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Screening Assessment

1,1-Ethanediol, 2,2,2-trichloro- (Chloral hydrate)

Chemical Abstracts Service Registry Number 302-17-0

Environment and Climate Change Canada
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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 1,1-Ethanediol, 2,2,2-trichloro-, hereinafter referred to as chloral hydrate. The Chemical Abstracts Service Registry Number (CAS RN[1]) for chloral hydrate is 302-17-0. This substance is among those substances identified as priorities for assessment as it met categorization criteria under subsection 73(1) of CEPA.

Chloral hydrate does not occur naturally in the environment. In Canada, it is primarily found in chlorinated drinking water as a disinfection by-product. It is also an active ingredient in prescription drugs used as sedatives and hypnotics, a medicinal ingredient in natural health products licensed as homeopathic medicines, and an intermediate for industrial metal plating.

The ecological risk of chloral hydrate was characterized using the ecological risk classification of organic substances (ERC). The ERC is a risk-based approach that employs multiple metrics for both hazard and exposure on the basis of weighted consideration of multiple lines of evidence for determining risk classification. Hazard profiles are established primarily on the basis of 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 then 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 chloral hydrate as having low potential to cause ecological harm.

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

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

Drinking water is the primary source of exposure to chloral hydrate for the general population of Canada. Exposure to the general population through its use in the metal plating industry is not expected as chloral hydrate is consumed in the plating process.

Chloral hydrate was previously assessed by Health Canada, and a drinking water guidance document was published that determined that the amount of chloral hydrate typically found in drinking water is well below the level at which health effects may be observed. A health-based value was derived, with an increased incidence of liver histopathology as the critical health effect.

On the basis of the information presented in this screening assessment, it is concluded that chloral hydrate 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 concluded that chloral hydrate does not meet any of the criteria under section 64 of CEPA.

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 chloral hydrate to determine whether this substance 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]).

Chloral hydrate was previously assessed by Health Canada, and a guidance document on chloral hydrate in drinking water is available (Health Canada 2008). Such assessments undergo a similar review and approval process to that used for drinking water guideline documents, including international peer review and public consultations. The drinking water guidance document was used to inform this screening assessment as drinking water is the primary source of exposure in Canada.

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

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 which was subject to an external peer-review. Additionally, the ERC document (published July 30, 2016) and the draft of this screening assessment (published December 17, 2016) were each subject to 60-day public comment periods. While external comments were taken into consideration, the final content and outcome of the screening assessment remain the responsibility of Environment and Climate Change Canada and Health Canada.

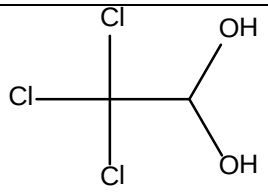
This screening assessment focuses on information critical to determining whether chloral hydrate meets the criteria set out in section 64 of CEPA by examining scientific information and incorporating a weight of evidence approach

and precaution[2]. The screening assessment presents the critical information and considerations on which the conclusion is based.

2. Substance Identity, Physical and Chemical Properties

The substance 1,1-Ethanediol, 2,2,2-trichloro-, hereinafter referred to as chloral hydrate, is an organic chemical belonging to a substance class known as chlorinated alcohols. The CAS RN, Domestic Substances List (DSL) name and common name for this substance, as well as additional information regarding substance identity, are presented in Table 2-1.

Table 2-1. Substance identity

CAS RN	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
302-17-0	1,1-Ethanediol, 2,2,2-trichloro- (chloral hydrate)	 $C_2H_3Cl_3O_2$	165.40

The physical and chemical properties of chloral hydrate can be found in Health Canada's guidance document (Health Canada 2008). Additional physical and chemical properties are presented in ECCC (2016b). This substance has high water solubility and a low organic carbon-water partitioning coefficient.

3. Sources and Uses and Environmental Fate

Chloral hydrate does not occur naturally in the environment. In Canada, chloral hydrate is primarily found in chlorinated drinking water as a disinfection by-

[2]A determination of whether one or more of the criteria of section 64 of CEPA are met is based on 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 hazardous products intended for workplace use, handling and storage. 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.

product. There are no data on the levels of chloral hydrate in air or soil, but given its physical and chemical properties, it is not expected to partition to these media.

Chloral hydrate is an active ingredient in four prescription drugs for use as sedatives and hypnotics (DPD 2017). It is also a medicinal ingredient in natural health products licensed as homeopathic medicines, identified as “Chloralum”, and is present in these homeopathic medicines at quantities of either 12 CH or 6X (LNHPD [modified 2016]).

On the basis of information submitted pursuant to section 71 of CEPA (Canada 2009), in 2008, a quantity of chloral hydrate lower than the reporting threshold of 100 kg was manufactured and up to 11 000 kg was imported into Canada.[3] In Canada, chloral hydrate is used as a plating and surface treating agent (Canada 2009). One use of chloral hydrate is as a brightener in nickel plating; in general, brighteners are added in low concentrations and consumed in the electrolysis process (Nickel Institute 2013).

4. Potential to Cause Ecological Harm

4.1 Characterization of Ecological Risk

The ecological risk of chloral hydrate was characterized using the ecological risk classification of organic substances (ERC) (ECCC 2016a). The ERC is a risk-based approach that employs 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., LC_{50}) for characterization. The following section summarizes the approach, which is described in detail in ECCC (2016a).

Data on physical and chemical properties, fate (chemical half-lives in various media and biota, partition coefficients, and fish bioconcentration), acute fish ecotoxicity, and chemical import or manufacture volume in Canada were collected from the scientific literature and from available empirical databases (e.g., OECD QSAR Toolbox) in response to surveys under section 71 of CEPA, or were generated using selected quantitative structure-activity relationship

[3] Values reflect quantities reported in response to surveys. See survey schedule 2 and 3 for specific inclusions and exclusions.

(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 established based principally on metrics regarding mode of toxic action, chemical reactivity, food web-derived internal toxicity thresholds, bioavailability, and chemical and biological activity. Exposure profiles were also composed of multiple metrics including potential emission rate, overall persistence, and long-range transport potential. Hazard and exposure profiles were compared to decision criteria in order to classify the hazard and exposure potential for each organic substance as low, moderate, or high. Additional rules were applied (e.g., classification consistency and 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 which had a low estimated rate of emission to water after wastewater treatment, representing a low potential for exposure. The second step reviewed low risk potential classification outcomes using relatively conservative, local-scale (i.e., in the area immediately surrounding a point-source of discharge) risk scenarios designed to be protective of the environment, to determine whether the classification of potential risk should be increased. ERC uses a weighted approach to minimize the potential for both over- and under-classification of hazard and exposure and subsequent risk. The balanced approaches for dealing with uncertainties are described in greater detail in ECCC (2016a). Two of the more substantial areas of uncertainty are as follows: (1) 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. However, the impact of this error is mitigated by the fact that overestimation of median lethality will result in a conservative (protective) tissue residue value used for critical body residue (CBR) analysis. (2) 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. Because exposure and risk classifications are highly sensitive to emission rate and use quantity, changes or errors in chemical quantity could result in differences in classification of exposure. 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.

Critical data and considerations used to develop the substance-specific profiles for chloral hydrate and to determine the hazard, exposure and risk classifications are presented in ECCC (2016b).

On the basis of low hazard and low exposure classifications according to ERC for chloral hydrate, this substance was classified as having a low potential for ecological risk. It is therefore unlikely that this substance result in concerns for organisms or the broader integrity of the environment in Canada.

5. Potential to Cause Harm to Human Health

5.1 Characterization of Risk to Human Health

In Canada, chloral hydrate is found in chlorinated drinking water as a disinfection by-product. Given the physical and chemical properties and partitioning behaviour of this substance, exposure to chloral hydrate from air and soil are not expected for the general population.

Exposure to chloral hydrate found in the limited number of prescription drugs used as sedatives and hypnotics is not expected to be significant for the general population. Exposure is also not expected to be significant from its use in the limited number of homeopathic medicines licensed as natural health products due to the significant dilution characteristic of such products.

Exposure of the general population to chloral hydrate from its use as an intermediate for industrial metal plating is not expected as this substance is added in low concentrations and consumed in the industrial process.

The current use pattern of chloral hydrate suggests that drinking water is the primary source of exposure for the general population of Canada. Surveys conducted in 1995 and 1997 in Canada showed that the mean concentration of chloral hydrate in drinking water ranged from 1.2 to 8.4 µg/L, with a maximum value of 22.5 µg/L (Health Canada 2008). A more recent survey conducted in 2009-2010 (National Drinking Water Survey), and the subsequent Targeted Survey conducted in 2011-2012, reported maximum concentrations of 42.86 and 32.07 µg/L, respectively, indicating values are similar (personal communication, email from the Water and Air Quality Bureau, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated May 12, 2017; unreferenced).

Chloral hydrate was previously assessed by Health Canada, and the drinking water guidance document, as well as the more recent surveys, determined that the amount of chloral hydrate typically found in drinking water (as described above) is well below the level at which health effects may be observed. A health-based value of 200 µg/L was derived in the guidance document, on the basis of a tolerable daily intake of 0.0045 mg/kg bw/day, with an increased incidence of liver histopathology as the critical health effect (Health Canada 2008).

In a more recent monograph published by the International Agency for Research on Cancer (IARC 2014), chloral hydrate was classified as a Group 2A substance (probably carcinogenic to humans), whereas it had previously been classified as a Group 3 substance (not classifiable as to its carcinogenicity to humans). Health Canada reviewed the updated monograph and determined that the health-based value established in Health Canada's guidance document (Health Canada 2008) remains protective of human health (personal communication, email from the Water and Air Quality Bureau, Health Canada (HC), to the Existing Substances Risk Assessment Bureau, HC, dated July 30, 2015; unreferenced).

While exposure of the general population to chloral hydrate is not of concern at current levels, this substance is considered to have a health effect of concern on the basis of its potential carcinogenicity. Therefore, there may be a concern for human health if exposures were to increase.

6. Conclusion

Considering all available lines of evidence presented in this screening assessment, there is low risk of harm to organisms and the broader integrity of the environment from chloral hydrate. It is concluded that chloral hydrate 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 screening assessment, it is concluded that chloral hydrate 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 concluded that chloral hydrate does not meet any of the criteria set out in section 64 of CEPA.

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