Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

PHMB (1600; 1.8)

(polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8)

Product type: 1

ECHA/BPC/058/2015

Adopted

16 June 2015

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Opinion of the Biocidal Products Committee

on the application for approval of the active substance PHMB (1600; 1.8) for product type 1

In accordance with Article 89(1) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products (BPR), the Biocidal Products Committee (BPC) has adopted this opinion on the non-approval in product type 1 of the following active substance:

Common name:	PHMB (1600; 1.8) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8)
Chemical name:	CoPoly(bisiminoimidocarbonyl, hexamethylene hydrochloride), (iminoimidocarbonyl, hexamethylene hydrochloride)
EC No.:	None
CAS No.:	27083-27-8 and 32289-58-0

Existing active substance

This document presents the opinion adopted by the BPC, having regard to the conclusions of the evaluating Competent Authority. The assessment report, as a supporting document to the opinion, contains the detailed grounds for the opinion.

Process for the adoption of BPC opinions

Following the submission of an application by Lonza (previously Arch Chemicals Ltd) on 30 July 2007, the evaluating Competent Authority France submitted an assessment report and the conclusions of its evaluation to the European Chemicals Agency on 5 September 2013. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC and its Working Groups. Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Information on the fulfilment of the conditions for considering the active substance as a candidate for substitution was made publicly available at http://echa.europa.eu/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations on 9 February 2015, in accordance with the requirements of Article 10(3) of Regulation (EU) No 528/2012. Interested third parties were invited to submit relevant information by 10 April 2015.

Adoption of the BPC opinion

Rapporteur: BPC member of France

The BPC opinion on the non-approval of the active substance PHMB (1600; 1.8) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8) in product type 1 was adopted on 16 June 2015.

The BPC opinion takes into account the comments of interested third parties provided in accordance with Article 10(3) of BPR.

The BPC opinion was adopted by consensus.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that the PHMB (1600; 1.8) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8) in product type 1 may not be approved. The detailed grounds for the overall conclusion are described in the assessment report.

2. BPC Opinion

2.1. BPC Conclusions of the evaluation

a) Presentation of the active substance including the classification and labelling of the active substance

This evaluation covers the use of PHMB (1600; 1.8) (polyhexamethylene biguanide hydrochloride which is identified and characterised with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8) in product type 1. PHMB (1600; 1.8) is a polymer that is directly manufactured as an aqueous solution, at a concentration of 20% w/w. Specifications for the reference source are established.

The physico-chemical properties of the active substance as manufactured are deemed acceptable for the appropriate use, storage and transportation of the biocidal product. Not all impurities have been identified or quantified. Validated analytical methods that were required have not been submitted for some impurities and the active substance as well as for the determination of residues in drinking water, body fluids and tissues and food stuff.

A harmonised classification is available and is given below. The current harmonised classification and labelling for PHMB (according to Regulation (EC) No 1272/2008 (CLP Regulation)) is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox 4; H302 Skin Sens. 1B; H317 Eye Dam. 1; H318 Carc. 2; H351 STOT RE 1; H372 (respiratory tract) (Inhalation) Aquatic Acute 1; H400 Aquatic Chronic 1; H410
Labelling	
Pictograms	GHS07, GHS09, GHS05, GHS08
Signal Word	Dgr
Hazard Statement Codes	H302: Harmful if swallowed. H317: May cause an allergic skin reaction. H318: Causes serious eye damage. H351: Suspected of causing cancer. H372 (respiratory tract) (Inhalation): Causes damage to organs through prolonged or repeated exposure by inhalation. H410: Very toxic to aquatic life with long lasting effects.

Specific Concentration limits, M-Factors	M = 10 (acute, chronic)

An opinion of the Risk Assessment Committee (RAC) was adopted in March 2014 for acute toxicity by inhalation:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox 2; H330
Labelling	
Hazard Statement Codes	H330: Fatal if inhaled.

b) Intended use, target species and effectiveness

PHMB (1600; 1.8) is used for hygienic hand wash (PT 1). The representative product contains 0.9% w/w of active substance. The product would be supplied in a container into which a small finger operated pump is integrated. Operating the pump dispenses 3 mL of product directly onto the hand. The hand washing is followed by a rinsing with water.

The product would be used primarily by professional users, but potential use by non-professionals in a domestic setting is also considered.

The lethal action of PHMB (1600; 1.8) is an irreversible loss of essential cellular components as a direct consequence of cytoplasmic membrane damage. It is concluded that cytoplasmic precipitation is a secondary event to the death of the bacterial cell.

The data on PHMB (1600; 1.8) and the representative biocidal product have demonstrated sufficient efficacy against bacteria at the application rate of 3 mL of product containing 0.9% w/w of active substance.

The evaluation of the literature studies provided by the applicant does not show particular resistance to PHMB (1600; 1.8) with bacteria. Nevertheless, cross resistance and modifications of the expression of genes as a mechanism of tolerance to sublethal concentrations of PHMB (1600; 1.8) are described in the literature and should be taken into account, if needed, in a strategy for resistance management at product authorisation stage.

c) Overall conclusion of the evaluation including need for risk management measures

Human health

PHMB (1600; 1.8) is harmful if inhaled and may cause an allergic skin reaction. By inhalation, it causes damage to organs through repeated exposure and is also suspected of causing cancer. It has no irritant properties and is not genotoxic or reprotoxic.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusions**
Hygienic hand wash	*Primary exposure* Dermal exposure 3 mL of product is dispensed onto the hand via a small finger operated pump. The hands are rubbed together and then rinsed with water.	Professionals (10 washes/day)	Acceptable
		General public: toddlers (5 washes/day)	Not acceptable
Toddler mouthing on hands	*Secondary exposure* Oral exposure	General public	Acceptable

The risk related to primary exposure to PHMB (1600; 1.8) is considered as acceptable for professionals.

The risk related to primary exposure for the general public is unacceptable for toddlers. It has to be noted that, in absence of an acceptable dermal absorption study, the dermal absorption taken into account for the assessment (4%) is a default value based on the oral absorption value. In consequence, it is not possible to determine an absorption rate over time (µg/cm^2/min) that would allow to estimate the exposure during washing and after rinsing the hands. Consequently, the exposure is calculated based on the leftover product after rinse only, which underestimates the exposure. Even in this context, the risk for the general public is not acceptable.

The risk related to secondary exposure is considered as acceptable. No combined exposure was estimated considering that the risk related to primary exposure is unacceptable for toddlers.

No risk mitigation measure was envisaged for the general public (such as a restriction to adults) since an unacceptable risk was identified for the environment as well.

Environment

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusions**
Private use of PHMB (1600; 1.8) for hand disinfection based on: - annual tonnage approach - average consumption approach	For all 4 scenarios, the product will ultimately be discharged to drain and will enter a municipal sewage treatment plant (STP). As a result, there will be potential for exposure of both the aquatic (surface water and sediment) and the terrestrial (soil and groundwater) compartments, the latter as a result of contaminated sewage sludge spreading on land.	Not acceptable
Professional use of PHMB (1600; 1.8) for hand disinfection (hospital scenario) based on: - annual tonnage approach - average consumption approach		Not acceptable

The risk assessment was performed applying the consumption approach and tonnage approach. The consumption approach was considered more relevant than the tonnage approach for the risk assessment.

Based on the consumption approach, the risk is acceptable for the terrestrial compartment, groundwater and the STP for private and professional use.

Based on the consumption approach, the risk is unacceptable for sediment when considering private use and for freshwater and sediment when considering professional use. Since for the private use scenario the fraction of inhabitants using the product and the market share of products containing the active substance were already refined compared to default values, it is not realistic to refine the assessment further. Market share was reduced from 0.5 (default value) to 0.2 and the fraction of inhabitants for private use was reduced from 1 to 0.2.

2.2. Exclusion, substitution and POP criteria

2.2.1. Exclusion and substitution criteria

The table below summarises the relevant information with respect to the assessment of exclusion and substitution criteria:

Property		Conclusions
CMR properties	Carcinogenicity (C)	Carc 2
	Mutagenicity (M)	No classification required
	Toxic for reproduction (R)	No classification required
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	P and vP
	Bioaccumulative (B) or very Bioaccumulative (vB)	not B or vB
	Toxic (T)	T
Endocrine disrupting properties	PHMB (1600; 1.8) is not considered to have endocrine disrupting properties.	
Respiratory sensitisation properties	No classification required.	
Concerns linked to critical effects	PHMB (1600; 1.8) does not fulfil criterion (e) of Article 10(1).	
Proportion of non-active isomers or impurities	With regard to the proportion of non-active isomers or impurities, PHMB (1600; 1.8) is put on the market as a 20 % aqueous solution of the active substance which has a minimum purity of 95.6%. Given this, PHMB (1600; 1.8) does not fulfil criterion (f) of Article 10(1).	

Consequently, the following is concluded:

PHMB (1600; 1.8) does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

PHMB (1600; 1.8) meets the conditions laid down in Article 10(1)(d) of Regulation (EU) No 528/2012, and is therefore considered as a candidate for substitution. PHMB (1600; 1.8) fulfils the P, vP and T criteria.

The exclusion and substitution criteria were assessed in line with the "Note on the principles for taking decisions on the approval of active substances under the BPR"[1] and in line with "Further guidance on the application of the substitution criteria set out under Article 10(1) of the BPR"[2] agreed at the 54th and 58th meeting respectively, of the representatives of Member States Competent Authorities for the implementation of Regulation 528/2012 concerning the making available on the market and use of biocidal products. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution criteria is based on Article 10(1)(a, b, d, e and f).

During public consultation, three confidential and eleven non-confidential comments were received from third parties. Comments included information on the availability of alternative active substances, on the essentiality of the active substance PHMB (1600; 1.8) for the control of bacteria, viruses and other pathogens, and on the properties of PHMB (1600; 1.8). There are several other active substances intended for use in the same product type already approved or currently being reviewed under Regulation (EU) No 528/2012.

2.2.2. POP criteria

PHMB (1600; 1.8) does not fulfil criteria for being a persistent organic pollutant (POP). PHMB (1600; 1.8) does not have potential for long-range transboundary atmospheric transport.

2.3. BPC opinion on the application for approval of the active substance PHMB (1600; 1.8) in product type 1

In view of the conclusions of the evaluation, the use of PHMB (1600; 1.8) in hygienic hand wash product gives rise to concerns for human health, when considering primary exposure of the general public, and for the aquatic compartment (including sediment) when considering general public and professional uses.

The overall conclusion from the evaluation of PHMB (1600; 1.8) for use in product type 1 is that biocidal products containing PHMB (1600; 1.8) as an active substance may not be expected to meet the criteria laid down in point (iii) and (iv) of Article 19(1)(b). Subsequently, it is proposed that PHMB (1600; 1.8) shall not be approved and included in the Union list of approved active substances.

According to Article 28(2) of Regulation (EU) No 528/2012, PHMB (1600; 1.8) gives rise to the following concerns: it is classified as skin sensitizer (Skin Sens. 1B), carcinogenic of category 2 (Carc. 2), specific target organ toxicant by repeated exposure by inhalation (STOT RE 1), toxic to aquatic life of acute category 1 (Aquatic Acute 1). In addition, it fulfils the substitution criteria vP and T. Therefore inclusion in Annex I of Regulation (EU) No 528/2012 is not acceptable.

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[1] See document: Note on the principles for taking decisions on the approval of active substances under the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/c41b4ad4-356c-4852-9512-62e72cc919df/CA-March14-Doc.4.1%20-%20Final%20-%20Principles%20for%20substance%20approval.doc).
2 See document: Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/dbac71e3-cd70-4ed7-bd40-fc1cb92cfe1c/CA-Nov14-Doc.4.4%20-%20Final%20-%20Further%20guidance%20on%20Art10(1).doc).