle diameter: 23.3 um (lognormal distribution; CV = 1.3; based on penetrating spray lubricants (RIVM 2009) Inhalation cut off diameter: 15 um Airborne fraction (non-volatile fraction that becomes airborne): 0.2 (Fscale default value particles < 22.5 um for penetrating spray lubricants (RIVM 2009) Mass generation rate: 1.2 g/s (default for DIY products) Spray duration: 170 seconds (based on DIY glue spray) Exposure duration: 30 minutes (based on DIY putty spray in garage) Product amount: 255 g Concentration of DIDA: 14.2% Room volume: 34 m^3 (garage) Room height: 2.25 m
Aerosol lubricant (dermal)	Model: ConsExpo aerosol spray (contact rate) Contact rate: 100 mg/min (default value for surface spraying aerosol) Release duration: 170 s Product amount: 283 mg Concentration of diisodecyl adipate: 14.2%
Acne treatment sulphur wash (using face cleanser scenario)	Adult: Product applied: 2.6 g/application (Loretz et al. 2008) Frequency per day: 2 per day (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada (HC), to the Existing Substances Risk Assessment

	Bureau, HC, dated September 19, 2016; unreferenced) Teen: Product applied: 2.6 g/application (Loretz et al. 2008) Frequency per day: 2 per day (personal communication, email from the Natural and Non-prescription Health Products Directorate, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated September 19, 2016; unreferenced) Concentration of 5%
Mouthing toys	Exposure = amount of substance available for migration out of toy/body weight Amount of substance: 180 µg (study using representative surface area of toy (10 cm^2) and duration of exposure (3 hours)) body weight = 15.5 kg (toddlers 0.5-4 years)

Table C-2: Maximal estimates of daily intake (ug/kg-bw/day) of DIDA

Estimated Intake (µg/kg-bw/day) of DIDA by Various Age Groups								
Age group:	0 - 0.5 yr[a]	0 - 0.5 yr[a]	0 - 0.5 yr[a]	0.5–4 yr[d]	5–11 yr[e]	12–19 yr[f]	20–59 yr[g]	60 + yr[h]
Route of exposure	(breast milk fed[b)]	(formula fed[c])	(not formula fed)	N/A	N/A	N/A	N/A	N/A
Ambient air[i]	0.0008	0.0008	0.0008	0.002	0.001	0.0007	0.0006	0.0006
Indoor air[j]	0.005	0.005	0.005	0.02	0.009	0.005	0.005	0.004
Drinking water[k]	0.00	0.12	0.04	0.05	0.04	0.02	0.03	0.03
Breast milk[l]	N/A	N/A	0.00	N/A	N/A	N/A	N/A	N/A
Soil[m]	0.0005	0.0005	0.0005	0.0008	0.0003	0.00006	0.00005	0.00005
Total intake[n]	0.005	0.12	0.05	0.06	0.05	0.03	0.03	0.03
Maximum Total Intake from All Routes of Exposure:								0.12

[a] Assumed to weigh 7.5 kg, to breathe 2.1 m^3 of air per day, to drink 0.2 L/day (not formula fed) and to ingest 30 mg of soil per day.
[b] Infants 0 – 6 months assumed to ingest 0.742 litre breast milk/day (US EPA 2011).
[c] Formula-fed infants are assumed to have an intake rate of 0.75 kg of formula per day.
[d] Assumed to weigh 15.5 kg, to breathe 9.3 m^3 of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day
[e] Assumed to weigh 31.0 kg, to breathe 14.5 m^3 of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day.
[f] Assumed to weigh 59.4 kg, to breathe 15.8 m^3 of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day.
[g] Assumed to weigh 70.9 kg, to breathe 16.2 m^3 of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day.
[h] Assumed to weigh 72.0 kg, to breathe 14.3 m^3 of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day.
[i] No ambient air data for DIDA were available; ambient air estimates were based on environmental concentrations for ambient air derived from ChemCAN simulations (in the case of air, using output of air concentration from one simulation as advective inflow concentration in second simulation)
[j] No indoor air data for DIDA were available so ambient air estimates were used for indoor air concentrations.
[k] No drinking water data for DIDA were available; drinking water concentration estimates were based on environmental concentrations for surface water derived from ChemCAN simulations (in the case of water, using output of surface water concentration from one simulation as advective inflow concentration in second simulation)
[l] DIDA was not found in breast milk.
[m] No soil or dust data for DIDA were available; concentrations were based on environmental concentrations for soil derived from ChemCAN simulations. The amount of indoor dust ingested each day is based on Wilson et al. (2013).
[n] Exposure from food from DIDA was not expected.