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: 5

ECHA/BPC/123/2016

Adopted

12 October 2016

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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 5

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 approval in product type 5 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 Agency (ECHA) on 23 November 2015. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-17) and its Working Groups (WG III 2016). 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 https://echa.europa.eu/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations/-/substance-rev/12541/term on 22 February 2016 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 21 April 2016.

Adoption of the BPC opinion

Rapporteur: 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 5 was adopted on 12 October 2016.

No comments were received from interested third parties during the public consultation in accordance with Article 10(3) of BPR.

The BPC opinion was adopted by consensus. The opinion is published on the ECHA webpage at:

http://echa.europa.eu/regulations/biocidal-products-regulation/approval-of-active-substances/bpc-opinions-on-active-substance-approval.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that 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 5 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 with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8) in product type 5. PHMB (1600; 1.8) is a polymer that is directly manufactured as an aqueous solution, at a concentration of 20% w/w. PHMB (1600; 1.8) acts by performing a series of cytological and physiological changes which culminate in the death of the cell. Specifications for the reference source are established.

The physico-chemical properties of the active substance as manufactured and biocidal product have been evaluated and are deemed acceptable for the appropriate use, storage and transportation of the active substance and biocidal product.

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 according to Regulation (EC) No 1272/2008 (CLP Regulation) as reported in Regulation (EU) 2016/1179 (9th ATP):

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox 2 Acute Tox 4 Skin Sens. 1B Eye Dam. 1 Carc. 2 STOT RE 1 Aquatic Acute 1 Aquatic Chronic 1
Labelling	
Pictograms	GHS06, GHS09, GHS05, GHS08
Signal Word	Danger
Hazard Statement Codes	H330: Fatal if inhaled 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. H400: Very toxic to aquatic life. H410: Very toxic to aquatic life with long lasting effects.
Specific Concentration limits, M-Factors	M = 10 (acute, chronic)

b) Intended use, target species and effectiveness

PHMB (1600; 1.8) is used for the disinfection of animal drinking water (PT5). It is intended to be used, as a bactericide, for the disinfection of animal drinking water stored in a tank. PHMB (1600; 1.8) is only used by professional users.

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 concentration of 0.008% 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 resistances 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 it is swallowed and fatal if it is inhaled. It may cause an allergic skin reaction and serious eye damage. By inhalation, it causes damage to organs through repeated exposure and is suspected of causing cancer. It has no skin irritant properties and is not genotoxic or reprotoxic.

The table below summarises the exposure scenarios assessed. The conclusions of the scenarios reflect the outcome of both local and systemic risk assessments.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Mixing and loading	*Primary exposure* - Manual pouring of the product into water storage tanks	Professionals	Acceptable with gloves and coverall
Exposure to disinfected water	*Secondary exposure* - Dermal contact with treated drinking water	Professionals	Acceptable
Combined exposure	*Combined exposure* - Manual pouring of the product into water storage tanks and, - Dermal contact with treated drinking water	Professionals	Acceptable with gloves and coverall
Indirect exposure via food and products from animal origin	*Secondary exposure* - Consumption of products from animal origin, considering animals having ingested water treated by PHMB	General public	Not finalised

With regards to systemic effects, for the mixing and loading and exposure to disinfected water risk for professionals are acceptable even without PPE. However, as the representative product is classified as skin senzitiser, acceptable risks for mixing and

loading are only identified when using gloves and protective clothes. No local effects are expected from contact with the treated water, the secondary exposure scenario is acceptable. For combined exposure, risks are acceptable when wearing appropriate ppe during the mixing and loading phase to avoid sensitization.

The preliminary dietary assessment from exposure of food producing animals to PHMB (1600; 1.8) via animal drinking water shows a potential concern for consumers. However, this was based on a guidance under development, based on a worst-case assessment without further possibility for refinement. Until the draft guidance is finalized and further information is provided, the assessment of human exposure via food consumption is considered not finalized, and no conclusion can be drawn.

Assessment of safety for livestock and domestic animals

The table below summarises the exposure scenarios assessed.

Summary table: livestock and domestic animals scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Livestock and domestic animals feed with treated water	*Primary exposure* - Feeding of animals (domestic and livestock) with water treated with PHMB	Animals	Not finalised

In order to assess the risk for livestock and domestic animals exposed to drinking water, a comparision of exposure of animals to the critical NOAEL was performed. In the preliminary assessment, low margins of exposure were observed, which might be a cause for concern. However, in the absence of guidance and further information, the preliminary assessment is considered not finalized and no conclusion can be drawn.

Environment

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Disinfection of animal drinking water	For animal housings where releases to the environment are expected only *via* the manure or slurry, which induces a potential exposure of the terrestrial compartments (soil and groundwater) and surface water and sediment *via* run-off, following the spreading of contaminated slurry/manure on land (arable land or grassland).	Acceptable **only for parent broilers in free range** - **grating floor** when slurry/manure is spread on **arable land only**

	For animal housing where releases to the environment are expected: - *via* the manure or slurry, which induces a potential exposure of the terrestrial compartments (soil and groundwater) and surface water and sediment via run-off, following the spreading of contaminated slurry/manure on land (arable land or grassland), and; - via the STP for the animal housings such as poultries.	Not Acceptable

For animal housings where releases occur via the manure or slurry spreading on soil:

- When manure/slurry is spread on grassland, the use of PHMB based products for disinfection of animal drinking water is not acceptable for aquatic compartment (including sediment) and the soil compartment for all housing types.
- When manure/slurry is spread on arable land, the use of PHMB based products for disinfection of animal drinking water is not acceptable for the soil compartment, except for the housing type "*Parent broilers in free range - grating floor"* for which an acceptable risk for all relevant environmental compartments is identified.

For animal housings where releases occur via waste water and manure or slurry spreading:

- The use of PHMB based products for disinfection of animal drinking water is not acceptable for the soil compartment for all the housing types.

Overall conclusion

A safe use for human health is identified provided adequate ppe is worn. The risk assessments for the general public *via* food consumption and for livestock and domestic animals have to be finalised when appropriate guidance is available. For the environment a safe use is identified for the disinfection of drinking water only for parent broilers in free range - grating floor, when the manure/slurry is spread on arable land whereas an unacceptable risk is identified for spreading on grassland. Consequently, the spreading of manure/slurry will have to be restricted to arable land by introducing a label provision. This risk mitigation measure is considered not feasible for the following reasons:

- in several Member States manure/slurry from farms with different animal categories is collected for further use or treatment. Manure/slurry from parent broilers in free range on a grating floor would have to be separated from other slurries/manures in order to ensure it is not applied on arable land. This separation will lead to a significant increase in costs regarding management of slurry/manure (specific disposal, transport and reuse) at national level.
- in several Member States the quality of manure/slurry is controlled via analytical measurements. The analysis of PHMB as an additional parameter of contamination will lead to a significant increase of the costs for these measurements.

It is concluded that the risks for the environment cannot be mitigated by introducing risk mitigation measures and therefore PHMB shall not be approved for use as a disinfectant in animal drinking water in product type 5.

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	PHMB (1600; 1.8) does not fulfil criterion (a), (b) and (c) of Article 5(1)]
	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	PHMB (1600; 1.8) does not fulfil criterion (e) of Article 5(1) and does fulfil criterion (d) of Article 10(1)
	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. PHMB (1600; 1.8) does not fulfil criterion (d) of Article 5(1).		
Respiratory sensitisation properties	No classification required. PHMB (1600; 1.8) does not fulfil criterion (b) of Article 10(1).		
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% w/w purity. 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) does meet the conditions laid down in Article 10 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

[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)

substitution criteria is based on Article 10(1) (a, b, d, e and f).

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.

2.2.3. Public consultation for potential candidates for substitution

No comments were received from interested third parties during the public consultation in accordance with Article 10(3) of BPR. There are several other active substances intended for use in the same product type currently being reviewed under Regulation (EU) No 528/2012.

2.3. BPC opinion on the application for approval of the active substance PHMB (1600; 1.8) in product type 5

In view of the conclusions of the evaluation it is concluded that biocidal products containing PHMB (1600; 1.8) as an active substance for the use in animal drinking water may not be expected to meet the criteria laid down in point (b) of Article 19(1)(b)(iv). Consequently, it is proposed that PHMB (1600; 1.8) shall not be approved and included in the Union list of approved active substances in product type 5.

PHMB (1600; 1.8) does not fulfil the criteria according to Article 28(2) to enable inclusion in Annex I of Regulation (EU) 528/2012 as PHMB (1600; 1.8) gives rise to the following concerns: it is classified as skin sensitizer (Skin Sens. 1B), carcinogenic 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 criterion of Article 10(1)(d) being P and vP and T.

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