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: 11

ECHA/BPC/064/2015

Adopted

17 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 11

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 11 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 29 October 2008, the evaluating Competent Authority France submitted an assessment report and the conclusions of its evaluation to the European Chemicals Agency on 14 November 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 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 11 was adopted on 17 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 11 may 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 11. 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 the preservation of liquid-cooling and processing systems in closed systems (PT11).

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 (containing 20% w/w of the active substance) have demonstrated sufficient bacteriostatic efficacy for 28 days at the concentration of 0.02% v/v of the product, corresponding to a concentration of 0.004% w/w of the 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.

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 risk assessment is performed at the highest claimed dose of 0.005% w/w of active substance.

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**

Mixing and loading (dosing of closed recirculating cooling systems)	*Primary exposure* Manual pouring/loading: dermal exposure • tier 1: without personal protective equipment (PPE) • tier 2: with gloves and impermeable coveralls Automated loading (pumped transfer): dermal exposure. • without PPE	Industrials and professionals	Acceptable
Post-application	*Primary exposure* Cleaning dispensing pumps: dermal exposure • tier 1: without PPE • tier 2a: with gloves and impermeable coveralls • tier 2b: with gloves and impermeable coveralls and rinse before cleaning Cooling water monitoring: dermal exposure • without PPE	Industrials and professionals	Acceptable
Combined exposure mixing/loading and post-application)	*Primary exposure* Loading, cleaning dispensing pump and monitoring: dermal exposure • manual loading tier 1, post-application tier 1 as described above • manual loading tier 2, post-application tier 2a as described above • manual loading tier 2, post-application tier 2b as described above • automated loading, post-application tier 1 as described above • automated loading, monitoring, cleaning tier 2b as described above	Industrials and professionals	Acceptable
	Secondary exposure Not expected as the system is closed		

The risk is acceptable only when the loading is automated. The risk during the cleaning phase is acceptable only when gloves and impermeable coveralls are worn and the pump is rinsed beforehand. The risk during monitoring is acceptable without personal protective equipment.

No secondary exposure is expected as the system is closed.

Environment

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusions**
Release of PHMB from dosing events. Dosing aims at compensate losses of PHMB from the cooling water. There may be spillage or leaks when dosing the formulation (losses during chemical fill). These are estimated to be 0.5% of the total system volume per dosing event.	For all the scenarios, emissions are discharged to drains and enter a sewage treatment plant (STP). Consequently, 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.	Acceptable
Release of PHMB from design losses. According to ESD for PT11, a loss of around 1% of the total system volume per month is anticipated from an existing system being routinely checked and treated.		Acceptable
Release of PHMB from complete system drainage from the closed recirculating system. This scenario considers complete drainage of the cooling system for maintenance or in case of uncontrolled microbial growth, resulting from lack of a routine monitoring programme.		Acceptable

The risk is acceptable for all compartments when considering the release from dosing events and from design losses.

When considering the phase of complete drainage of the closed recirculating system:

- the risk is acceptable for STP and groundwater;
- the risk is acceptable for freshwater, sediment, and soil only when the cooling system is completely disposed of as hazardous waste (for example draining by specialised companies that disposes the drain liquid via high-temperature incineration).

General conclusion

In conclusion, safe use for human health and the environment is identified when:

- the loading of the product in the closed recirculating system is automated;
- the cleaning is done wearing gloves and impermeable coveralls and when the pump is rinsed beforehand;
- disposal following drainage of the cooling system is handled as hazardous waste.

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 purity of 95.6% w/w. 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 currently being reviewed under Regulation (EU) No 528/2012.

[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).

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 11

In view of the conclusions of the evaluation, it is proposed that PHMB (1600; 1.8) shall be approved and be included in the Union list of approved active substances, subject to the following specific conditions:

1. The active substance as manufactured is an aqueous solution of 20% w/w of PHMB (1600; 1.8). The dry weight specification (calculated) minimum purity of PHMB (1600; 1.8) is 956 g/kg. The maximum content of the relevant impurity hexamethylene-1,6-diamine hydrochloride is 0.4% (w/w).

2. PHMB (1600; 1.8) is considered a candidate for substitution in accordance with Article 10(1)(d) of Regulation (EU) No 528/2012.

3. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

4. For industrial and professional users, safe operational procedures, appropriate organisational and technical risk mitigation measures shall be established. Products shall be used with appropriate personal protective equipment where exposure cannot be reduced to an acceptable level by other means.

5. In view of the risk identified for human health, labels and, where provided, safety data sheets, shall indicate that loading of product into the cooling system shall be automated, that the pump shall be rinsed before cleaning and that appropriate personal protective equipment (gloves and impermeable coveralls) shall be worn during the cleaning phase, unless it can be demonstrated that risks can be reduced to an acceptable level by other means.

6. In view of the risk identified for the environment, labels and, where provided, safety data sheets, shall indicate that disposal following drainage of the closed recirculating system shall be handled as hazardous waste, unless it can be demonstrated at product authorisation that risks to the environment can be reduced to an acceptable level by other means.

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.

2.4. Elements to be taken into account when authorising products

1. The active substance PHMB (1600; 1.8) is considered as a candidate for substitution, and consequently the competent authority shall perform a comparative assessment as part of the evaluation of an application for either national or Union authorisation.

2. The bacteriostatic efficacy of the active substance is demonstrated at the concentration of 0.004% w/w of active substance. At product authorisation stage, efficacy will have to be demonstrated according to the uses claimed.

3. Cross-resistance and tolerance to sublethal concentrations of active substance are described in literature. Therefore, Member States should pay attention to possible occurrence of resistance before authorising products.

2.5. Requirement for further information

Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of PHMB (1600; 1.8). However, further data shall be required as detailed below:

1. Additional information about some impurities, dimers, monomers and the fraction < 1000 Daltons should be provided to the Competent Authority (France) as soon as possible but no later than six months before the date of approval of the active substance.

2. Additional information about (eco)toxicity of some impurities has to be provided to the Competent Authority (France) as soon as possible but no later than six months before the date of approval of the active substance.

3. As PHMB (1600; 1.8) is a polymer, it may be difficult to develop an adequate residue analytical method. A limited residue definition in form of a marker for drinking water, body fluid and tissues has to be provided to the Competent Authority (France) as soon as possible but no later than six months before the date of approval.

4. For drinking water, a validated method for determination of PHMB (1600; 1.8) has to be provided to the Competent Authority (France) as soon as possible no later than six months before the date of approval.

5. An analytical method for determination of PHMB (1600; 1.8) in body fluids and tissues or an acceptable justification of non-submission of data has to be provided to the Competent Authority (France) as soon as possible but no later than six months before the date of approval.

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