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: 2

ECHA/BPC/171/2017

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 PT2

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 2 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 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 2 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 2 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 (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 2. 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 equipment and areas (PT2). A risk assessment was conducted for the following uses:

- Disinfection of surface by mopping or wiping (professional and non-professional uses),
- Disinfection of surface using ready to use trigger spray (only professional uses),
- Disinfection of surface by wiping using impregnated wipes (only professional uses),
- Disinfection of small object by dipping (professional and non-professional uses),
- Disinfection with cleaning in place system (only professional uses).

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 yeasts at the concentration of 0.03% w/w active substance for disinfection of hard surfaces by soaking in disinfection solutions or applied for Cleaning-in-Place (CIP) systems and at the concentration of 0.016% w/w active substance for ready to use application.

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 asssessments.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Surface disinfection by mopping	*Primary exposure* Dermal exposure - Mixing and loading of product with water, - Application of the product by mopping	Professionals	Acceptable with goggles* and gloves
		Non-professionals	Not acceptable
Surface disinfection by wiping	*Primary exposure* Dermal exposure - Mixing and loading of product with water, - Application of the product by wiping	Professionals	Not acceptable
		Non-professionals	Not acceptable
Small surface disinfection by trigger spray	*Primary exposure* Dermal and inhalation exposure - Spraying of ready-to-use product using a trigger spray - Wiping of the sprayed product on surface to disinfect	Professionals	Not finalised**
Small surface disinfection by impregnated wipes	*Primary exposure* Dermal exposure - Application of the product by wiping by using impregnated wipes	Professionals	Acceptable
Disinfection by dipping of small objects	*Primary exposure* Dermal exposure - Mixing and loading of product with water, - Application by dipping of objects in the solution	Professionals	Acceptable with goggles*, gloves and coverall
		Non-professionals	Not acceptable
Disinfection with cleaning in place system (CIP)	*Primary exposure* Dermal exposure - Mixing and loading of product in the CIP system,	Professionals	Acceptable with goggles*

Surface disinfection by mopping or wipping	*Secondary exposure* Dermal exposure - Exposure to disinfected surfaces	General public	Not acceptable
Small surface disinfection by impregnated wipe	*Secondary exposure* Dermal exposure - Exposure to dried small surfaces only	General public	Acceptable (only after drying of the treated surface)
Disinfection by dipping of small objects	*Secondary exposure* Dermal exposure - Exposure to dried small objects only	General public	Acceptable (only after drying of the treated object)
Disinfection with cleaning in place system (CIP)	*Secondary exposure* Dermal exposure - Exposure to surfaces	General public	Acceptable
Toddler crawling on disinfected surface (relevant for surface application only)	*Secondary exposure* Dermal and oral exposure - Exposure of toddler crawling on disinfected surface with a hand to mouth transfer	General public (toddlers)	Not acceptable (Acceptable only when access to treated aera is restricted)

* goggles are necessary when considering local risks
** as local risk assessment cannot be performed

Systemic effects:

With regards to systemic effects, the risk related to primary exposure to PHMB (1415; 4.7) is considered as acceptable for **professional users** during:

- mopping when gloves are worn,
- spraying with trigger spray gloves are worn
- dipping of small objects when gloves and coverall are worn.
- wiping with impregnated wipes without wearing protective equipement,
- disinfection with cleaning in place system without wearing protective equipement.

Disinfection by wiping leads to unacceptable risks.

Risks related to surface disinfection and dipping of small objects are considered unacceptable for **non-professional users**.

The risk related to secondary exposure is considered acceptable regarding the exposure to disinfected areas only for small surfaced totally dried for CIP, dipping of small object and trigger spray applications.

A small surface should be regarded as a potential dermal contact aera of 0.12 m^2 within a day when considering disinfection of small objects by dipping or disinfection via CIP, and of 0.19 m^2 within a day when considering disinfection by impreniated wipes.

The risk is also considered as unacceptable for toddlers crawling on surface disinfected by trigger spray application, impregnated wiping or wiping/mopping. In consequence, the use of biocidal products containing the active substance should be restricted to areas not accessible to toddlers.

Local effects:

Regarding local effects, only mixing and loading phases and trigger spray application were considered relevant in the assessment. Risks are acceptable for mixing and loading phase while using goggles and appropriated risk mitigation measures. Risk cannot be assessed due to a lack of appropriate data for trigger spray application and thus risk is considered unacceptable at this 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**
Disinfection of surfaces used in institutional areas by professional users based on tonnage approach	PHMB will ultimately be discharged to drains and will enter a municipal STP. As a result of this, 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
Disinfection of surfaces for sanitary purposes in hospitals by professional users based on: - consumption approach - tonnage approach		Not acceptable
Disinfection of surfaces for sanitary purposes by non-professional users based on: - consumption approach - tonnage approach		Not acceptable
Disinfection of scopes and other articles in washers/disinfectors		Not acceptable
Disinfection of medical equipment by dipping		Not acceptable
Disinfection in industrial aeras		Not acceptable
Small scale disinfection in institutional areas using ready to use applications		Acceptable

The risk for the environment is considered as unacceptable for the aquatic compartement (including sediment) and the terrestrial compartment for all assessed uses except for ready-to-use impregnated wipes for small scale disinfection in institutional areas. For the latter, risk is acceptable for all environmental compartments.

Overall conclusion

A safe use for human health and the environment is identified only for small scale surface disinfection by professional users using ready-to-use impregnated wipes in areas not accessible to toddlers.

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;
  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.

[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)

Several other active substances are already approved for PT 2 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 2 and are not candidates for substitution: active chlorine released from sodium hypochlorite, active chlorine released from calcium hypochlorite, active chlorine released from chlorine, ampholyt, biphenyl-2-ol, burnt dolomitic lime, burnt lime, C(M)IT/MIT, chlorocresol (CMK), citric acid, hydrated dolomitic lime, hydrated lime, hydrogen peroxide, L(+) lactic acid, peracetic acid, peeracetic generated from TAED and sodium percarbonate, 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 PT2

In view of the conclusions of the evaluation, it is proposed that PHMB (1415; 4.7) 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 (1415; 4.7). The minimum purity of PHMB (1415; 4.7) is 943 g/kg on a dry weight basis.

2. PHMB (1415; 4.7) is considered a candidate for substitution in accordance with Article 10(1)(d) of Regulation (EU) No 528/2012.

3. The authorisations of biocidal products are subject to the following condition(s):

    a. 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.

    b. In view of the risks identified for the uses assessed, the product assessment shall pay particular attention to:

        i. Professional users;

        ii. Non professional users;

        iii. General public;

        iv. Toddlers;

        v. Environment: surface water, sediment and soil.

4. The person responsible for the placing on the market of a treated article treated with or incorporating the active substance PHMB (1415; 4.7) shall ensure that the label of that treated article provides the information listed in the second subparagraph of Article 58(3) of the Regulation (EU) No 528/2012.

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.

2.4. Elements to be taken into account when authorising products

1. The active substance PHMB (1415; 4.7) 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 following recommendations and risk mitigation measures have been identified for the uses assessed. Authorities should consider these risk mitigation measures when authorising products, together with possible other risk mitigation measures, and decide whether these measures are applicable for the concerned product:

    a. If an unacceptable risk is identified for professional users, safe operational procedures and appropriate organizational 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.

    b. An unacceptable risk for professionals when considering surface disinfection by wiping or when considering small surface disinfection by trigger spray is identified. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, these uses should not be authorised.

    c. An unacceptable risk for non-professionals when considering surface disinfection by wiping or mopping or when considering disinfection of small objects by dipping is identified. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, these uses should not be authorised.

    d. An unacceptable risk for the general public when considering surface disinfection by wiping or mopping is identified. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, these uses should not be authorised.

    e. An unacceptable risk for the general public in contact with wet cleaned surface when considering small surface disinfection by impregnated wipes is identified. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures, i.e. by restricting the access of the general public to dried surface only or by other means, this use should not be authorised.

    f. An unacceptable risk for toddlers crawling on surfaces cleaned with the biocidal product is identified. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures, e.g. labels, and where provided, safety data sheets, should indicate that the products shall be restricted to areas not accessible to toddlers, or by other means, these uses should not be authorised.

    g. An unacceptable risk for the environment when considering article/equipment disinfection or surface disinfection, except small surface disinfection in institutional areas using ready to use applications is identified. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, these uses should not be authorised.

    h. An assessment of the risk in food and feed areas may be required at product authorisation where use of the product may lead to contamination of food and feeding stuffs.

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 (1415; 4.7). However, further data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (France).

- For confirming that all impurities have a similar (eco) toxicological profile, in the form of QSAR/expert statement to justify the pooling of the impurities in the reference specifications.
- Validation of the methods for the determination of most of the impurities of the active substance.
- A validated method for determination of the active substance in drinking water.
- A validated method for determination of residue of the active substance in body fluid or an acceptable justification of non-submission.
- An analytical method for determination of the active substance in food and feeding stuffs or an acceptable justification of non-submission.

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