

Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

PHMB (1415; 4.7)

Polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1415 and a mean polydispersity (PDI) of 4.7)

Product type: 6

ECHA/BPC/174/2017

Adopted

4 October 2017

Opinion of the Biocidal Products Committee

on the application for approval of the active substance PHMB (1415; 4.7) for product type PT6

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 (1415; 4.7) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1415 and a mean polydispersity (PDI) of 4.7)
Chemical name:	CoPoly(bisiminoimidocarbonyl, hexamethylene hydrochloride), (iminoimidocarbonyl, hexamethylene hydrochloride)
EC No.:	None
CAS No.:	32289-58-0 and 1802181-67-4
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 Laboratoire PAREVA on July 2007, the evaluating Competent Authority France submitted an assessment report and the conclusions of its evaluation to the European Chemicals Agency on December 2016. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-22) and its Working Groups (WG III 2017). 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/fr/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations/-/substance-rev/15711/term> on 12 February 2017, 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 2017.

Adoption of the BPC opinion

Rapporteur: France

The BPC opinion on the non-approval of the active substance PHMB (1415; 4.7) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1415 and a mean polydispersity (PDI) of 4.7) in product type 6 was adopted on 4 October 2017.

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. 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 PHMB (1415; 4.7) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1415 and a mean polydispersity (PDI) of 4.7) 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 (1415; 4.7) (polyhexamethylene biguanide hydrochloride which is identified and characterised with a mean number-average molecular weight (Mn) of 1415 and a mean polydispersity (PDI) of 4.7) in product type number 6. PHMB (1415; 4.7) is a polymer that is directly manufactured as an aqueous solution, at a concentration of 20% w/w. PHMB (1415; 4.7) 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 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) for PHMB:

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	
Pictogram codes	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): 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)

This CLP entry for PHMB lists the CAS numbers 32289-58-0 and 27083-27-8. These CAS numbers originate from the already approved PHMB (1600; 1.8) (Regulation (EU) No 2016/125). The conclusion of the evaluating Competent Authority (France) is that this classification – as presented in the table - covers also PHMB (1451; 4.7). A CLH dossier will therefore be submitted to ECHA by the evaluating Competent Authority (France).

b) Intended use, target species and effectiveness

PHMB (1415; 4.7) is intended to be used as an antimicrobial preservative for aqueous manufactured products in cans, tanks or other closed containers during storage. PHMB (1415; 4.7) is used as preservative by professional users against potentially harmful and spoilage microorganisms (bacteria and yeasts).

The representative product is intended to be used as a preservative for detergents used in many applications, as liquid for dishwashing.

The lethal action of PHMB (1415; 4.7) 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 (1415; 4.7) and the representative biocidal product have demonstrated sufficient efficacy against bacteria and yeast at the concentration of 0.06% w/w of active substance.

The evaluation of the literature studies provided by the applicant does not show particular resistance to PHMB (1415; 4.7) with bacteria, fungi and yeasts. Nevertheless, cross resistance and modifications of the expression of genes as a mechanism of tolerance to sublethal concentrations of PHMB (1415; 4.7) 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 (1415; 4.7) 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	Conclusion
Formulation of product to be preserved			
Formulation of product to be preserved (mixing and loading)	<i>Primary exposure</i> Dermal exposure during manual addition of biocidal product into product to be preserved (liquid detergents)	Professionals	Acceptable with gloves and protection clothes
Use of liquid detergents			
Liquid detergent for hand wash laundry	<i>Primary exposure</i> Dermal exposure Mixing and loading detergent	Professionals	Acceptable
		Non-professionals	Acceptable
	<i>Primary exposure</i> Dermal exposure Application phase : hand washing	Professionals	Not acceptable
		Non-professionals	Acceptable
	<i>Secondary exposure</i> Dermal exposure from wearing clothes washed with preserved product	General public	Not acceptable
Liquid detergent for pre-treatment of clothes	<i>Primary exposure</i> Dermal exposure Application as spot removers	Professionals	Acceptable
		Non-professionals	Acceptable
Liquid detergent for hand dishwashing	<i>Primary exposure</i> Dermal exposure Mixing and loading the detergent	Professionals	Acceptable
		Non-professionals	Acceptable
	<i>Primary exposure</i> Dermal exposure Application phase : hand dishwashing	Professionals	Acceptable
		Non-professionals	Acceptable
	<i>Primary exposure</i> Combined exposure (mixing/loading and hand dishwashing)	Professionals	Acceptable
		Non-professionals	Acceptable
<i>Secondary exposure</i> Dermal exposure from dish/ustensils washed with preserved product	General public	Acceptable	
Liquid detergent for surface cleaning	<i>Primary exposure</i> Dermal exposure - Mixing and loading detergent - Hard surface disinfection by mopping or wiping	Professionals	Not acceptable

		Non-professionals	Not acceptable
	<i>Secondary exposure</i> Oral and dermal exposure for an infant crawling on surface cleaned with preserved product and ingesting product via hand to mouth transfer	General public	Not acceptable
Indirect exposure via food			
Indirect exposure via food	<i>Secondary exposure</i> Indirect exposure via food in contact with dish/utensils cleaned with preserved product, to food in contact with surface cleaned with preserved product	General public	Not finalised

Formulation of preserved products

For the formulation of preserved products, the risk is acceptable when gloves and coverall are worn.

Liquid detergents

Considering systemic effects for primary exposure, the risk is considered acceptable for professionals and non-professionals when using preserved detergent without PPE for spot pre-treatment of clothes and for manual dishwashing and combined tasks. Risk is also acceptable for non-professional use as hand wash laundry.

The risk is not considered acceptable for the use as surface disinfection with preserved product by professional and non-professional users.

Considering systemic effects for secondary exposure, the risk is acceptable when considering the dermal contact with residues on dish/utensils. However, the risk is unacceptable regarding dermal contact with surfaces cleaned with preserved detergent and the wear of clothes washed with preserved detergent.

A preliminary assessment of indirect exposure via food contaminated by the active substance from treated dishware and cleaned surfaces has been performed and shows acceptable risks for consumers. As currently no guidance is available, acceptable risk related to food consumption after dish washing or after disinfection of surfaces via mopping/wiping has to be confirmed at product authorisation stage.

Environment

PHMB (1415; 4.7) is a persistent substance regarding the results of degradation studies in soil and water/sediment compartments. This substance has high adsorption properties. Nevertheless, PHMB (1415; 4.7) shows no potential for bioaccumulation. It is classified as very toxic to aquatic life and can cause long lasting effects.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	Description of scenario including environmental compartments	Conclusion
Formulation phase considering tonnage approach	<p>In all cases, the STP is the primary compartment of exposure for the proposed uses.</p> <p>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.</p>	Not acceptable
Application phase of detergent for professional uses considering consumption approach or tonnage approach		Not acceptable
Application phase of detergent for non-professional uses considering consumption approach or tonnage approach		Not acceptable
Application phase of detergent when cumulating the professional and non-professional uses considering consumption approach		Not acceptable

In conclusion for all scenarios, the risk for at least one environmental relevant compartment is considered not acceptable.

Overall conclusion

When considering both human health and environment, no safe use is identified for use of PHMB (1415; 4.7) as preservative of detergents.

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 (1415; 4.7) 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)	vP	PHMB (1415; 4.7) 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	No classification required. PHMB (1415; 4.7) does not fulfil criterion (b) of Article 10(1).		
Respiratory sensitisation properties	Not considered to have endocrine disrupting properties. PHMB (1415; 4.7) does not fulfil criterion (d) of Article 5(1).		
Concerns linked to critical effects	PHMB (1415; 4.7) does not fulfil criterion (e) of Article 10(1).		
Proportion of non-active isomers or impurities	Not relevant. PHMB (1415; 4.7) does not fulfil criterion (f) of Article 10(1).		

Consequently, the following is concluded:

PHMB (1415; 4.7) does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

PHMB (1415; 4.7) 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 (1415; 4.7) fulfils the 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

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](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))

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).

2.2.2. POP criteria

PHMB (1415; 4.7) does not fulfil criteria for being a persistent organic pollutant (POP). PHMB (1415; 4.7) does not have potential for long-range transboundary atmospheric transport.

2.2.3. Public consultation for potential candidates for substitution

As PHMB (1415; 4.7) is considered a candidate for substitution, ECHA launched the public consultation in accordance with Article 10(3) of Regulation (EU) No 528/2012. The public consultation took place from 10/02/2017 to 10/04/2017. Six contributions were submitted: three by individual companies and three by the applicant.

In the three industry contributions and the three applicant contributions, information is submitted on the importance of the active substance compared to possible alternatives such as chlorine or alcohol based products and quaternary ammonium compounds:

- First, regarding the efficacy, it is stated that these alternative substances have no bacteriostatic properties and lose their effectiveness too quickly. PHMB (1415; 4.7) has a powerful broad-spectrum microbicide; it is claimed effective against gram-positive and gram-negative bacteria, highly effective against algae, and effective in slightly acidic or alkaline environments. The efficacy is also claimed even in hard water and in presence of organic matter.
- Second, regarding the chemical hazard profile, the quaternary ammonium compounds have foaming properties, and present problem such as stability over large pH range, stability in the long term, to high temperature, sunlight, flammability, compatibility, corrosivity, generation of by-products (chloramines), risk of violent chemical reaction, pH dependence, and sensibility to organic matter.
- Third, regarding the conditions of use, it is also stated that the possible alternative solutions with other biocide active substances do not meet all the benefits provided by PHMB (1415; 4.7):
 - a) PHMB (1415; 4.7) has to be dosed only once a year when used as an "overwintering agent" for public and private swimming pools;
 - b) The effectiveness range of PHMB (1415; 4.7) is 5-6 months in swimming pool water;
 - c) PHMB (1415; 4.7) has no degreasing effect on skin and mucous membranes;
 - d) PHMB (1415; 4.7) disintegrated in swimming pool water after 5-6 months, so that the basin water can be drained into the canalisation;
 - e) 1L of undiluted PHMB (1415; 4.7) based product treats 50m³ of water;
 - f) PHMB (1415; 4.7) based products are tasteless, odourless and non-foaming.

Several other active substances are already approved for PT 6 with intended uses similar to PHMB (1415; 4.7). The evaluation performed on PHMB (1415; 4.7) does not confirm the statements and information provided during the public consultation. It is noted that the information provided during the public consultation has not been peer reviewed.

It is therefore concluded that based on the information provided and the assessment performed, other chemical alternatives which would provide a significant lower risk profile compared to PHMB (1415; 4.7) in the field of intended uses which has been assessed could be identified. The following active substances are approved for PT 6 and are not candidates for substitution: biphenyl-2-ol, C(M)IT/MIT, chlorocresol (CMK), DBDCB, folpet, hydrogen peroxide, MBIT and peracetic acid.

2.2. BPC opinion on the application for approval of the active substance PHMB (1415; 4.7) in product type PT6

In view of the conclusions of the evaluation, it is concluded that biocidal products containing PHMB (1415; 4.7) as an active substance for the use as a preservative for aqueous manufactured products in cans, tanks or other closed containers during storage 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 (1415; 4.7) shall not be approved and included in the Union list of approved active substances in product type 6.

PHMB (1415; 4.7) does not fulfil the criteria according to Article 28(2) to enable inclusion in Annex I of Regulation (EU) 528/2012 as PHMB (1415; 4.7) 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 vP and T.

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