Screening Assessment

Organic Peroxides Group

Chemical Abstracts Service Registry Numbers
80-15-9
80-43-3

Environment and Climate Change Canada
Health Canada

June 2019

En14-378/2019E-PDF

ISBN 978-0-660-30906-4

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 two of six substances referred to collectively under the Chemicals Management Plan as the Organic Peroxides Group. These two substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA. The other four substances were subsequently determined to be of low concern through other approaches, and decisions for these substances are provided in a separate report.[1] Accordingly, this screening assessment addresses the two substances listed in the table below, which will hereinafter be referred to as the Organic Peroxides Group. The Chemical Abstracts Service Registry Numbers (CAS RN[2]), their *Domestic Substances List* (DSL) names and their common names are listed in the table below.

Table 1: Substances in the Organic Peroxides Group

CAS RN	DSL name	Common name
80-15-9	Hydroperoxide, 1-methyl-1-phenylethyl	Cumene hydroperoxide (CHP)
80-43-3	Peroxide, bis(1-methyl-1-phenylethyl)	Dicumyl peroxide (DCUP)

Cumene hydroperoxide (CHP) and dicumyl peroxide (DCUP), herein referred to as CHP and DCUP, do not occur naturally in the environment. According to information submitted pursuant to a survey under section 71 of CEPA, there were no reports of manufacture in Canada for either CHP or DCUP in 2011. In the same calendar year, 10 319 kg of CHP and 100 000 to 1 000 000 kg of DCUP were imported into Canada. Both CHP and DCUP are used as industrial processing agents and are expected to be present in negligible quantities in finished materials after processing. CHP has been reported under CEPA section 71 noticeto be used in commercial products such as adhesives and sealants, building and construction materials, and paints and coatings. DCUP has been reported under CEPA section 71 notice to be used in commercial products such as building and construction materials and plastic and rubber materials, as well as in products used in automotive, aircraft and transportation applications.

The ecological risks of the substances CHP and DCUP were characterized using the ecological risk classification of organic substances (ERC), which is a risk-based

[1] Conclusions for CAS RNs 133-14-2, 614-45-9, 3006-86-8, 3851-87-4 are provided in the Substances Identified as Being of Low Concern based on on the Ecological Risk Classification of Organic Substances and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Screening Assessment.

[2] 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.

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, CHP and DCUP are considered unlikely to be causing ecological harm.Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to the environment from CHP and DCUP. It is concluded that CHP and DCUP do not meet the criteria under paragraphs 64(*a*) or (*b*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that have or may have an immediate or long-term harmful effect on the environment or its biological diversity or that constitute or may constitute a danger to the environment on which life depends.

CHP was reviewed internationally as part of a hydroperoxides group through the Organisation for Economic Co-operation and Development (OECD) in 2008 and was also one of the organic peroxides reviewed by the Australian Government Department of Health (AGDH) in 2016. General toxicity for the oral, inhalation, and dermal routes of exposure were identified for the hydroperoxides group.

Exposures of the general population of Canada to CHP through environmental media and food are expected to be negligible. Exposure to CHP for the general population can occur from its use in adhesive products available to consumers. The margins between estimated dermal and inhalation exposures to CHP and the no adverse health effect levels derived from laboratory studies are considered adequate to address uncertainties in the health effects and exposure databases.

DCUP can cause adverse effects on the reproductive system. Exposure of the general population of Canada to DCUP from environmental media, food, and products is not expected, and the risk to human health is therefore considered to be low.

On the basis of the information presented in this screening assessment, it is concluded that CHP and DCUP do not meet the criteria under paragraph 64(*c*) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that CHP and DCUP do not meet any of the criteria set out in section 64 of CEPA.

Table of contents

List of tables

1. Introduction

Pursuant to section 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 on two of six substances, referred to collectively under the Chemicals Management Plan as the Organic Peroxides Group, to determine whether these two substances present or may present a risk to the environment or to human health. These two substances were identified as priorities for assessment as they met categorization criteria under subsection 73(1) of CEPA (ECCC, HC [modified 2017]).

The other four substances (listed in Table 1-1) were considered in the Ecological Risk Classification of Organic Substances (ERC) Science Approach Document (ECCC 2016a), and in the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Science Approach Document (Health Canada 2016), and were identified as being of low concern to both human health and the environment. As such, they are not further addressed in this report. Conclusions for these four substances are provided in the Substances Identified as Being of Low Concern using the Ecological Risk Classification of Organic Substances and the Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances Draft Screening Assessment (ECCC, HC 2018).

Table 1-1. Substances in the Organic Peroxides Group that were addressed under other approaches

CAS RN[3]	Domestic Substances List (DSL) name	Approach under which the substance was addressed	References
133-14-2	Peroxide, bis(2,4-dichlorobenzoyl)	ERC/TTC	ECCC, HC 2018
614-45-9	Benzenecarboperoxoic acid, 1,1-dimethylethyl ester	ERC/TTC	ECCC, HC 2018
3006-86-8	Peroxide, cyclohexylidenebis[(1,1-dimethylethyl)	ERC/TTC	ECCC, HC 2018
3851-87-4	Peroxide, bis(3,5,5-trimethyl-1-oxohexyl)	ERC/TTC	ECCC, HC 2018

[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.

The two substances addressed in this screening assessment are hereinafter referred to as the Organic Peroxides Group.

The two substances currently being assessed were previously reviewed internationally. Cumene hydroperoxide, herein referred to as CHP, has been reviewed internationally through the Organisation for Economic Co-operation and Development (OECD) in 2008 as a member of the hydroperoxides and reviewed by the Australian Government Department of Health (AGDH) in 2016 as a member of the organic peroxides. Dicumyl peroxide, herein referred to as DCUP, has been reviewed internationally through the OECD in 2012 as a member of the aryl substituted dialkyl peroxides. OECD 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 reliable. The OECD Screening Information Data Set (SIDS) Initial Assessment Profiles (SIAP) and Australian Human Health Tier II Assessment by AGDH were used to inform the health effects characterizations in this screening assessment.

The ecological risks of CHP and DCUP were characterized using the ERC (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 based on 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 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 August 2017. Empirical data from key studies as well as some results from models were used to reach conclusions. When available and relevant, information presented in assessments from other jurisdictions was considered.

This 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 peer-review and a 60-day public comment period. Additionally, the draft of this screening assessment (published April 28, 2018) was subject to a 60-day public comment period. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Health Canada and Environment and Climate Change Canada.

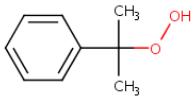
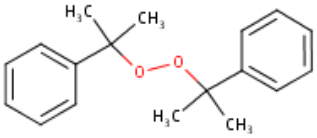
This screening assessment focuses on information critical to determining whether substances meet the criteria as set out in section 64 of CEPA by examining scientific

information and incorporating a weight of evidence approach and precaution.[4] This screening assessment presents the critical information and considerations that form the basis of the conclusion.

2. Identity of substances

The substances, hydroperoxide, 1-methyl-1-phenylethyl herein referred to as CHP, and peroxide, bis(1-methyl-1-phenylethyl), herein referred to as DCUP, are organic chemicals belonging to a substance group known as organic peroxides. The CAS RNs and DSL names for these substances, as well as additional information regarding substance identity, are presented in Table 2-1.

Table 2-1. Substance identities

CAS RN (abbreviation)	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
80-15-9 (CHP)	Hydroperoxide, 1-methyl-1-phenylethyl (Cumene hydroperoxide)	 $C_9H_{12}O_2$	152.192
80-43-3 (DCUP)	Peroxide, bis(1-methyl-1-phenylethyl) (Dicumyl Peroxide)	 $C_{18}H_{22}O_2$	270.37

Organic peroxides are liquid or solid organic substances that contain the bivalent -O-O structure and may be considered derivatives of hydrogen peroxide, where one or both

[4] 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.

of the hydrogen atoms have been replaced by organic radicals. Organic peroxides are thermally unstable substances or mixtures that can undergo exothermic self-accelerating decomposition. In addition, they can be liable to explosive decomposition, burn rapidly, be sensitive to impact or friction, or react dangerously with other substances. In general, organic peroxides have no or only weak oxidizing properties (ECHA 2017).

3. Characterization of ecological risk

The ecological risks of CHP and DCUP were characterized using the ERC (ECCC 2016a). The ERC is a risk-based approach that considers multiple metrics for both hazard and exposure, on the basis of weighted consideration of multiple lines of evidence for determining risk classification. The various lines of evidence are combined to discriminate between substances of lower or higher potency and lower or higher potential for exposure in various media. This approach reduces the overall uncertainty with risk characterization compared to an approach that relies on a single metric in a single medium (e.g., median lethal dose [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 (Q)SAR Toolbox 2016), 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 substances 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, exposure, and subsequent risk. The balanced approaches for dealing with uncertainties are described in greater detail in ECCC 2016a. The following describes two of the more substantial areas of uncertainty. Error with empirical or 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 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 believed to be the current use quantity and may not reflect future trends.

4. Cumene hydroperoxide (CHP)

4.1 Physical and chemical properties

A summary of physical and chemical properties of CHP is presented in Table 4-1. Additional physical and chemical properties are presented in ECCC (2016b).

Table 4-1. Physical and chemical property values (at standard temperature) for CHP

Property	Value	Type of data	Reference
Physical state	Liquid at 25°C		OECD 2008
Melting point (°C)	-9	experimental	ChemIDplus 1993-
Vapour pressure (Pa)	2 at 25°C	modelled	OECD 2008
Henry's law constant ($Pa \cdot m^3/mol$)	4.77×10^{-3}	modelled	ChemIDplus 1993-
Water solubility (mg/L)	13 900 at 25°C	experimental	ChemIDplus 1993-
log K_{ow} (dimensionless)	1.6	experimental	OECD 2008

Abbreviations: K_{ow}, octanol–water partition coefficient

4.2 Sources and uses

CHP does not occur naturally in the environment.

CHP was included in a survey issued pursuant to a CEPA section 71 notice(Canada 2012). Table 4-2 presents a summary of the reported manufacture and import quantities for CHP.

Table 4-2. Summary of information on Canadian manufacturing and imports of CHP submitted pursuant to a CEPA section 71 survey

Common name	Total manufacture[a] (kg)	Total imports[a] (kg)	Reporting year
Cumene hydroperoxide (CHP)	None reported[b]	10 319	2011

[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) (Canada 2012).
[b] No manufacture above the reporting threshold of 100 kg was reported.

CHP is used as an industrial processing agent, namely as a raw material in the synthesis of other organic peroxides and resins, as a polymerization initiator and as a modifier with certain resins. Negligible amounts are expected to be present in final products as the process materials are held at a thermal decomposition temperature for extended periods of time (OECD 2008). CHP is also used in anaerobic adhesives and two-component epoxies as a polymerization aid (OECD 2008; Raftery et al. 1997). CHP may also be used as a component in lubricants and thread sealants, neither of which have direct food contact, and as a component in plasticizers used in plasticized films and PVC articles for repeated use in food packaging materials that come into direct contact with various food types (personal communication, email from the Food Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated June 2015; unreferenced).

Table 4-3 presents a summary of the major uses of CHP according to information reported pursuant to a CEPA section 71 survey (Canada 2012).

Additional use of CHP may include food packaging materials (personal communication, email from the Food Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated June 2015; unreferenced).

Table 4-3. Summary of the major uses of CHP in Canada (on the basis of consumer and commercial DSL codes reported by the user, pursuant to a CEPA section 71 survey)

Major uses[a]	CHP
Adhesives and sealants	Y
Building or construction materials not otherwise covered in this table	Y
Paints and coatings	Y
Other - Polymer initiator	Y

Abbreviations: Y= use was reported for this substance; N= use was not reported for this substance
[a] Non-confidential uses reported in response to the surveys conducted under section 71 of CEPA (Environment Canada 2013). See surveys for specific inclusions and exclusions (schedules 2 and 3) (Canada 2012).

Globally, production of neat CHP in 2006 was in the range of 1 000 000 to 10 000 000 kg (reported as 1 000 to 10 000 tonnes) (OECD 2008). The national aggregate production volume (includes both manufactured and imported volumes) in the United States was in the range of 450 000 to 4 500 000 kg (reported as 1 000 000 to 10 000 000 lb) per year from 2012 to 2015 (US EPA 2017a). CHP is manufactured and/or imported in the European Economic Area in the range of 1 000 000 to 10 000 000 kg (reported as 1 000 to 10 000 tonnes) per year (ECHA c2007-2017a).

CHP is on the US FDA List of Indirect Food Additives Used in Food Contact Substances, specifically used as components in adhesives and components of coatings (21CFR175), paper and paperboard (21CFR176) and polymers (21CFR177) (US eCFR 2017). In Europe, CHP is reported to have uses in the following products: adhesives and sealants; air care products; biocidal products (e.g. disinfectants, pest control); coatings, paints, thinners, and paint removers; fillers, putties, plasters and modelling clay; finger paints; ink and toners; polishes and wax blends; washing and cleaning products; and cosmetics and personal care products (ECHA c2007-2017a).

4.3 Potential to cause ecological harm

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

Given the low hazard and low exposure classification according to information considered under ERC, CHP 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.

4.4 Potential to cause harm to human health

4.4.1 Exposure assessment

4.4.1.1 Environmental media and food

No environmental monitoring data were identified for CHP in air, water, or soil in Canada. Considering its uses, it is not expected to be found in significant quantities in these media. Concentrations of CHP were predicted from environmental modeling estimates using ChemCAN (2003), where a scenario was derived from the Canadian import quantity of 10 319 kg (Environment Canada 2013). Predicted concentrations of CHP in air, water, and soil were negligible. Though not manufactured in Canada, CHP has been reported to the National Pollutant Release Inventory (NPRI), with total on-site releases of 5 kg (reported as 0.005 tonnes) in both 2014 and 2015 after reported releases of 0 tonnes from 2011 to 2013.

CHP may be used as a component in lubricants and thread sealants, neither of which have direct food contact, and as a component in plasticizers in plasticized films and PVC articles for repeated-use food packaging materials that come into direct contact with various food types. The estimated dietary exposure for the general population to

CHP from these uses is negligible (personal communication, email from the Food Directorate, Health Canada, to the Existing Substances Risk Assessment Bureau, Health Canada, dated June 2015; unreferenced).

Exposures of the general population of Canada to CHP through environmental media and food are expected to be negligible.

4.4.1.2 Products available to consumers

CHP is used in adhesives as a polymerization initiator, since a key decomposition pathway produces free radicals (Raftery et al. 1997; OECD 2008). Products available to consumers include two-component epoxies (MSDS 2014) and thread sealants (SDS 2015). Both types of adhesive cure rapidly and are able to withstand high pressures once fully cured.

Thread sealants containing CHP are anaerobic adhesives available to consumers for use in securing metal, tapered pipe thread fittings (e.g., automotive and plumbing applications) (TDS 2008). CHP is typically present in thread sealants at 1% to 5% w/w (SDS 2015). The redox decomposition of CHP by metal ions, and thus the initiation of polymerization, requires anaerobic conditions, and it therefore begins when the fitting is screwed together (Raftery 1997). Such adhesives are typically fully cured within 24 hours at room temperature (TDS 2008).

Two-component epoxies containing CHP are available to consumers for use in bonding rigid materials, including plastics, composites and wood (TDS 2002). CHP is included in the adhesive component at 1% to 10% w/w (MSDS 2014). It is mixed with the activator component for about 1 to 3 minutes (“mixing and loading” stage) for polymerization initiation. The epoxy is then applied to the surfaces being bound together, with a typical working time of about 5 to 6 minutes. Full cure of the epoxy is reached at room temperature in about 4 hours (TDS 2002).

Table 4-4 summarizes the sentinel scenario for exposure to CHP via use of two-component epoxy glues. The two-component glue fact sheet (RIVM 2007) on ConsExpo Web (2017) was used to estimate exposure to CHP through the dermal and inhalation routes (the parameters used are summarized in Appendix A). Dermal absorption values for CHP were estimated and applied to the per-external-event exposures calculated using the ConsExpo model (see Appendix B for details).

Table 4-4. Estimated exposures to CHP from the use of two-component epoxy glue as a sentinel scenario[a]

Concentration of CHP in product (% w/w)	Inhalation - mean event concentration[b] (mg/m^3)	Systemic exposure[c] (mg/kg bw)
0.5–5 (in 1 of 2 components)	5.20×10^{-2}–2.86×10^{-1}	9.27×10^{-3}

[a] Considering use by adults 20 years of age and over with a body weight of 70.9 kg (Health Canada 1998).
[b] CHP is expected to be readily absorbed following inhalation exposure (AGDH 2016), therefore estimated inhalation exposures assume absorption of 100%.

[c] Estimated dermal exposures were adjusted using calculated dermal absorption values as detailed in Appendix B.

4.4.2 Health effects assessment

CHP was reviewed internationally as a member of hydroperoxides by the OECD and as a member of organic peroxides by the AGDH. A preliminary SIDS Initial Assessment Profile (SIAP) was published by OECD in 2008. Both categories of chemicals were determined to possess properties indicating hazard for human health. Thus, the OECD SIAP (2008) and AGDH Human Health Tier II Assessment (2016) were used to inform the hazard assessment of CHP. A literature search was conducted from the year prior to the OECD assessment to July 2017. The significant new studies of CHP conducted after the aforementioned reviews were also considered in this assessment.

The reactivity of the hydroperoxide moiety of CHP is expected to contribute more to its toxicity than that of the aryl functional group, and the hydroperoxide moiety is considered by OECD (2008) to be the primary cause of the biological effects observed for CHP. The major metabolic pathway for organic hydroperoxides is a two-electron reduction to the corresponding alcohol by glutathione (GSH) peroxidases (AGDH 2016). Thus, cumyl alcohol is the anticipated metabolite of CHP (OECD 2008).

4.4.2.1 Genotoxicity and carcinogenicity

CHP was considered by OECD (2008) to be potentially genotoxic in vitro. In an in vivo study, repeated intraperitoneal injection of CHP in mice resulted in a significant increase in DNA damage in the testicular tissues of male mice at a dose level of 23 mg/kg bw/day and above (OECD 2008). However, in a recent dermal study, CHP did not increase the number of micronucleated peripheral erythrocytes in mice or rats after application of CHP on dorsal skin at up to 100 mg/kg bw/day for 14 days or up to 12 mg/kg bw/day for 90 days (Rider et al. 2016).

There were limited chronic dermal studies available for CHP, but they were not considered by OECD (2008) to be reliable (carcinogenicity) studies. The (Q)SAR predicted profile of CHP recorded in the Danish (Q)SAR Database (2015) showed a positive prediction in “FDA RCA Cancer Female Mouse” with the CASE Ultra model. However, the cancer predictions with other models in the same report were mainly negative, inconclusive, or positive but outside of the applicability domains.

4.4.2.2 Reproductive and developmental toxicity

No developmental or reproductive toxicity data for CHP were available during OECD (2008) or AGDH (2016) review periods. Two unpublished developmental toxicity studies were submitted to ECHA (c2007-2017b) after the aforementioned assessments. A preliminary developmental dose-finding study was conducted in 2015. In this study, pregnant female Wistar rats were administered CHP via gavage at 0, 15, 30, 60, and

120 mg/kg bw/day from gestation day (GD) 6 to 19. Maternal toxicity (mortality, clinical signs, body weight loss and decreased food consumption) and embryo toxicity (increased incidence of early embryonic loss) were reported in the top dose group. A lowest-observed-adverse-effect level (LOAEL) of 120 mg/kg bw/day and a no-observed-adverse-effect level (NOAEL) of 60 mg/kg bw/day for maternal and developmental health effects were determined by the dossier submitter. However, the developmental health effects were observed only in the presence of maternal toxicity. A follow-up developmental toxicity study was conducted from 2015 to 2016. In that study, the same strain of pregnant rats were administered CHP at 0, 5, 13.3, and 33.3 mg/mL via gavage (equivalent to 0, 15, 40, and 100 mg/kg bw/day) from GD 6 to 19. There were no reproductive, developmental health effects or maternal systemic health effects observed. The necropsy examination in dams showed clear treatment-related local effects, such as multifocal/diffuse thickness of non-glandular stomach mucosa in all dose groups. These effects were considered to be adverse in the high- and mid-dose groups. A LOAEL of 40 mg/kg bw/day and a NOAEL of 15 mg/kg bw/day were therefore determined for local effects in dams (ECHA c2007-2017a).

4.4.2.3 Other repeated-dose toxicity

No valid oral repeated-dose toxicity study was identified by OECD (2008) for CHP. In an unpublished repeated-dose inhalation study cited in the OECD initial report (2008), rats were dosed with CHP via aerosol to the whole body for 6 hours per day, 5 days per week for 3 months at 0, 1, 6 or 31 mg/m^3 (equivalent to 0, 0.008, 0.46 or 2.4 mg/kg bw/day, respectively). The clinical signs of exposure included skin and respiratory irritation (dose groups were not specified in OECD 2008). The NOAEL was determined by OECD (2008) and AGDH (2016) to be 31 mg/m^3 (2.4 mg/kg bw/day) as no toxicologically relevant health effects were observed in the study.

In a dermal study published after the aforementioned international reviews, both sexes of B6C3F1/N mice or F344/N rats were administered varying doses of CHP applied topically for 14 or 90 days (Rider et al. 2016). In the 14-day studies, CHP was applied on the dorsal skin of animals at 0, 6.25, 12.5, 25, 50, or 100 mg/kg bw/day, 5 times per week for a total of 12 days in rats and 13 days in mice. In the 90-day studies**,** 0, 0.75, 1.5, 3, 6, or 12 mg/kg bw/day of CHP were applied to both mice and rats. No significant changes in survival or body weight in mice and rats were observed following 14 days of exposure (NOAEL = 100 mg/kg bw/day). In the 90-day studies, the top dose triggered a significant decrease (15%) in body weight in male rats only. In both the 14-day and 90-day studies, the histopathological findings were limited to the site of the application in rats and mice and were characterized as inflammation and epidermal hyperplasia. The study authors concluded that the topical CHP application caused skin damage only at the application site and did not cause systemic effects. In addition, the AGDH (2016) did not identify any treatment related systemic health effects that were associated with dermal exposure to organic peroxides.

4.4.3 Characterization of risk to human health

General toxicity for the oral, inhalation and dermal routes of exposure were identified for CHP by both OECD (2008) and AGDH (2016).

Exposure of the general population to CHP through environmental media and food (e.g., from food packaging materials) is expected to be negligible. Therefore, no risk from these sources is expected.

Exposure of the general population to CHP is expected to occur mainly from the intermittent use of adhesive products available to consumers, such as two-component epoxies and thread sealants, via dermal and inhalation routes. There were no systemic health effects noted for CHP up to the highest treatment dose of 100 mg/kg/day in a 14-day dermal toxicity study or up to the highest treatment dose of 31 mg/m^3 in a 3-month inhalation study. The estimated systemic exposure to CHP from two-component epoxies via the dermal route is four orders of magnitude lower than the highest treatment dose in the dermal study. Comparison of the estimated inhalation exposures to CHP from two-component epoxies with the highest treatment dose in the inhalation study results in margins of exposure ranging from 108 to 596. The highest treatment doses in both dermal and inhalation studies did not induce adverse health effects. Therefore, the risk from intermittent dermal or inhalation exposure to CHP is expected to be low.

On the basis of the conservative parameters used in modelling exposure to CHP in products available to consumers and the application of the NOAELs of CHP from the relevant toxicity studies, the margins for the intermittent use of these products are considered adequate to address uncertainties in the health effects and exposure databases.

4.4.4 Uncertainties in evaluation of risk to human health

There is uncertainty with respect to the general population of Canada’s exposure to CHP through environmental media and food as no studies on CHP levels in these media in Canada were found.

There is uncertainty with respect to the inhalation scenario for two-component epoxies containing CHP. The model used to estimate inhalation exposure is very conservative as it is assumed that 100% of the CHP in the product evaporates and that none remains in the applied portion. Furthermore, the model assumes that all of the CHP remains in the air of the room after the epoxy is applied even though CHP decomposes into radicals in this type of product, thus being used up. Additionally, the resultant material is typically hardened within 10 minutes, limiting the timeframe over which evaporation of CHP may occur.

Despite the uncertainty with respect to application of the critical effect level of a subchronic inhalation study to the intermittent exposure scenarios, this approach is conservative and the margin is considered adequate to account for this uncertainty.

5. Dicumyl peroxide (DCUP)

5.1 Physical and chemical properties

A summary of physical and chemical properties of DCUP is presented in Table 5-1. Additional physical and chemical properties are presented in ECCC (2016b).

Table 5-1. Physical and chemical property values (at standard temperature) for DCUP

Property	Value	Type of data	Reference
Physical state	Solid at 25°C		OECD 2012
Melting point (°C)	39.8	experimental	OECD 2012
Vapour pressure (Pa)	1×10^{-3} at 25°C	experimental	ECHA c2007-2017b
Henry's law constant ($Pa \cdot m^3/mol$)	4.48	modelled	ChemIDplus 1993-
Water solubility (mg/L)	0.43 at 20°C	experimental	OECD 2012
log K_{ow} (dimensionless)	5.6	experimental	OECD 2012

Abbreviations: K_{ow}, octanol–water partition coefficient

5.2 Sources and uses

DCUP does not occur naturally in the environment.

DCUP was included in a survey issued pursuant to CEPA section 71 notice(Canada 2012). Table 5-2 presents a summary of the reported manufacture and import quantities for DCUP.

Table 5-2. Summary of information on Canadian manufacturing and imports of DCUP submitted pursuant to a CEPA section 71 survey

Common name	Total manufacture[a] (kg)	Total imports[a] (kg)	Reporting year
Dicumyl peroxide (DCUP)	None reported[b]	100 000 to 1 000 000	2011

[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) (Canada 2012).
[b] No manufacture above the reporting threshold of 100 kg was reported.

DCUP is used as an industrial processing agent (polymerization catalyst or vulcanization agent in plastic and rubber products) (Lewis 1993). It is used for crosslinking of polyethylene and acrylic resin, as well as in the production of electric cables (Arkema Innovative Chemistry 2017). DCUP is also used as a flame retardant

synergist in polystyrene (AkzoNobel Polymer Chemistry 2017). Because of the high temperature and extended duration of processing during the manufacture of these materials, negligible quantities of DCUP are expected to remain after processing (OECD 2012).

Table 5-3 presents a summary of the major uses of DCUP according to information reported pursuant to a CEPA section 71 survey (Canada 2012). Additional Canadian uses of DCUP were not identified.

Table 5-3. Summary of the major uses of DCUP in Canada (on the basis of consumer and commercial DSL codes reported by the user, pursuant to a CEPA section 71 survey)

Major Uses[a]	DCUP
Building or construction materials not otherwise covered in this table	Y
Plastic and rubber materials not otherwise covered in this table	Y
Other - Polymer initiator	Y
Automotive, aircraft and transportation	Y
Other - Fully reacted chemical intermediate	Y
Metal materials not otherwise covered in this table	Y

Abbreviations: Y, yes; N, no

[a] Non-confidential uses reported in response to the surveys conducted under section 71 of CEPA (Environment Canada 2013). See surveys for specific inclusions and exclusions (schedules 2 and 3) (Canada 2012).

Globally, production of neat DCUP in 2010 was in the range of 10 000 000 to 50 000 000 kg (reported as 10 to 50 kilotonnes) (OECD 2008). The national aggregate production volume (includes both manufactured and imported volumes) in the United States was in the range of 450 000 to 4 500 000 kg (reported as 1 000 000 to 10 000 000 lb) per year from 2012 to 2015 (US EPA 2017b). DCUP is manufactured and/or imported in the European Economic Area in the range of 10 000 000 to 100 000 000 kg (reported as 10 000 to 100 000 tonnes) per year (ECHA c2007-2017b).

DCUP is on the US FDA List of Indirect Food Additives Used in Food Contact Substances, specifically adhesives and components of coatings (21CFR175) and polymers (21CFR177) (US eCFR 2017). In Europe, DCUP is not reported to have any consumer uses (ECHA c2007-2017b), but is reported to be found in products with materials such as plastic (e.g. food packaging and storage, toys, mobile phones), wood (e.g. floors, furniture, toys) and stone, plaster, cement, glass or ceramic (e.g. dishes, pots/pans) (ECHA 2017).

5.3 Potential to cause ecological harm

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

DCUP was assigned a moderate exposure classification according to the information considerd under ERC because of long overall persistence and a moderate current use quantity (ECCC 2016b)It was also classified as having a low hazard potential and an overall low potential for ecological risk. It is unlikely that this substance is resulting in concerns for the environment in Canada.

5.4 Potential to cause harm to human health

5.4.1 Exposure assessment

5.4.1.1 Environmental media and food

No environmental monitoring data were identified for DCUP in air, water, or soil in Canada. Considering its physical-chemical properties and uses, it is not expected in these media. Concentrations of DCUP were predicted from environmental modeling estimates using ChemCAN (2003), where a scenario was derived from a maximum Canadian import quantity of approximately 1 000 000 kg (range imported presented in Table 5-2; Environment Canada 2013). Predicted concentrations of DCUP in air, water, and soil were minimal.

No data were identified for DCUP in food or food packaging materials in Canada.

Exposure of the general population to DCUP from environmental media and food is not expected.

5.4.1.2 Products available to consumers

DCUP is used as an industrial processing agent. Unreacted DCUP is thermally decomposed following its use in the polymerization of plastics and rubbers and is therefore not found in products used by consumers (OECD 2012). Exposure of the general population to DCUP from products available to consumers is not expected.

5.4.2 Health effects assessment

A harmonized classification of DCUP for reproductive toxicity based on a new developmental toxicity study received during the registration period was proposed by the Norwegian Environment Agency (ECHA 2017). The proposed classification (Repr. 1B) was recently adopted by the Committee for Risk Assessment (RAC) of ECHA (ECHA 2018). As an aryl substituted dialkyl peroxide, DCUP was reviewed together with other structurally similar substances by OECD (2012), and the OECD review was used to inform the hazard assessment of DCUP. A literature search was conducted from the year prior to the OECD review to July 2017. The significant new studies conducted after the OECD review were also considered in this assessment.

5.4.2.1 Reproductive and developmental toxicity

No developmental or reproductive toxicity data for DCUP were available during the OECD (2012) review period. In an unpublished developmental toxicity study conducted after the OECD Cooperative Chemicals Assessment Meeting (OECD 2012), pregnant Wistar rats were administered DCUP at 0, 50, 150, or 450 mg/kg bw/day from GD 5 to 19 via gavage. Maternal health effects observed in the high-dose group included death, vaginal and uterine bleeding, enlarged adrenals and spleen, significantly reduced food consumption, and body weight gain. Health effects in high-dose embryos included significantly increased post implantation loss, decreased foetal weight, malrotated fore- and hind-limbs, and significantly increased skeletal malformations and variations. A LOAEL of 450 mg/kg bw/day and a NOAEL of 150 mg/kg bw/day for maternal and developmental health effects were determined by an ECHA dossier submitter (c2007-2017b). A further assessment of the relationship between the individual dams with symptoms of maternal toxicity and the individual pups with symptoms of developmental toxicity was conducted by the Norwegian Environment Agency (ECHA 2017). The assessment concluded that the observed developmental effects following exposure to DCUP were not secondary non-specific consequences of maternal toxicity.

5.4.3 Characterization of risk to human health

Although DCUP can cause adverse effects on the reproductive system, the exposure of the general population in Canada to DCUP through environmental media, food, or the use of products available to consumers is not expected, and the potential risk to human health is therefore considered to be low.

While exposure of the general population to DCUP is not of concern at current levels, this substance is considered to have health effects of concern given its hazard potential. Therefore, there may be a concern for human health if exposures were to increase.

5.4.4 Uncertainties in evaluation of risk to human health

Although there are some limitations in the exposure database for DCUP (e.g., no data about levels in environmental media or food in Canada), given that general population exposure is not expected, a qualitative approach to risk characterization is considered appropriate for this substance.

6. Conclusion

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

On the basis of the information presented in this screening assessment, it is concluded that CHP and DCUP do not meet the criteria under paragraph 64(c) of CEPA as they are not entering the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.

It is therefore concluded that CHP and DCUP do not meet any of the criteria set out in section 64 of CEPA.

References

[AGDH] Australian Government Department of Health. 2016. Sydney (AU): Department of Health, National Industrial Chemicals Notification and Assessment Scheme (NICNAS). Human Health Tier II Assessment for selected organic hydroperoxides. [accessed 2017 Jun 13].

AkzoNobel Polymer Chemistry. 2017.Flame retardant & Synergists. [accessed 2018 Feb 20].

Arkema Innovative Chemistry. 2017. DiCup® R / Luperox® DCP dicumyl peroxide. [accessed 2017 Aug 9].

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

Canada, Dept. of the Environment. 2012. *Canadian Environmental Protection Act, 1999: Notice with respect to certain substances on the Domestic Substances List* [PDF] Canada Gazette, Part I, vol. 146, no. 48, Supplement.

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.

ChemIDplus [database]. 1993- . Bethesda (MD): US National Library of Medicine. [updated 2017 Aug 6; accessed 2017 Aug 17].

[ConsExpo Web] Consumer Exposure Web Model. 2017. Ver. 1.0.1. Bilthoven (NL): Rijksinstituut voor Volksgezondheid en Milieu [National Institute for Public Health and the Environment].

Danish (Q)SAR Database [database]. 2015. Division of Diet, Disease Prevention and Toxicology, National Food Institute, Technical University of Denmark. [accessed 2017 Jun 13].

[DPD] Drug Product Database online query [database]. [modified 2017 Feb 17]. Ottawa (ON): Health Canada. [accessed 2015 June].

[ECCC, HC] Environment and Climate Change Canada, Health Canada. [modified 2017 Mar 12]. Categorization. Ottawa (ON): Government of Canada. [accessed 2017 Jun 1].

[ECCC, HC] Environment and Climate Change Canada, Health Canada. 2018. Screening assessment: substances identified as being of low concern using the ecological risk classification of organic substances and the threshold of toxicological concern (TTC)-based approach for certain substances. Ottawa (ON):Government of Canada.

[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. Data used to create substance-specific hazard and exposure profiles and assign risk classifications in the Ecological Risk Classification of organic substances. Gatineau (QC). Available from: eccc.substances.eccc@canada.ca

[ECHA] European Chemicals Agency. 2017. CLH report, Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2. International Chemical Identification: Bis(α,α-dimethylbenzyl) peroxide. CAS Number: 80-43-3 [PDF].

[ECHA] European Chemicals Agency. c2007-2017a. Registered substances database; search results for CAS RN 80-15-9. Helsinki (FI): ECHA. [updated 2017 Aug 30; accessed 2017 May].

[ECHA] European Chemicals Agency. c2007-2017b. Registered substances database; search results for CAS RN 80-43-3. Helsinki (FI): ECHA. [updated 2017 Aug 30; accessed 2017 May].

[ECHA] European Chemicals Agency. 2018. Annex to a news release. Helsinki, 15 June 2018. [accessed 2017 July].

Environment Canada. 2013. DSL Inventory Update data collected under the Canadian Environmental Protection Act, 1999, section 71: Notice with respect to certain substances on the Domestic Substances List. Data prepared by: Environment Canada, Health Canada; Existing Substances Program.

Gimenez-Conti I, Viaje A, Chesner J, Conit C, Slaga TJ. 1991. Induction of short-term markers of tumor promotion by organic peroxides. Carcinogenesis. 12(4), 563-569 [cited in ECHA dossier c2007-2017b].

Gimenez-Conti IB, Binder RL, Johnston D, Slaga TJ. 1998. Comparison of the skin tumor-promoting potential of different organic peroxides in SENCAR mice. Toxicol Appl Pharmacol. 149:73-79 [cited in ECHA dossier c2007-2017b].

Guy RH. 2010. Predicting the rate and extent of fragrance chemical absorption into and through the skin. Chem Res Toxicol. 23:864-870.

Health Canada. 1998. Exposure factors for assessing total daily intake of priority substances by the general population of Canada. Unpublished report. Ottawa (ON): Government of Canada.

Health Canada. [modified 2017 May 3]. Lists of permitted food additives. Ottawa (ON): Government of Canada. [accessed 2017 Mar 31].

Health Canada. 2016. Science Approach Document: Threshold of Toxicological Concern (TTC)-based Approach for Certain Substances.Ottawa (ON): Government of Canada.

[HSDB] Hazardous Substances Data Bank [database]. 1983-2017. Bethesda (MD): National Library of Medicine (US). [updated 2017 July; accessed 2017 Apr 12].

Lewis RJ Sr, editor. 1993. Hawley's condensed chemical dictionary, 12th ed. New York (NY): Van Nostrand Rheinhold Co., p. 386. [cited in HSDB 1983-2017].

[LNHPD] Licensed Natural Health Products Database [database]. [modified 2016 Aug 10]. Ottawa (ON): Health Canada. [accessed 2015 June].

[MSDS] Material Safety Data Sheet. 2014. PC perma poxy 5 minute plastic weld. Halton Hills (ON): ITW Permatex Canada. [accessed 2017 Jun 19].

[NHPID] Natural Health Products Ingredients Database [database]. [modified 2017 Jun 21]. Ottawa (ON): Health Canada. [accessed 2015 June].

[NPRI] National Pollutant Release Inventory. 2011-2015. NPRI Datasets: Online query tool. Ottawa (ON): Government of Canada. Search results for cumene hydroperoxide, CAS RN 80-15-9. [modified 2017 June 15; accessed 2017 August].

[OECD] Organisation for Economic Co-operation and Development. 2008. SIDS Initial Assessment Profile[PDF]: hydroperoxide, 1-methyl-1-phenylethyl (CHP); hydroperoxide, 1,1-dimethylpropyl (TAHP). SIAM [SIDS initial assessment meeting] 27, 14-16 October 2008: Ottawa, Canada. [accessed 2017 June].

[OECD] Organisation for Economic Co-operation and Development. 2012. SIDS Initial Assessment Profile [PDF]: Aryl Substituted Dialkyl Peroxides. CoCAM [Cooperative Chemicals Assessment Meeting] 3, 16-18 October 2012: Lucerne, Switzerland. [accessed 2017 June].

Potts RO, Guy RH. 1992. Predicting skin permeability. Pharm Res. 9(5):663-669.

Raftery D, Smyth MR, Leonard RG. 1997. Investigations into the cumene hydroperoxide-based cure chemistry of anaerobic adhesives. Int J Adhes Adhes. 17(4):349-352.

Rider CV, Chan P, Herbert RA, Kissling GE, Fomby LM, Hejtmancik MR, Witt KL, Waidyanatha S, Travlos GS, Kadiiska MB. 2016. Dermal exposure to cumene hydroperoxide: assessing its toxic relevance and oxidant potential. Toxicol Pathol. 44(5):749-762.

[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 [PDF]. Bilthoven (NL): RIVM. Report No.: 320104007/2007. [accessed 2017 Jun 21].

[SDS] Safety Data Sheet. 2015. Permatex® High Performance Thread Sealant [PDF]. Halton Hills, ON, Canada: ITW Permatex Canada. [accessed 2017 Jun 19].

[TDS] Technical Data Sheet. 2002. Permatex® PermaPoxy™ Plastic Weld [PDF]. Hartford, CT, USA: Permatex, Inc. [accessed 2017 June 19].

[TDS] Technical Data Sheet. 2008. High Performance Thread Sealant [PDF]. Hartford, CT, USA: Permatex, Inc. [accessed 2017 Jun 19].

[US eCFR] US Electronic Code of Federal Regulations. 2017. Title 21, vol. 3, c I, part 175, Indirect food additives: adhesives and components of coatings; part 176, Indirect food additives: paper and paperboard components; and part 177, Indirect food additives: polymers.. Washington (DC): National Archives and Records Administration’s Office of the Federal Register (OFR); Government Publishing Office. [accessed 2017 Oct 3].

[US EPA] US Environmental Protection Agency. 2016 Chemical Data Reporting Results [database]. 2017a. Search results for CAS RN 80-15-9.Washington (DC): US EPA, Office of Chemical Safety and Pollution Prevention. [updated 2017 Aug 17; accessed 2017 Aug 17].

[US EPA] US Environmental Protection Agency. 2016 Chemical Data Reporting Results [database]. 2017b. Search results for CAS RN 80-43-3.Washington (DC): US EPA, Office of Chemical Safety and Pollution Prevention. [updated 2017 Aug 17; accessed 2017 Aug 17].

Appendix A. Exposure scenario parameters for two-component epoxies

ConsExpo Web (2017) was used to estimate inhalation and dermal exposures to CHP from two-component epoxies. The Do-it-yourself products fact sheet (RIVM 2007) was used as guidance in determining the exposure intake estimates, with some refinements based on product details. The results from the two stages of use (mixing and loading; application) were added together to provide conservative estimates of exposure for a consumer performing both steps.

Table A-1. Two-component epoxy – inhalation

Parameter	Two-component epoxy glue – mixing and loading	Two-component epoxy glue – application
Exposure to vapour	Evaporation constant release	Evaporation from increasing area
Exposure duration (min.)	5	20
Application duration (min.)	5	10
Product amount (g)	20	20
Room volume (m^3)	1	20
Ventilation rate (h^{-1})	0.6	0.6
Release area (cm^2)	20	500
Temperature (°C)	20	20
Mass transfer rate	14.7	14.7
Mol. weight matrix (g/mol)	3000	3000

Table A-2. Two-component epoxy – dermal

Parameter	Two-component epoxy glue – mixing and loading	Two-component epoxy glue – application
	Instant application	Instant application
Surface area (cm^2)	2	43
Product amount (mg)	50	100

Appendix B. Calculation of dermal absorption for CHP

Maximum flux (J_{max}) is the theoretical upper-limit rate at which a chemical can be dermally absorbed from a given vehicle. It was calculated using physical-chemical properties of CHP (see section 4.1, Table 4-1) and the sums of parameters from the two-component epoxy scenario detailed in Appendix A (i.e. the mixing and loading stage and the application stage were considered as one exposure). The following steps were used to calculate J_{max} and to then estimate dermal absorption of CHP.

Table B-1. Calculation of dermal absorption of CHP in two-component epoxies

Calculation	Result
$\log K_p = -2.71 + 0.71 (\log K_{ow}) – 0.0061 (MW)$ [a]	-2.502
$Kp = 10^{logKp}$	3.145×10^{-3} cm/hr
Jmax = Kp × WS [b]	4.372×10^{-2} mg/(cm^2·hr)
Qmax = Jmax × SA × ED [b,c]	6.557×10^{-1} mg
Qapp = PA × C [b,d]	0.75 mg (for 0.5% w/w CHP) 7.5 mg (for 5% w/w CHP)
DA = (Qmax / Qapp) ×100% [b]	87% (for 0.5% w/w CHP) 8.7% (for 5% w/w CHP)

Abbreviations: Kp, permeability coefficient (cm/hr); K_{ow}, octanol-water partition coefficient; MW, molecular weight (g/mol); J_{max}, maximum flux (mg/[cm^2·hr]); WS, water solubility (mg/cm^3); Q_{max}, maximum amount of substance that could be absorbed at saturation concentration (mg); SA, surface area (cm^2); ED, exposure duration (hr); PA, product amount (g); Q_{app}, total amount of substance on the skin (mg); C, concentration (mg/g); DA, dermal absorption (%)

[a] Potts and Guy, 1992.

[b] Guy 2010.

[c] Sum of surface areas (SA) for both stages of epoxy use was used (45 cm^2, Table A-2); exposure duration (ED) of 20 minutes was assumed based on curing time of epoxies

[d] Sum of product amounts (PA) for both stages of epoxy use was used (0.15 g, Table A-2); the reported concentration (C) range of CHP in a sample epoxy was used as minimum and maximum concentration values (0.5% w/w and 5% w/w in final formulation)

Table B-2. Calculation of systemic exposure of CHP from two-component epoxies

Concentration of CHP in product (% w/w)[a]	Dermal – dermal deposition (mg/kg bw)[b]	Systemic exposure[c] (mg/kg bw/event)
0.5	1.06×10^{-2}	9.27×10^{-3}
5	1.06×10^{-1}	9.27×10^{-3}

[a] MSDS 2014.

[b] Calculated using ConsExpo Web (2017) as detailed in Appendix A.

[c] Concentration-specific dermal absorption values (Table B-1) were applied to estimated external event doses to obtain dermal uptake.