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: 1

ECHA/BPC/170/2017

Adopted

4 October 2017

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Opinion of the Biocidal Products Committee

on the application for approval of the active substance PHMB (1415; 4.7) for product type PT1

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 (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 1 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 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 (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 1. 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 for 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 used for hygienic hand wash (PT 1). The representative product contains 0.4% w/w of active substance. The product would be supplied in a container into which a small finger operated pump is integrated. After cleaning, the hands are rinsed and dried.

The product would be used by professional and non-professional users.

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 at the application rate of 5 mL of product containing 0.4% w/w of active substance and a contact time of 30 seconds.

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**
Hygienic hand wash	*Primary exposure* Dermal exposure 5 mL of product is dispensed onto the hand via a small finger operated pump. The hands are rubbed together, then rinsed with water and dried.	Professionals (10 washes/day)	Not acceptable
		Non-professionals (5 washes/day)	Not acceptable
Toddler mouthing on hands	*Secondary exposure* Oral exposure	General public	Not acceptable

With regards to systemic effects, the risk related to primary exposure to PHMB (1415; 4.7) is considered as unacceptable for professional users and non-professionals (adults and toddlers).

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

Residues in food from the intended professional use of PHMB in PT 1 biocidal products are not expected. Nevertheless, regarding non-professional use, no indirect exposure via food assessment was performed.

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**
Professional use of PHMB (1415; 4.7) 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
Private use of PHMB (1415; 4.7) for hand disinfection 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 groundwater and the STP for private and professional use.

Based on the consumption approach, the risk is unacceptable for sediment, soil and surface water when considering private and professional uses.

Overall conclusion

No safe use was identified either for human health or environment for scenarios considering the use of the biocidal product for hygienic hand wash by professional and non-professionel users.

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 (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 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;

[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)

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) 1 L of undiluted PHMB (1415; 4.7) based product treats 50 m^3 of water;
f) PHMB (1415; 4.7) based products are tasteless, odourless and non-foaming.

Several other active substances are already approved for PT 1 with intended uses similar to PHMB (1415; 4.7). The evaluation performed on PHMB (1415; 4.7) does not confirm the above 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 1 and are not candidates for substitution: active chlorine released from sodium hypochlorite, biphenyl-2-ol, chlorocresol (CMK), hydrogen peroxide, L(+) lactic acid, peracetic acid, propan-1-ol and propan-2-ol.

2.3. BPC opinion on the application for approval of the active substance PHMB (1415; 4.7) in product type PT1

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 hygienic hand wash 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 1.

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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