Government of Canada / Gouvernement du Canada

Risk Management Scope

for

Poly(iminocarbonimidoyliminocarbonimidoylimino-1,6-hexanediyl), hydrochloride

AND

Guanidine, N,N'''-1,6-hexanediylbis[N'-cyano-, polymer with 1,6-hexanediamine, hydrochloride

referred to as

Poly(hexamethylenebiguanine) (PHMB)

Chemical Abstracts Service Registry Number (CAS RN): 27083-27-8 and 32289-58-0

Environment and Climate Change Canada

Health Canada

October 2020

Canada

Summary of Proposed Risk Management

This document outlines the risk management options under consideration for poly(hexamethylenebiquanine) (PHMB), which has been proposed to be harmful to human health.

In particular, the Government of Canada is considering the following risk management actions:

- Cosmetics:
  1) Communicating measures to reduce exposures of Canadians to PHMB from certain cosmetics, including dermally applied products and cosmetic spray applications, by describing PHMB as a prohibited or restricted ingredient on the Health Canada Cosmetic Ingredient Hotlist.

- Other products available to consumers:
  1) Applying Significant New Activity (SNAc) provisions under CEPA. These provisions would require any proposed manufacture, import or distribution for sale of products available to consumers containing PHMB, that constitutes a significant new activity, to be notified to the Government of Canada and to be subject to further assessment. The SNAc provisions would be applied to products from which the substance is proposed or intended to be diffused or to be released as a vapour, mist or aerosol.

Moreover, because certain data gaps remain, further information on the following item should be provided on or before December 2, 2020, to the contact details identified in section 8 of this document, to inform risk management decision-making:

- Current quantities (in kilograms) and concentrations of PHMB used in cosmetics and other products available to consumers (such as spray products or products that diffuse or release the substance as a vapour, mist or aerosol)

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.

Note: The above summary is an abridged list of options under consideration to manage this substance and to seek information on identified gaps. Refer to section

3 of this document for more complete details in this regard. It should be noted that the proposed risk management option(s) may evolve through consideration of additional information obtained from the public comment period, literature and other sources.

Table of Contents

1. Context

The *Canadian Environmental Protection Act, 1999* (CEPA) (Government of 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 based on the criteria set out in section 64 of CEPA[1,2], and if so to manage the associated risks.

The substance poly(hexamethylenebiguanine) (PHMB) Chemical Abstracts Service Registry Number (CAS RN[3]) [32289-58-0 and 27083-27-8] (alternatively CAS RN 27083-27-8), referred to throughout this document as PHMB, is included in the screening assessment of the Poly Others Group of the Chemicals Management Plan (Canada 2020).

2. Issue

Health Canada and Environment and Climate Change Canada conducted a joint scientific assessment of substances in the Other Polymers Group. A notice summarizing the scientific considerations of the draft screening assessment for these substances was published in the *Canada Gazette*, Part I, on October 3, 2020 (Canada 2020). Refer to the draft screening assessment report for PHMB for further information.

2.1 Draft Screening Assessment Conclusion

Based on the information available, the draft screening assessment proposes that PHMB (CAS RN 32289-58-0 and CAS RN 27083-27-8) is toxic under section 64(*c*) of CEPA because it is entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in

[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] 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.

Canada to human life or health (Canada, 2020). It proposed that there was not concern for ecological harm from the substance.

The draft screening assessment also proposes that PHMB (CAS RN 32289-58-0 and CAS RN 27083-27-8) meets the persistence criteria but not the bioaccumulation criteria, as defined in the *Persistence and Bioaccumulation Regulations* made under CEPA (Government of Canada, 2000).

The exposure sources of concern, identified in the draft screening assessment, are based on the potential dermal sensitization from the use of cosmetics and the potential inhalation toxicity of PHMB from the use of cosmetic spray applications. In addition, there could be a concern of increased exposure if other products available to consumers, other than cosmetics, where PHMB can be diffused or released to air and potentially available for inhalation, entered the Canadian market. As such, this document focuses on these applications and exposures of greatest concern (refer to section 5).

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 PHMB (CAS RN 32289-58-0 and CAS RN 27083-27-8) 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 PHMB and its associated Risk Management Scope document.

If the ministers finalize the recommendation to add PHMB to Schedule 1, risk management instruments must be proposed and finalized within a set period of time, as outlined in sections 91 and 92 of CEPA (refer to section 8 for publication timelines applicable to this group of substances).

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.

[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.

For PHMB, 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 this substance is to reduce exposure of the general population to PHMB 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. In this case, the proposed risk management objectives for PHMB are:

- to reduce dermal exposure from cosmetics available to consumers;
- to reduce inhalation exposure from cosmetic spray applications available to consumers;
- to prevent inhalation exposure from products available to consumers, other than cosmetics, since exposures from these products, such as sprays, mist, vapour or aerosol applications or products where the substance may be diffused into air, may be a concern if these products were to become available in Canada.

The proposed risk management objectives may be revised in the Risk Management Approach document that will be published concurrently with the 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

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

- Cosmetics:
  1) Communicating measures to reduce exposures of Canadians to PHMB from certain cosmetics, including dermally applied products and cosmetic spray applications, by describing PHMB as a prohibited or restricted ingredient on the Health Canada Cosmetic Ingredient Hotlist.

- Other products available to consumers:
  1) Applying Significant New Activity (SNAc) provisions under CEPA. These provisions would require any proposed manufacture, import or distribution for sale of products available to consumers containing PHMB, that constitutes a significant new activity, to be notified to the Government of Canada and to be subject to further assessment. The

SNAc provisions would be applied to products from which the substance is proposed or intended to be diffused or to be released as a vapour, mist or aerosol.

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 ensure that risks are managed effectively over time. To achieve this, the Government of Canada will review, on a regular basis, the effectiveness of the risk management action(s) for PHMB.

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 current

[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).

quantities (in kilograms) and concentrations of PHMB used in cosmetics and other products available to consumers where PHMB can be released to air and inhaled (i.e., spray application products, products intended to result in the release the substance as a vapour mist or aerosol or products that diffuse the substance in the air).

Should stakeholders have further information to help address these gaps, they should provide it on or before December 2, 2020 to the contact identified in section 8 of this document. Such information can help inform the risk management decision-making process.

4. Background

4.1 General Information on PHMB

PHMB is an organic substance which is part of the CMP Other Polymers Group. The draft screening assessment identified the substance PHMB as having two equivalent CAS RN depending on how the polymer is described; CAS RN 27083-27-8 expresses the PHMB hydrochloride in terms of its starting monomers, and CAS RN 32289-58-0 for the PHMB hydrochloride as the resultant polymer (SCCS, 2017; CIR, 2017; ECHA, 2017). It is additionally noted that PHMB may also be identified by two other CAS RNs (28757-47-3 and 1802181-67-4) outside of Canada. Additionally, PHMB may have several common names associated with it, including an International Nomenclature of Cosmetic Ingredients (INCI) name for identification in cosmetics, “polyaminopropyl biguanide”.

4.2 Current Uses and Identified Sectors

PHMB has been included in a voluntary survey (ECCC, 2015) as well as a mandatory survey conducted under section 71 of CEPA (Canada, 2015). Total reported imports of PHMB for 2014 ranged from 100 to 1000 kg and no manufacturing activities were reported. According to the mandatory and voluntary surveys, the major use reported in Canada for PHMB is as an antimicrobial preservative in cosmetics, natural health products and topical pharmaceuticals.

PHMB is also identified as being used in cosmetics, based on notifications submitted under the *Cosmetic Regulations* to Health Canada (personal communication, email from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the New Substances Assessment and Control Bureau, Health Canada, dated September 2017; unreferenced).

PHMB is listed in the Natural Health Products Ingredients Database with a non-medicinal role for external use only as a preservative (antimicrobial) and not permitted in sprayable formulations, and listed in the Licensed Natural Health Products Database as a non-medicinal ingredient in a limited number of currently

licensed topical natural health products, such as sunscreen, pain relief ointments, lotion and contact lens solutions (LNHPD [modified 2018], NHPID [modified 2018]). PHMB is also listed in the internal Drug Product Database as a non-medicinal ingredient in over the counter disinfectants in Canada (personal communication, email from the Therapeutic Products Directorate, Health Canada, to the New Substances Assessment and Control Bureau, Health Canada, dated December 2017; unreferenced).

Globally, PHMB was also identified as a preservative and antimicrobial agent in cosmetics, personal care products, wet wipes, hand washes, pharmaceuticals and contact lens solutions. The substance is also used to disinfect medical utensils, farm equipment and may be used as a component in sanitizers for disinfecting various surfaces.

5. Exposure Sources and Identified Risks

Direct exposures from use of cosmetic products were evaluated. Product scenarios that result in the highest levels of potential exposure for each substance by the dermal and inhalation routes, or sentinel scenarios, were presented in the screening assessment. The critical health effects associated with PHMB identified in the draft screening assessment (Canada, 2019) are dermal sensitization and inhalation toxicity.

In the assessment, dermal exposure to PHMB in body moisturizer was identified as a potential concern for skin sensitization. Given the information available, it is proposed that the dermal exposure to cosmetics may pose a risk of dermal sensitization in adults and children as the concentrations in these products are higher than levels at which sensitization can occur.

Inhalation exposure was also considered, but was not found to be a concern at current levels of exposure when used in non-spray applications given PHMB has a low vapour pressure and not expected to evaporate from a product. However, if PHMB is used in products where it is dispersed into the air or released as a vapour, mist or aerosol, these are considered forms that may pose an inhalation risk to human health. Cosmetic spray applications containing PHMB are available to Canadians.

No current sources of exposure other than cosmetics were identified as a concern in the draft screening assessment (Canada, 2019). It was found that an analogous substance to PHMB, polyhexamethylene guanidine phosphate (PHMG-P), is an antimicrobial with similar product applications suspected to be responsible for serious adverse health effects from humidifier disinfectants in Korea (Kim, 2016). To date, other types of spray products (e.g., humidifier disinfectants, air fresheners or other such products available to consumers) containing PHMB are not known to be in use in Canada, however there may be a concern for increased exposure should these products become available in Canada.

6. Risk Management Considerations

6.1 Alternatives and Alternate Technologies

It is not known whether there are safe alternatives available to replace PHMB in cosmetic or disinfectant applications. Consideration will be given to the likelihood that its presence in these products is for functional purposes as a preservative or disinfectant.

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

Domestically, risk management actions for PHMB include:

- *Natural Health Products Ingredients Database* – Listed with a non-medicinal role as a preservative/antimicrobial for topical use only, up to 0.1% and not permitted in sprayable formulations (NHPID, 2018);
- *Licensed Natural Health Products Database* – Listed as a non-medicinal ingredient in a limited number of currently licensed topical natural health products, such as makeup, pain relief ointments, lotion and contact lens solutions (LNHPD [modified 2018]); and
- *Food and Drug Regulations*, *Food and Drugs Act* - listed as a non-medicinal disinfectant permitted in drugs for external use (Canada, 2017).
- The safety of PHMB used in incidental additives is subject to provisions under paragraph 4(1)(a) of the *Food and Drugs Act*.

7.2 Pertinent International Risk Management Context

Internationally, PHMB is subject to the following risk management actions:

United States

- Protection of the Environment, Title 40 of the Code of Federal Regulation (CFR):
    - Part 180 – Tolerances and Exemptions for Pesticide Chemical Residues in Food. PHMB is exempt from the requirement of a tolerance for residues of the antimicrobial in or on all food commodities when the residues are the result of the lawful application of a food contact surface sanitizer containing PHMB at 550 parts per million (ppm) (US eCRF, 2018a).
- Food and Drugs Act, Title 21 of the Code of Federal Regulation (CFR):
    - Part 170.39 – Threshold of Regulation for Substances used in Food-Contact Articles, where PHMB is exempt as an antimicrobial agent at levels up to 1000 ppm (0.1% by weight) in water-based latex adhesives complying with 21 CFR 175.105 for use at temperatures that do not exceed 120 F (US eCRF, 2018b).

<u>European Union</u>

- Included in Annex V, List of Preservatives Allowed in Cosmetic Products, of European Commission Regulation No 1223/2009 (EC, 2009), up to 0.1% in ready to use preparations. Not allowed to be used in applications that may lead to exposure via inhalation.

7.3 Regulatory Alignment

Canada is aligned in regulating the preservative/anti-microbial use of PHMB. By taking action on PHMB in cosmetics, Canada would be aligning with similar actions in the EU.

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 PHMB are encouraged to identify themselves as stakeholders. The stakeholders will be informed of future decisions regarding PHMB and may be contacted for further information.

8.2 Timing of Actions

Electronic consultation on the draft screening assessment report and Risk Management Scope: October 3, to December 2, 2020.This should include the submission of public comments, additional studies or information on PHMB.

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

Publication of responses to public comments on the Risk Management Approach, if applicable and if required, the proposed instruments: At the latest, 24-month from the date on which the Ministers recommended that PHMB be added to Schedule 1 of CEPA.

Consultation on the proposed instrument if required: 60-day public comment period starting upon publication of the proposed instrument

Publication of the final instruments, if required: At the latest, 18-month from the publication of the proposed instrument

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 eCFR] United States Code of Federal Regulations. 2018b. Title 21: Part 170 (Food Additives), Subpart 170.39