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: 6

ECHA/BPC/062/2015

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 6

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 6 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 14 February 2014. 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 6 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 6 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 6. 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 as preservatives for products during storage (PT6). The following uses were claimed when the dossier was submitted by the applicant:

- preservatives for detergents (e.g. wet wipes liquor);
- preservatives for fluids used in paper production (e.g. polymer emulsion);
- preservatives for fluids used in textile production (e.g. polymer emulsion);
- preservatives for leather production (e.g. polymer emulsion);
- preservatives for timber products;
- preservatives for glues and adhesives (e.g. polymer emulsions, wall paper paste).

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 active substance) has demonstrated sufficient efficacy for:

- preservative for detergent (e.g. fabric conditioners) against bacteria, at the concentration of 0.04% w/w of active substance;
- preservative for fluids used in paper, textile and leather production (e.g. polymer emulsion) against bacteria, at the concentration of 0.02% 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 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.

Exposure calculations were performed on the basis of the highest claimed concentration (0.08% w/w a.s. for detergents and 0.06% w/w a.s. for polymer emulsions).

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**
Formulation of product to be preserved			
Formulation of product to be preserved (mixing and loading)	*Primary exposure to the biocidal product* Manual addition of biocidal product into product to be preserved (detergents and polymer emulsions): dermal exposure • tier 1: without personal protective equipment (PPE) • tier 2: with gloves and protective clothes	Industrials/ Professionals	Acceptable
Detergents			
Liquid detergent for laundry washing	*Primary exposure to the preserved liquid detergent* Mixing and loading detergent: without PPE Washing: without PPE • manual wash • machine wash Combined exposure (mixing/loading and washing)	Professionals	Acceptable
		Non-professionals	Acceptable
	Secondary exposure to the preserved liquid detergent Dermal exposure from wearing clothes washed with preserved product	General public	Acceptable
Liquid detergent for cloth pre-treatment	*Primary exposure to the preserved liquid detergent* Use of liquid detergent for cloth pre-treatment: without PPE	Professionals	Acceptable
		Non-professionals	Acceptable
	Secondary exposure to the preserved liquid detergent Dermal exposure from wearing clothes washed with preserved product (same as above)	General public	Acceptable
Liquid detergent for dishwashing (mixing/loading, washing)	*Primary exposure to the preserved liquid detergent* Mixing and loading: without PPE Manual washing: without PPE Combined exposure (mixing/loading and washing)	Professionals	Acceptable
		Non-professionals	Acceptable
	Secondary exposure Dermal exposure from dish/utensils washed with preserved product	General public	Acceptable

Combined scenario (spot pre-treatment, manual laundry washing, manual dishwashing)	*Primary exposure to the preserved liquid detergent* Dermal exposure, as described above	Professionals	Acceptable
		Non-professionals	Acceptable
Liquid detergent for surface cleaning	*Primary exposure to the preserved liquid detergent* Use of liquid detergent for surface cleaning (household): mixing/loading and wiping/mopping hard surfaces such as floors • tier 1: without PPE • tier 2: with gloves (professionals only)	Professionals	Acceptable
		Non-professionals	Acceptable
	Secondary exposure to the preserved liquid detergent Oral and dermal exposure for an infant crawling on surface cleaned with preserved product	General public	Acceptable
Polymer emulsions			
Polymer emulsion in paper industries	*Primary exposure to the preserved polymer emulsion* Formulation of paper pulp: Manual addition of preserved polymer into pulp preparation: dermal exposure Pump cleaning after mixing and loading: dermal exposure • tier 1: without PPE • tier 2: with a previous rinsing	Industrials/ Professionals	Acceptable
	Secondary exposure to the preserved liquid detergent Dermal exposure from handling dry paper	Professionals	Acceptable
	Secondary exposure to the preserved liquid detergent Oral exposure to paper by an infant (ingestion of paper)	General public	Acceptable
Polymer emulsion in textile/leather industries	*Primary exposure to the preserved polymer emulsion* Addition of preserved polymer emulsion in the system: dermal exposure Pump cleaning after mixing and loading: dermal exposure • tier 1: without PPE • tier 2: with a previous rinsing	Industrials/ Professionals	Acceptable

	Secondary exposure to the preserved polymer emulsion Dermal exposure from contact with processed leather • tier 1: without PPE • tier 2: with gloves and impermeable coverall	Professionals	Acceptable
	Secondary exposure to the preserved polymer emulsion Dermal exposure of general public from contact with textile/leather (wear of leather clothes as a worst case)	General public	Not acceptable
Combined indirect exposure via food (detergents and polymer emulsions)			
Combined scenario (indirect exposure via food)	*Secondary exposure to the preserved detergents and polymer emulsions* Combined exposure to food in contact with dish/utensils cleaned with preserved product, to food in contact with surface cleaned with preserved product and to food in contact with paper	General public	Acceptable

– Formulation of preserved products:

For the formulation of preserved products, the risk is acceptable with the wear of gloves and coverall.

– Leather/textile:

Leather was considered as a worst case for this use. The risk related to secondary exposure to the active substance in leather is acceptable for professionals handling freshly processed leather, with the wear of gloves and impermeable coverall.

The risk related to dermal contact with leather (e.g. clothes) is unacceptable for the general public, even when considering the lowest efficacious concentration (0.02%). It has to be noted that this assessment is a worst case that should be refined if further data are available.

– Paper:

The risks are acceptable when considering the secondary exposure of professionals handling processed (dry) paper, the ingestion of paper by an infant and the exposure via food in contact with wrapping paper.

– Detergents:

The risks are acceptable for professionals and non-professionals when using preserved detergent without PPE, for manual laundry washing, manual dishwashing, spot pre-treatment of clothes, separately and combined. It is also acceptable without PPE for the use of preserved surface cleaner.

The risks are acceptable when considering the dermal contact with residues on dish/utensils and surfaces cleaned with preserved detergent, the wear of clothes washed with preserved detergent, and the exposure via food in contact with residues of the active substance on dish/utensils and surfaces cleaned with preserved detergent.

Environment

Exposure calculations were performed on the basis of the efficient concentration (0.04% w/w a.s. for detergents and 0.02% w/w a.s. for polymer emulsions).

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusions**
Scenario 1: **detergents** (liquid fabric softeners, dishwashing detergents, liquid laundry detergents, liquid soaps and hand cleaners, and surfactants used to formulate such products). Exposure and risk were assessed considering tonnage and consumption approaches for the formulation phase (professional); the use phase (professional and amateur) and aggregated uses.	In all cases, the STP is the primary compartment of exposure for the proposed uses. As a result of this, there will be a potential for exposure of STP and 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
Scenario 2: **pulp and paper additives** (water-soluble and water-dispersed pulp and paper additives in storage containers before use). Exposure and risk were assessed considering the consumption approach for newsprint; printing and writing paper; tissue paper; and mill producing all type of paper.		Not acceptable
Scenario 3: **textile additives** (water-soluble and water-dispersed textile additives in storage containers before use). Exposure and risk were assessed considering the consumption approach for pre-treatment phase; exhaust process; padding, printing, and coating processes and whole textile production.		Not acceptable
Scenario 4: **leather additives** (water-soluble and water-dispersed leather additives in storage containers before use). Exposure and risk were assessed considering the consumption approach for raw hide treatment; pelt treatment; shaved treatment; crust leather treatment and whole leather production process.		Not acceptable except for preservation of additives for crust leather treatment
Scenario 5: **wide-dispersive use** taking into account the total tonnage claimed for PT6 (cumulative assessment).		Not acceptable

Based on the consumption approach:

- for the preservations of detergents, the risk is considered unacceptable for the aquatic compartment (including sediment) both for professional and amateur uses;

- for the preservation of pulp and paper treatment additives, the risk is considered unacceptable for the aquatic compartment (including sediment);

- for the preservation of textile treatment additives, the risk is considered unacceptable for the aquatic compartment (including sediment) for all types of use, and for the terrestrial compartment except for the use in additives for textile exhaust process;

- for leather processing fluids, the risk assessment is considered acceptable for the aquatic compartment (including sediment) and for terrestrial compartment only if PHMB (1600; 1.8) is used in additives for crust leather treatment, corresponding to the skin type at the finishing process; the risk is considered unacceptable for the other sub-uses.

Based on the tonnage approach:

- for the preservation of detergents, the risk is considered unacceptable for the sediment compartment for the formulation phase, the professional use and the total use (professional and amateur) of detergents;

- when a wide dispersive use scenario is applied considering the global tonnage for PHMB (1600; 1.8) as PT06, the risk is unacceptable for the sediment compartment.

General conclusion

It is concluded that risks are acceptable for human health except for the preservation of leather additives. It is also concluded that risks are unacceptable for the environment taking into account the total tonnage claimed for PT6 (cumulative exposure for wide-dispersive use). Regarding the preservation of leather additives, in particular, the conclusion is based on the 3 following considerations:

- the secondary exposure for general public is unacceptable;
- one very minor use only is acceptable for the environment (crust leather treatment phase), based on the consumption approach;
- cumulative assessment for the environment based on wide-dispersive use leads to unacceptable risks.

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% 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 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 6

In view of the conclusions of the evaluation, the use of PHMB (1600; 1.8) as preservatives

[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).

for products during storage gives rise to concerns for human health, when considering the secondary exposure of the general public from uses in the preservation of leather additives, and for the aquatic compartment (including sediment) and terrestrial compartment.

The overall conclusion from the evaluation of PHMB (1600; 1.8) for use in product type 6 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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