

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: 5

ECHA/BPC/173/2017

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 PT5

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 5 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 5 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 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 (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 5. 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 used for the disinfection of animal drinking water (PT 5). It is intended to be used, as bactericide and yeasticide, for the disinfection of animal drinking water stored in a tank. PHMB (1415; 4.7) is only used by 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 and yeast at the concentration of 0.04% 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. 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	<i>Primary exposure</i> Dermal exposure Manual pouring of the product into water storage tanks	Professionals	Acceptable with goggles*
Exposure to disinfected water	<i>Secondary exposure</i> Dermal contact with treated drinking water	Professionals	Not acceptable
Indirect exposure via food and products from animal origin	<i>Secondary exposure</i> Consumption of products from animal origin, considering animals having ingested water treated by PHMB	General public	Not finalised

*goggles are necessary when considering local risks

With regards to systemic effects, the risk related to the mixing and loading phase is acceptable without personal protective equipment. However, as the representative product is classified for eye irritation, acceptable risk for mixing and loading is only identified when wearing goggles and applying appropriate risk mitigation measures.

Considering the secondary exposure, the risk for professionals having contact with treated water is acceptable only with the wearing of gloves. Nevertheless, as there is a doubt regarding the relevance and the applicability of such risk mitigation measure, risk is considered unacceptable. No local effects are expected from contact with the treated water.

The preliminary dietary assessment from exposure of food producing animals to PHMB (1415; 4.7) 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 finalised and further information is provided, the assessment of human exposure via food consumption is considered not finalised, and no conclusions 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	<i>Primary exposure</i> 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 treated with PHMB (1415; 4.7), a comparison 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 finalised and no conclusion can be drawn.

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
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).	Not acceptable
	For animal housing where releases to the environment are expected 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:

Either manure/slurry is spread on grassland or arable land, 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.

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 aquatic compartment (including sediment) and the soil compartment for all the housing types when considering releases via waster water.

Overall conclusion

No safe use for human health is identified. It is concluded that the risks for human health cannot be mitigated by introducing risk mitigation measures. 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, no safe use is identified for the disinfection of drinking water intended to feed animals.

When considering both human health and environment, no safe use is identified for use of PHMB (1415; 4.7) for the disinfection of drinking water intended to feed animals.

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

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>)

the BPR² 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;
 - 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 5 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.

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))

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 5 and are not candidates for substitution: active chlorine released from sodium hypochlorite, active chlorine released from calcium hypochlorite, active chlorine released from chlorine, hydrogen peroxide and peracetic acid.

2.3. BPC opinion on the application for approval of the active substance PHMB (1415; 4.7) in product type PT5

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 disinfection for 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 (1415; 4.7) shall not be approved and included in the Union list of approved active substances in product type 5.

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.