Government of Canada / Gouvernement du Canada

Risk Management Scope

for

Hexanoic acid, 2-ethyl-, 2-ethylhexyl ester

(2-ethylhexyl-2-ethylhexanoate)

Chemical Abstracts Service Registry Number 7425-14-1

Environment and Climate Change Canada

Health Canada

March 2017

Canada

Summary of Proposed Risk Management

This document outlines the risk management options under consideration for the substance 2-ethylhexyl-2-ethylhexanoate. In particular, the Government of Canada is considering:

1. adding 2-ethylhexyl-2-ethylhexanoate to the Health Canada Cosmetic Ingredient Hotlist;
2. applying Significant New Activity provisions under CEPA to 2-ethylhexyl-2-ethylhexanoate.

The risk management options outlined in this Risk Management Scope document may evolve through consideration of assessments and risk management options published for other Chemicals Management Plan (CMP) substances as required to ensure effective, coordinated, and consistent risk management decision-making.

Note: The above summary is an abridged list of options under consideration to manage this substance and to seek information on identified information gaps and uncertainties. Refer to section 3 of this document for more complete details in this regard.

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1. Context

The *Canadian Environmental Protection Act, 1999* (CEPA) (Canada 1999) provides the authority for the Minister of the Environment and the Minister of Health (the Ministers) to conduct assessments to determine if substances are toxic to the environment and/or harmful to human health as set out in section 64 of CEPA,[1,2] and if so to manage the associated risks.

The substance hexanoic acid, 2-ethyl-, 2-ethylhexyl ester, Chemical Abstracts Service Registry Number (CAS RN)[3] 7425-14-1, referred to throughout this document as "2-ethylhexyl-2-ethylhexanoate", is included in the assessment of calcium 2-ethylhexanoate and 2-ethylhexyl-2-ethylhexanoate, as part of the CMP (Canada 2016).

2. Issue

2.1 Draft Screening Assessment Conclusion

Health Canada and Environment and Climate Change Canada conducted a joint screening assessment relevant to the evaluation of 2-ethylhexyl-2-ethylhexanoate and calcium 2-ethylhexanote (hexanoic acid, 2-ethyl-, calcium salt, CAS RN 136-51-6, referred to throughout this document as calcium 2-

[1] Section 64 [of CEPA]: *For the purposes of* [Parts 5 and 6 of CEPA]*, except where the expression "inherently toxic" appears, a substance is toxic if it is entering or may enter the environment in a quantity or concentration or under conditions that*

- *(a) have or may have an immediate or long-term harmful effect on the environment or its biological diversity;*
- *(b) constitute or may constitute a danger to the environment on which life depends; or*
- *(c) constitute or may constitute a danger in Canada to human life or health.*

[2] A determination of whether one or more of the criteria of section 64 of CEPA are met is based upon an assessment of potential risks to the environment and/or to human health associated with exposures in the general environment. For humans, this includes, but is not limited to, exposures from ambient and indoor air, drinking water, foodstuffs, and products available to consumers. A conclusion under CEPA is not relevant to, nor does it preclude, an assessment against the hazard criteria specified in the *Hazardous Products Regulations*, which are part of the regulatory framework for the Workplace Hazardous Materials Information System for products intended for workplace use. Similarly, a conclusion based on the criteria contained in section 64 of CEPA does not preclude actions being taken under other sections of CEPA or other Acts.

[3] CAS RN: Chemical Abstracts Service Registry Number. The Chemical Abstracts Service information 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.

ethylhexanoate) in Canada. A notice summarizing the scientific considerations of the draft screening assessment for these substances was published in the *Canada Gazette*, Part I, on March 25, 2017 (Canada 2017).

Based on the information available, the draft screening assessment proposes that 2-ethylhexyl-2-ethylhexanoate is harmful to human health under section 64(*c*) of CEPA because it is 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 (Canada 2016). It is proposed that calcium 2-ethylhexanoate is not harmful to human health under section 64(*c*) of CEPA because 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. However, calcium 2-ethylhexanoate has effects of concern based on potential developmental toxicity in laboratory animals. While available information does not indicate a risk to human health for Canadians at current levels of exposure, there may be a concern if exposures were to increase.

It is proposed that 2-ethylhexyl-2-ethylhexanoate and calcium 2-ethylhexanoate 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 under section 64(*a*) or 64(*b*) of CEPA, respectively (Canada 2016).

The exposure source of concern, identified in the draft screening assessment, is dermal exposure to 2-ethylhexyl-2-ethylhexanoate from foot lotion and face make-up (refer to section 5).

Of note, the proposed risk management options described in this document and the proposed conclusion outlined in the draft screening assessment are preliminary and may be subject to change. For further information on the draft screening assessment for 2-ethylhexyl-2-ethylhexanoate and calcium 2-ethylhexanoate, refer to www.ec.gc.ca/ese-ees/default.asp?lang=En&n=C78BFAB3-1

2.2 Proposed Recommendation under CEPA

Based on the findings of the draft screening assessment conducted as per CEPA, the Ministers propose to recommend that 2-ethylhexyl-2-ethylhexanoate be added to the *List of Toxic Substances* in Schedule 1 of the Act.[4]

[4] When a substance is found to meet one or more of the criteria under section 64 of CEPA, the Ministers can propose to take no further action with respect to the substances, add the substance to the Priority Substances List for further assessment, or recommend the addition of the substance to the List of Toxic Substances in Schedule 1 of the Act.

The Ministers will take into consideration comments made by stakeholders during the 60-day public comment period on the draft screening assessment and Risk Management Scope document in the preparation of the final screening assessment and Risk Management Approach document, if required. If it is concluded that 2-ethylhexyl-2-ethylhexanoate meets one or more of the criteria under section 64 of CEPA at the time of the final screening assessment and the Ministers recommend the addition of 2-ethylhexyl-2-ethylhexanoate to Schedule 1, risk management instrument(s) will be proposed within 24 months of the date on which the final screening assessment is published and will be finalized within 18 months of the date on which the risk management instrument(s) are proposed.

3. Proposed Risk Management

3.1 Proposed Human Health Objective

Proposed human health objectives are quantitative or qualitative statements of what should be achieved to address human health concerns.

The proposed human health objective for 2-ethylhexyl-2-ethylhexanoate is to reduce exposure of the general population to the substance to levels that are protective of human health.

3.2 Proposed Risk Management Objective and Options under Consideration

Proposed risk management objectives set quantitative or qualitative targets to be achieved by the implementation of risk management regulations, instrument(s) and/or tool(s) for a given substance or substances. In this case, the proposed risk management objectives for 2-ethylhexyl-2-ethylhexanoate are:

(1) to reduce dermal exposure to the sources of greatest concern, specifically cosmetics containing 2-ethylhexyl-2-ethylhexanoate; and
(2) to prevent increases in exposure to 2-ethylhexyl-2-ethylhexanoate.

To achieve the proposed risk management objectives and to work towards achieving the proposed human health objective, the risk management options under consideration are:

(1) Add 2-ethylhexyl-2-ethylhexanoate to Health Canada's Cosmetic Ingredient Hotlist, which is 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* (FDA) or may contravene one or more provisions of the *Cosmetic Regulations*. Section 16 of the FDA states that "No person shall sell any cosmetic that has in or on it any substance that may cause injury to the health of the user." In addition, the hotlist includes certain substances that may make it unlikely for a product to be classified as a cosmetic under the FDA. Compliance with the provisions of section 16 are monitored, in part, through the mandatory notification provisions of section 30 of the *Cosmetic Regulations* of the *Food and Drugs Act*, which requires that all manufacturers and importers provide a list of the cosmetic's ingredients to Health Canada.

(2) Apply Significant New Activity provisions under CEPA to 2-ethylhexyl-2-ethylhexanoate that would require that any proposed new manufacture, import or use be subject to further assessment and that would determine if the new activity requires further risk management consideration.

Following the publication of this Risk Management Scope document, additional information obtained from the public comment period and from other sources will be considered, along with the information presented in this document, in the instrument selection and development process.[5] The risk management options outlined in this document may evolve through consideration of assessments and risk management options published for other CMP substances to ensure effective, coordinated, and consistent risk management decision-making.

3.3 Risk Management Information Gaps

At this time, no additional information is required from industry.

4. Background

4.1 General Information on 2-Ethylhexyl-2-ethylhexanoate

2-Ethylhexyl-2-ethylhexanoate is an organic substance and is based on the parent structure 2-ethylhexanoic acid (2-EHA), CAS RN 149-57-5, which was

[5] The proposed risk management regulation(s), instrument(s) or tool(s) will be selected using a thorough, consistent and efficient approach and will take into consideration available information in line with the Government of Canada's Cabinet Directive on Regulatory Management (TBS 2012a), the Red Tape Reduction Action Plan (TBS 2012b) and the *Red Tape Reduction Act* (Canada 2015).

evaluated by Health Canada and Environment and Climate Change Canada as part of the Challenge initiative (Health Canada 2011). 2-Ethylhexyl-2-ethylhexanoate is the ester of 2-EHA and 2-ethylhexanol.

4.2 Current Uses and Identified Sectors

Responses to a 2011 survey indicated that there were no reports of manufacture or import of 2-ethylhexyl-2-ethylhexanoate in Canada above the reporting threshold of 100 kg in that year (Environment Canada 2013).

According to notifications submitted under the Cosmetic Regulations to Health Canada (Canada 2016), 2-ethylhexyl-2-ethylhexanoate is used in certain cosmetic products in Canada, such as foot lotion and face make-up. No occurrence data regarding 2-ethylhexyl-2-ethylhexanoate in food in Canada were identified. It was reported as a volatile component of certain foreign food samples, such as wild peanuts (Cherif et al. 2013), muskmelon (Priyanka et al. 2015), roasted barley (Bianchi et al. 2007), and beef (Tansawat et al. 2013). Given the very low concentration present, the limited number of foods in which 2-ethylhexyl-2-ethylhexanoate has been detected, and the fact that the substance is volatile, with expected losses during food preparation, the level of exposure from these sources is likely to be negligible. It is also unlikely that many of the foods in which 2-ethylhexyl-2-ethylhexanoate has been reported to be present would be consumed by the general population of Canadians (Canada 2016). Based on these considerations, exposure of the general population of Canadians to 2-ethylhexyl-2-ethylhexanoate from food is considered negligible.

In the United States, the national production volume of 2-ethylhexyl-2-ethylhexanoate in 2011 was 35 300 kilograms (78 000 pounds) (CDAT [modified 2014]). Globally, 2-ethylhexyl-2-ethylhexanoate has reported uses as an emollient in cosmetics (Fiume et al. 2015; CosIng 2016).

5. Exposure Source and Identified Risk

General population exposure to 2-ethylhexyl-2-ethylhexanoate may occur from the use of certain cosmetics, such as foot lotion and face make-up. According to the draft screening assessment of 2-ethylhexyl-2-ethylhexanoate (Canada 2016), dermal exposure was estimated to be 0.37-1.10 mg/kg/d from the use of foot lotion containing 1-3% w/w of 2-ethylhexyl-2-ethylhexanoate (use frequency of 2 times per day) and 0.91-3.05 mg/kg/d from the use of face make-up containing 3-10% w/w of 2-ethylhexyl-2-ethylhexanoate (use frequency of 1.8 times per day).

Substance-specific health effects data were not identified. However, 2-EHA and 2-ethylhexanol (i.e., CAS RNs 149-57-5 and 104-76-7, respectively) are considered relevant to 2-ethylhexyl-2-ethylhexanoate, and were used as analogues where critical health effects data were required. Based on oral studies, 2-EHA was determined to be the more potent of the two analogues, and thus a study for 2-EHA was selected to be conservative. An oral study conducted on laboratory animals revealed developmental health effects at the lowest dose (100 mg/kg-bw/day) following repeated exposure to 2-EHA in rat dams. Margins of exposure comparing effect levels from the oral dosing of 2-EHA in laboratory animals and upper-bounding estimates of dermal exposure ranged from 160-480 for foot lotion and 60-200 for face-makeup and were potentially inadequate to address uncertainties in the health effects and exposure databases for 2-ethylhexyl-2-ethylhexanoate (Canada 2016).

6. Risk Management Considerations

6.1 Alternatives and Alternate Technologies

With respect to foot lotion and face make-up, alternative cosmetic products are available that do not use 2-ethylhexyl-2-ethylhexanoate.

6.2 Socio-economic and Technical Considerations

Socio-economic factors will be considered in the selection process for a regulation and/or instrument respecting preventive or control actions, and in the development of the risk management objectives(s). Socio-economic factors will also be considered in the development of regulations, instrument(s) and/or tool(s) as identified in the *Cabinet Directive on Regulatory Management* (TBS 2012a) and the guidance provided in the Treasury Board document *Assessing, Selecting, and Implementing Instruments for Government Action* (TBS 2007).

7. Overview of Existing Risk Management

7.1 Related Canadian Risk Management Context

2-Ethylhexyl-2-ethylhexanoate is not currently subject to any substance-specific risk management in Canada.

7.2 Pertinent International Risk Management Context

Internationally, the following pertinent risk management action has been taken for 2-ethylhexyl-2-ethylhexanoate:

United States:

2-Ethylhexyl-2-ethylhexanoate is subject to the US Environmental Protection Agency's *Toxic Substances Control Act* (TSCA) 2016 Chemical Data Reporting (CDR) requirement for which companies must report certain manufacture, import or processing to the US EPA (US EPA 2016).

Europe:

2-Ethylhexyl-2-ethylhexanoate is subject to European Commission Regulations (EC) No 1223/2009 as a substance which is prohibited for use in cosmetics due to its classification as a Category 2 reprotoxic substance (EU 2008), unless an evaluation by the Scientific Committee on Consumer Safety (SCCS) has found the substance safe for use in cosmetic products (EU 2009). As of January 2016, the SCCS has not carried out a safety evaluation of 2-ethylhexyl-2-ethylhexanoate in cosmetics.

8. Next Steps

8.1 Public Comment Period

Industry and other interested stakeholders are invited to submit comments on the content of this Risk Management Scope or other information that would help to inform decision-making (such as outlined in sections 3.2). Please submit additional information and comments prior to May 24, 2017 The Risk Management Approach document, which will outline and seek input on the proposed risk management instrument(s), will be published at the same time as the final screening assessment. At that time, there will be further opportunity for consultation.

Comments and information submissions on the Risk Management Scope should be submitted to the address provided below:

Environment and Climate Change Canada
Chemicals Management Division
Gatineau Quebec K1A 0H3
Tel: 1-800-567-1999 | 819- 938-3232
Fax: 819-938-5212
Email: ec.substances.ec@canada.ca

Companies that have a business interest in 2-ethylhexyl-2-ethylhexanoate are encouraged to identify themselves as stakeholders. Stakeholders will be informed of future decisions regarding 2-ethylhexyl-2-ethylhexanoate and may be contacted for further information.

8.2 Timing of Actions

Action	Date
Electronic consultation on the Risk Management Scope	March 25, 2017 to May 24, 2017
Submission of additional studies or information on 2-ethylhexyl-2-ethylhexanoate	on or before May 24, 2017
Publication of responses to public comments on the draft screening assessment and Risk Management Scope	before March, 2018
Publication of the final screening assessment and, if required, the Risk Management Approach document	before March, 2018
Publication of responses to public comments on the Risk Management Approach, if applicable, and publication if required, of the proposed instrument(s)	24-months from the publication of the final screening assessment
Consultation on the proposed instrument(s), if required	60-day public comment period starting upon publication of the proposed instrument(s)
Publication of the final instrument(s), if required	18-months from the publication of the proposed instrument(s)

9. References

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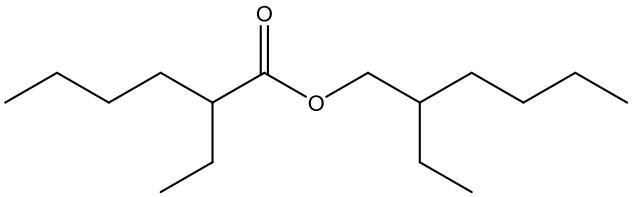
Appendix A. Substance Targeted for Risk Management

CAS RN	DSL name (common name)	Chemical structure and molecular formula	Molecular weight (g/mol)
7425-14-1	Hexanoic acid, 2-ethyl-, 2-ethylhexyl ester (2-Ethylhexyl-2-ethylhexanoate)	 $C_{16}H_{32}O_2$	256.43