Government of Canada / Gouvernement du Canada

Risk Management Scope

for

Certain Substances in the Hexamethylenetetramines Group

3,5,7-Triaza-1-azoniatricyclo[3.3.1.1³,7]decane, 1-(3-chloro-2-propenyl)-, chloride

(Cis/trans-CTAC)

3,5,7-Triaza-1-azoniatricyclo[3.3.1.1³,7]decane, 1-(3-chloro-2-propenyl)-, chloride, (Z)-

(Cis-CTAC)

Chemical Abstracts Service Registry Numbers (CAS RN):

4080-31-3

51229-78-8

Environment and Climate Change Canada

Health Canada

March 2021

Canada

Summary of Proposed Risk Management

This document outlines the risk management options under consideration for 3,5,7-Triaza-1-azoniatricyclo[3.3.1.1³,7]decane, 1-(3-chloro-2-propenyl)-, chloride and 3,5,7-Triaza-1-azoniatricyclo[3.3.1.1³,7]decane, 1-(3-chloro-2-propenyl)-, chloride, (Z)- which have been proposed to be harmful to human health, but not to the environment in Canada. The two substances are part of the Hexamethylenetetramines Group. The substances are commonly referred to as cis/trans-CTAC and cis-CTAC, and may also be referred to as Quaternium-15 for each or both substances.

In particular, the Government of Canada is considering the following risk management actions to address non-medicinal ingredients in natural health products and non-prescription drugs:

> Revising the listing for Quaternium-15 in the Natural Health Products Ingredients Database (NHPID) to reduce exposures of Canadian infants, toddlers, and children to Quaternium-15 in topical products (body moisturizer and sunscreen lotion)

To inform risk management decision-making, further information regarding the concentrations of cis/trans-CTAC and cis-CTAC used in products available to consumers, including body moisturizers and sunscreen lotion, to which dermal exposure may occur, should be provided (ideally on or before May 5, 2021), to the contact details identified in section 8 of this document.

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

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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 to human health as set out in section 64 of CEPA[1,2], and if so, to manage the associated risks.

The Hexamethylenetetramines Group is included in the third phase of the Chemicals Management Plan and includes:

- 3,5,7-Triaza-1-azoniatricyclo[3.3.1.1³,7]decane, 1-(3-chloro-2-propenyl)-, chloride [CAS RN 4080-31-3] (cis/trans-CTAC);
- 3,5,7-Triaza-1-azoniatricyclo[3.3.1.1³,7]decane, 1-(3-chloro-2-propenyl)-, chloride, (Z)- [CAS RN 51229-78-8] (cis-CTAC)[3]

The substances are commonly referred to as cis/trans-CTAC and cis-CTAC, and may also be referred to as Quaternium-15 for each or both substances.

2. Issue

Health Canada and Environment and Climate Change Canada conducted a joint scientific assessment of the Hexamethylenetetramines Group which includes cis/trans-CTAC and cis-CTAC. A notice summarizing the scientific considerations of the draft screening assessment for these substances was published in the *Canada Gazette*, Part I, on March 6, 2021 (Canada 2021). For further information, refer to the draft screening assessment report for the Hexamethylenetetramines Group.

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

[3] This substance was not identified under subsection 73(1) of CEPA but was included in this assessment as it was considered a priority on the basis of other human health concerns.

2.1 Draft screening assessment conclusion

Based on the information available, the draft screening assessment proposes that cis/trans-CTAC and cis-CTAC are toxic under section 64(*c*) of CEPA because they are entering or may enter 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, 2021).

It is proposed to conclude that the substances do not meet the criteria under paragraphs 64(*a*) or 64(*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.

The draft screening assessment also proposes that cis/trans-CTAC and cis-CTAC do not meet the criteria for persistence or bioaccumulation as defined in the *Persistence and Bioaccumulation Regulations* made under CEPA (Canada 2000).

The exposure source of concern, identified in the draft screening assessment, is based on dermal exposure of infants, toddlers, and children from the use of natural health product body moisturizers and non-prescription sunscreen lotion containing cis/trans-CTAC and/or cis-CTAC. This document focuses on the dermal exposures of greatest concern (refer to section 5).

Of note, the proposed risk management options described in this document and the proposed conclusions outlined in the draft screening assessment are preliminary and may be subject to change. For further information, refer to the draft screening assessment report for the Hexamethylenetetramines Group.

2.2 Proposed recommendation under CEPA

On the basis of the findings of the draft screening assessment conducted pursuant to CEPA, the ministers propose to recommend that cis/trans-CTAC and cis-CTAC be added to the List of Toxic Substances in Schedule 1 of the Act[4].

The ministers will take into consideration comments made by stakeholders during the 60-day public comment period on the draft screening assessment report for the Hexamethylenetetramines Group and the associated Risk Management Scope document.

If the ministers finalize the recommendation to add cis/trans-CTAC and cis-CTAC to Schedule 1, risk management instrument(s) must be proposed and finalized for cis/trans-CTAC within a set period of time, as outlined in sections 91 and 92 of CEPA (refer to section 8 for publication timelines applicable to these substances).

[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.

Cis-CTAC is not subject to sections 91 and 92 of CEPA since it was not identified under subsection 73(1) of CEPA.

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.

For cis/trans-CTAC and cis-CTAC, the proposed objective is focused on addressing the risks and exposure sources of concern outlined in section 5 of this document. As such, the proposed human health objective for these substances is to reduce exposure of infants and children to cis/trans-CTAC and cis-CTAC to levels that are protective of human health.

3.2 Proposed risk management objectives

Proposed risk management objectives set quantitative or qualitative targets to be achieved by the implementation of risk management regulations, instruments and/or tools for a given substance or substances. The proposed risk management objective for cis/trans-CTAC and cis-CTAC is to reduce dermal exposure of infants and children from body moisturizers and sunscreen lotion, to levels that are protective of human health.

The proposed risk management objective may be revised in the Risk Management Approach document that will be published concurrently with the final screening assessment for this substance, or in subsequent risk management documents (e.g., consultation document on proposed instrument), as the case may be.

3.3 Proposed risk management options under consideration

Cis/trans-CTAC and cis-CTAC may be referred to as Quaternium-15 for each or both substances; therefore to achieve the proposed risk management objective and to work towards achieving the proposed human health objective, the risk management options under consideration are as follows:

Addressing non-medicinal ingredients in natural health products and non-prescription drugs by:

> Revising the listing for Quaternium-15 in the Natural Health Products Ingredients Database (NHPID) to reduce exposures of Canadian infants, toddlers, and children to Quaternium-15 in topical products (body moisturizer and sunscreen lotion)

Following the publication of this 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 also evolve through consideration of assessments and risk management options or actions published for other CMP substances to ensure effective, coordinated, and consistent risk management decision-making.

3.4 Performance measurement and evaluation

Performance measurement evaluates the ongoing effectiveness and relevance of the actions taken to manage risks from toxic substances[6]. The aim is to determine whether human health and/or environmental objectives have been met and whether there is a need to revisit the risk management approach for that substance. To achieve this, the Government of Canada will review the effectiveness of the risk management action(s) for cis/trans-CTAC and cis-CTAC.

The Government of Canada plans to measure the effectiveness of the risk management action(s) by collecting and analyzing data to measure progress towards meeting the risk management objective(s).

The results of performance measurement and evaluation will be used to inform whether further risk management action is warranted and will be made available to Canadians along with recommendations for further action, if applicable.

3.5 Risk management information gaps

In order to make informed decisions on the proposed risk management, interested stakeholders are invited to provide further information regarding the concentrations of cis/trans-CTAC and cis-CTAC used in products available to consumers, including body moisturizers and sunscreen lotion, to which dermal exposure may occur.

Should stakeholders have relevant information on cis/trans-CTAC and cis-CTAC, they should provide it on or before May 5, 2021 to the contact identified in section

[5] The proposed risk management regulation, instrument or tool will be selected using a thorough, consistent and efficient approach and take into consideration available information in line with the Government of Canada's Cabinet Directive on Regulation (TBS, 2018), the Red Tape Reduction Action Plan (TBS, 2012), and in the case of a regulation, the *Red Tape Reduction Act* (Canada, 2015).

[6] Performance measurement can be performed at two levels:

- Instrument-based performance measurement evaluates the effectiveness of an individual instrument in meeting the specific risk management objectives that were set out when the risk management tool was designed. The results of performance measurement will help determine if additional risk management or assessment is needed (*i.e.*, evaluate whether risk management objectives have been met); and
- Substance-based performance measurement considers performance of all final risk management instruments applied to a chemical substance and relevant data or indicators of exposure to the environment or human health (*i.e.*, evaluate whether human health and/or environmental objectives have been met).

8 of this document. Such information can help inform the risk management decision-making process.

4. Background

4.1 General information on cis/trans-CTAC and cis-CTAC

Cis/trans-CTAC and cis-CTAC are organic substances included in the Hexamethylenetetramines Group in the third phase of the CMP. Cis/trans-CTAC and cis-CTAC are both associated with the common INCI name "Quaternium-15" (US EPA 1995; Becker et al. 2010; SCCS 2011). The former substance represents a mixture of isomers, which contains approximately 31% to 60% cis-CTAC and 20% to 53% trans-CTAC (US EPA 1995; SCCS 2011). Since toxicological studies conducted on the mixture do not always report the relative abundance of each isomer, it is not possible to definitively distinguish whether health effects are mediated by one isomer or the other. Cis/trans-CTAC and cis-CTAC were assessed together in the human health assessment and the toxicological data from both were taken into consideration.

4.2 Current uses and identified sectors

Cis/trans-CTAC and cis-CTAC were included in a mandatory survey issued pursuant to section 71 of CEPA (Canada 2012). Total reported imports of cis/trans-CTAC for 2011 ranged from 10 000 – 100 000 kg, and 1000 – 10 000 kg for cis-CTAC (Environment Canada 2013). No manufacturing activities above the reporting threshold of 100 kg were reported for either substance (Environment Canada 2013). According to information submitted in response to the section 71 survey, cis/trans-CTAC was reported to be used in the automotive sector, aircraft and transportation sector, and in paints and coatings. Cis-CTAC was reported to be used in personal care products.

Other uses in Canada identified for both substances include in cleaning products, paints, adhesives, self-care products (i.e., cosmetics, as a non-medicinal ingredient in non-prescription drugs), and as formulants in registered pest control products.[7,8,9,10,11,12] Cis/trans-CTAC is also a medicinal ingredient in drug products[7]; in self-care products (as a non-medicinal ingredient in licensed natural health products[8]); a component in hand cleaners used in food processing

[7] Personal communication, email from the Food Directorate (FD), Health Canada (HC), to the Existing Substances Risk Assessment Bureau (ESRAB), HC, dated Feb. 4, 2019; unreferenced
[8] Personal communication, email from the Therapeutic Product Directorate (TPD), HC, to the ESRAB, HC, dated Feb. 4, 2019; unreferenced
[9] LNHPD [modified 2019]
[10] Personal communication, email from the Consumer and Hazardous Products Safety Directorate (CHPSD), HC, to the ESRAB, HC, dated Feb. 4, 2019; unreferenced
[11] Any cosmetic notifications under the INCI name "Quaternium-15" may also refer to cis-CTAC as it is not possible to know if cosmetics contain cis/trans-CTAC or cis-CTAC
[12] Personal communication, email from the Pest Management Regulatory Agency (PMRA), HC, to the ESRAB, HC, dated Feb. 4, 2019; unreferenced

establishments; and an active ingredient in pest control products[12], and may be used as a component in food packaging materials and in food contact surface cleaners and hand cleaners used in food processing establishments[7]. Cis-CTAC may also be used as a component in hand cleaners and lubricants used in food processing establishments[7].

5. Exposure Sources and Identified Risks

Direct exposures from use of self-care products and other products available to consumers, as well as exposure from food and environmental media, were evaluated. Product scenarios that result in the highest levels of potential exposure for the substances by the dermal routes were presented in the screening assessment. Inhalation exposure was also considered, but was not found to be a concern to human health at current levels of exposure.

The critical health effects associated with dermal exposure to cis/trans-CTAC and cis-CTAC are effects on the testes and liver, as identified in the draft screening assessment (Canada 2020). A comparison of the critical effect levels to exposure estimates from natural health product body moisturizers and non-prescription sunscreen lotion, resulted in margins of exposure (MOEs) that were considered potentially inadequate to address uncertainties in the health effects and exposure databases for relevant subpopulations, specifically infants, toddlers, and children. The resultant MOEs for the dermal route of exposure for facial moisturizer, body moisturizer (cosmetic), hair perm/straightener, wall paint, furniture cleaning wipe, and stain remover were considered adequate.

Developmental effects, such as malformations, were considered to be the critical health effects associated with oral exposure to cis/trans-CTAC and cis-CTAC. A comparison of critical effect levels to exposure estimates of oral exposure scenarios (i.e., dietary exposure from use in food packaging applications and drinking water), resulted in MOEs that are considered adequate to address uncertainties in the exposure and health effects databases.

6. Risk Management Considerations

6.1 Alternatives and alternate technologies

It is not known whether there are safe alternatives available to replace cis/trans-CTAC and cis-CTAC in body moisturizers and sunscreen lotion. Consideration will be given to the likelihood that their presence in these products may be for functional purposes as a preservative.

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 Regulation (TBS 2018) 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

Existing risk management for cis/trans-CTAC and cis-CTAC in Canada relates to its presence in natural health products, non-prescription drugs, food packaging materials and incidental additives, and pesticides.

Natural health products and non-prescription drugs:

Cis/trans-CTAC is listed by its CAS RN under Quaternium-15 as a permitted non-medicinal ingredient in the NHPID (NHPID 2019) and in currently licensed natural health products (LNHPD 2019) and non-prescription drugs.

Pesticides

Cis/trans-CTAC and cis-CTAC are permitted as formulants in pesticides under the *Pest Control Products Act*.[13]

Cis/trans-CTAC is registered as an active ingredient in pesticides.[12]

Food

In Canada, packaging materials in which food is sold must comply with safety provisions set out under Division 23 of the Canadian *Food and Drug Regulations* and section 4(1)(a) of the *Food and Drugs Act*.

In Canada, incidental additives used in food processing facilities are subject to safety provisions set out under section 4(1)(a) of the *Food and Drugs Act*.

Cosmetics

Cis/trans-CTAC and cis-CTAC are not subject to any specific risk management related to cosmetics.

[13] Personal communication, email from the Pest Management Regulatory Agency (PMRA), HC, to the ESRAB, HC, dated Feb. 4, 2019; unreferenced

7.2 Pertinent international risk management context

7.2.1 United States

Natural health products

Cis/trans-CTAC and cis-CTAC are not subject to any specific risk management related to natural health products.

Pesticides

Cis-CTAC is restricted to a concentration limit of 0.14% by weight of pesticide formulation as a preservative in pesticide residues in food (US EPA 2019a).

Cis/trans-CTAC and cis-CTAC are permitted as antimicrobial substances and are currently subject to a regulatory re-evaluation (US EPA 2019b).

Food

Cis/trans-CTAC is permitted for use as a preservative in certain types of food packaging materials including paper and paperboard in contact with aqueous fatty foods (US FDA 2019a), adhesives (US FDA 2019b) and polyurethane resins (US FDA 2019c).

Cosmetics

Cis/trans-CTAC and cis-CTAC are not currently included on the US Food and Drug Administration's List of Prohibited and Restricted Ingredients from use in cosmetics.

Assembly Bill No. 2762 in California will prohibit the manufacture, sale, delivery, holding, or offering for sale of cosmetics containing 24 chemicals, other than in trace amounts, including Quaternium-15. Only the CAS RN for cis-CTAC is identified with Quaternium-15. The ban will come into effect on January 1, 2025.

7.2.2 European Union

Natural health products

Cis/trans-CTAC and cis-CTAC are not subject to any specific risk management related to natural health products.

Pesticides

Cis/trans-CTAC and cis-CTAC are permitted as preservatives in slimicides (ECHA 2012).

Food

Cis/trans-CTAC is permitted for use in food packaging materials under Regulation (EU) No 10/2011 (Consolidated-2019-05-19): Plastic materials and articles intended to come into contact with food (European Union 2019b).

Cosmetics

Quaternium-15 is prohibited in cosmetics based on its hazard classification under Regulation (EC) No. 1223/2009 (European Union 2009, 2019a).

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 section 3.2).

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 report. 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
Gatineau, Quebec K1A 0H3
Telephone: 1-800-567-1999 (in Canada) or 819-938-3232
Fax: 819-938-5212
Email: eccc.substances.eccc@canada.ca

Companies who have a business interest in cis/trans-CTAC and cis-CTAC are encouraged to identify themselves as stakeholders. The stakeholders will be informed of future decisions regarding cis/trans-CTAC and cis-CTAC and may be contacted for further information.

8.2 Timing of actions

Electronic consultation on the draft screening assessment report and Risk Management Scope: March 6, 2021 to May 5, 2021.This should include the submission of public comments, additional studies and/or information on cis/trans-CTAC and cis-CTAC.

Publication of responses to public comments on the draft screening assessment report and Risk Management Scope: concurrent to the publication of the final screening assessment and, if required, the Risk Management Approach document.

These are planned timelines, and are subject to change. Please consult the schedule of risk management activities and consultations for updated information on timelines.

9. References

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[US FDA] US Food & Drug Administration. 2019c. Code of Federal Regulations Title 21, Volume 3: Section 177.1680 Indirect Food Additives: Polymers.