Government of Canada Gouvernement du Canada

Risk Management Approach

for

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

and

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

are referred to as

Poly(hexamethylenebiguanine) (PHMB)

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

Environment and Climate Change Canada

Health Canada

May 2023

Canada

Summary of Proposed Risk Management

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

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

- Cosmetics:

  Measures to reduce exposures of the general population to PHMB from dermally applied cosmetic products, including topical and spray applications, by describing PHMB as a prohibited or restricted ingredient on Health Canada's Cosmetic Ingredient Hotlist. The Hotlist is used to communicate that certain substances may not be compliant with requirements of the *Food and Drugs Act* or provisions of the *Cosmetic Regulations*.

- Other products available to consumers:

  Applying Significant New Activity (SNAc) provisions under the *Canadian Environmental Protection Act, 1999* (CEPA). These provisions would require any proposed manufacture or import 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 before being undertaken. 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. The SNAc provisions do not apply to uses of a substance that are regulated under any act of parliament listed in Schedule 2 or Schedule 4 of CEPA, including but not limited to the *Pest Control Products Act*, the *Fertilizers Act* and the *Feeds Act*.

The risk management options outlined in this Risk Management Approach may evolve through consideration of assessments and risk management options or actions published for other Chemicals Management Plan 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) 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) Chemical Abstracts Service Registry Number (CAS RN[3]) [32289-58-0 and 27083-27-8], referred to throughout this document as PHMB, is included in the screening assessment of the Other Polymers Group of the Chemicals Management Plan (CMP) (Canada, 2023).

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 screening assessment for these substances was published in the *Canada Gazette*, Part I, on May 13, 2023 (Canada, 2023). Refer to the screening assessment for PHMB for further information.

2.1 Screening Assessment Conclusion

Based on the information available, the screening assessment concludes that PHMB (CAS RNs 32289-58-0 and 27083-27-8) is toxic under paragraph 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 Canada to human life or health (Canada, 2023).

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[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. 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.

The screening assessment also concludes that PHMB meets the persistence criteria but not the bioaccumulation criteria, as defined in the *Persistence and Bioaccumulation Regulations* made under CEPA.

The exposure sources of concern, identified in the 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 that release PHMB to air as a vapour, mist or aerosol, entered the Canadian market. As such, this document focuses on these applications and exposures of greatest concern (refer to section 5).

2.2 Recommendation under CEPA

On the basis of the findings of the screening assessment conducted pursuant to CEPA, the ministers recommend that PHMB be added to Schedule 1 of the Act[4].

The ministers have taken into consideration comments made by stakeholders during the 60-day public comment period on the draft screening assessment for the Other Polymers Group and associated Risk Management Scope for PHMB. As the ministers finalize the recommendation to add PHMB to Schedule 1, risk management instruments will be proposed and finalized within the time frames prescribed in sections 91 and 92 of CEPA.

2.3 Public Comment Period on the Draft Screening Assessment and the Risk Management Scope

The draft screening assessment for the Other Polymers Group and associated Risk Management Scope for PHMB summarizing the proposed risk management options under consideration at that time were published on October 3, 2020 (Canada, 2020a and Canada, 2020b). Interested parties were invited to submit comments on both documents during a 60-day comment period. Comments received on the draft screening assessment and the Risk Management Scope were taken into consideration in the development of this document. A summary of responses to public comments received is available.

[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 substance, 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.

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 PHMB, the proposed objective is to reduce Canadian's dermal and inhalation exposure to PHMB to levels that are protective of human health. 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 levels that are protective of human health;
- to reduce inhalation exposure from cosmetic spray applications available to consumers to levels that are protective of human health; and
- 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.

3.3 Proposed Risk Management Actions under Consideration

To achieve the proposed risk management objectives and to work towards achieving the proposed human health objective, the risk management actions being considered for PHMB are:

- Cosmetics:

  Measures to reduce exposures to PHMB from certain dermally applied cosmetics products, including topical and spray applications, by describing PHMB as a prohibited or restricted ingredient on the Health Canada's Cosmetic Ingredient Hotlist. The Hotlist is used to communicate that certain substances may not comply with requirements of the *Food and Drugs Act* or provisions of the *Cosmetic*

Regulations. More information on the Hotlist consultation process is available.

- Other products available to consumers:

  Applying Significant New Activity (SNAc) provisions under CEPA. These provisions would require any proposed manufacture or import 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. The SNAc provisions do not apply to uses of a substance that are regulated under any act of parliament listed in Schedule 2 or Schedule 4 of CEPA, including but not limited to the *Pest Control Products Act*, the *Fertilizers Act* and the *Feeds Act*.

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 evaluate the effectiveness of the risk management action(s) for PHMB.

[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, 2015a).

[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 (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). The results of performance measurement will help determine if additional risk management or assessment is needed.

The Government of Canada plans to measure the effectiveness of the risk management action by collecting and analyzing data, including data on PHMB prevalence in cosmetics and other products available to consumers in order to measure progress towards meeting the risk management objective.

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.

4. Background

4.1 General Information on PHMB

PHMB is an organic substance that is part of the CMP's Other Polymers Group. The screening assessment identified the substance PHMB as having two equivalent CAS RNs 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 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 issued pursuant to section 71 of CEPA (Canada, 2015b). Total reported imports of PHMB for 2014 were in the range of 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 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 topical use only, up to 0.1%, as a preservative antimicrobial, and is not permitted in sprayable formulations. It is also listed in the Licensed Natural Health Products Database as being present as a non-medicinal ingredient in a

limited number of currently licensed topical and ophthalmic natural health products, such as sunscreens, pain relief ointments, and eye washes (LNHPD [modified 2021], NHPID [modified 2021]). 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, mostly in cosmetics, natural health products, non-prescription drugs, pesticides, fabric softeners, contact lens solutions, and hand washes. The substance is also used to disinfect medical utensils, farm equipment and may be used as a component in sanitizers for disinfecting various surfaces. PHMB is not currently registered as an antimicrobial active ingredient and has not been reported as a formulant in products registered in Canada under the *Pest Control Products Act.*

5. Exposure Sources and Identified Risks

According to notifications submitted under the *Cosmetic Regulations* to Health Canada, PHMB is used in a variety of cosmetics in Canada, such as cleansers, make-up removers, conditioners, moisturizers, shampoos and hair styling products (personal communication, emails from the Consumer and Hazardous Products Safety Directorate, Health Canada, to the New Substances Assessment and Control Bureau, Health Canada; dated June 2017; unreferenced). The data indicate that approximately 1.5% of these products contain PHMB at a concentration of 1% to 3%, while approximately 90% of the products contain a maximum concentration of 0.3%.

Direct exposures from use of cosmetics were evaluated. Product scenarios that result in the highest levels of potential exposure for the 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 screening assessment (Canada, 2023) are dermal sensitization and inhalation toxicity.

In the screening assessment, dermal exposure to PHMB in body moisturizer was identified as a potential concern for skin sensitization. Given the information available, it is concluded that dermal exposure to cosmetics (e.g., body lotion) 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. If PHMB is used in products where it is dispersed into the air or released as a vapour, mist or aerosol, there may be an inhalation risk to human health. A limited number of cosmetic spray applications (e.g., hair detanglers and body mists) containing PHMB have been identified to be

available to Canadians. PHMB 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 is not expected to evaporate from a product.

No current sources of exposure other than cosmetics were identified as a concern in the screening assessment (Canada, 2023). It was found that an analogous substance to PHMB, polyhexamethylene guanidine phosphate, an antimicrobial with similar product applications is suspected to be responsible for serious adverse health effects, including death, 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 for topical use only, up to 0.1%, as preservative antimicrobial, and is not permitted in sprayable formulations (NHPID [modified 2021]);
- *Licensed Natural Health Products Database* – Listed as a non-medicinal ingredient in a limited number of currently licensed topical and ophthalmic

natural health products, such as sunscreens, pain relief ointments, and eye washes (LNHPD [modified 2021]);

- *Internal Drug Product Database* - Listed 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);
- The safety of PHMB used in incidental additives is subject to provisions under paragraph 4(1)(a) of the *Food and Drugs Act*; and
- *Pest Control Product Act* - PHMB is not registered as an antimicrobial active ingredient and has not been reported as a formulant in pest control products registered in Canada (personal communication, email from the Pest Management Regulatory Agency, Health Canada, to the Risk Management Bureau, Health Canada, dated January 2022; unreferenced). PHMB containing products may be subject to registration requirements under the Pest Control Products Act, depending on their use.

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 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 ^{o}F (US eCRF, 2018b).

European Union

- 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.

Australia

- Included in Therapeutic Goods Administration to amend the Poisons Standard to allow the use of PHMB in cosmetic preparations containing

0.3% or less, when packed and labelled for therapeutic use, and in other preparations containing 5% or less (TGA, 2018).

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 Approach or other information that would help to inform decision-making (such as outlined in section 3.2). Please submit additional information and comments prior to July 14, 2023.

Comments and information submissions on the Risk Management Approach 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: substances@ec.gc.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 Risk Management Approach: May 13, 2023 to July 14, 2023.

Publication of responses to public comments on the Risk Management Approach, if applicable and if required, the proposed instruments: At the latest, 24 months 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 months 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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[CIR] Cosmetic Ingredient Review. 2017. Safety assessment of Polyaminopropyl Biguanide as used in cosmetics [PDF]. p. 1-41. [accessed 2018 Aug 17].

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[ECCC] Environment and Climate Change Canada. 2015. Data collected from Follow up on your submission for certain polymers under DSL IU2 (February 2015). Data prepared by ECCC, Health Canada; Existing Substances Program.

[ECHA] European Chemicals Agency. 2017. Registered substances database; search results for CAS RN 55818-57-0. Helsinki (FI): ECHA.

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[SCCS] Scientific Committee on Consumer Safety. 2017. Opinion on Polyaminopropyl Biguanide (PHMB)- Submission III [PDF]- European Commission SCCS/1581/16.

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[TGA] Therapeutic Goods Administration. 2018. PHMB, Department of Health, Australian Government.