Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1)

Product type: 11

ECHA/BPC/163/2017

Adopted

29 June 2017

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

Opinion of the Biocidal Products Committee

on the application for approval of the active substance Reaction products of para-formaldehyde and 2-hydroxypropylamine (ratio 1:1) for product type 11

In accordance with Article 90(2) 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 11 of the following active substance:

Common name:	**Formaldehyde released from the reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1);** **RP 1:1**
Chemical name(s):	**Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 1.1)**
EC No.:	**not applicable**
CAS No.:	**not applicable**
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 Task Force Lubrizol Deutschland GmbH and Schülke & Mayr GmbH. on 31 October 2008, the evaluating Competent Authority Austria submitted an assessment report and the conclusions of its evaluation to the Commission on 29 September 2016. 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 https://www.echa.europa.eu/web/guest/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations/-/substance-rev/5401/term%20on%209th%20February%202015 on 04 November 2016 , in accordance with the requirements of Article 10(3) of the BPR. Interested third parties were invited to submit relevant information by 3 January 2017.

Adoption of the BPC opinion

Rapporteur: Austria

The BPC opinion on the approval of the active substance reaction products of paraformaldehyde and 2-hydroxy-propylamine (ratio 1:1) in product type 11 was adopted on 29 June 2017.

The BPC opinion takes into account the comments of interested third parties provided in accordance with Article 10(3) of the 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

Since RP 1:1 fulfils the criteria set in Article 5(1) of Regulation (EU) No 528/2012, the overall conclusion of the BPC is that RP 1:1 in product type 11 should normally not be approved, unless one of the conditions for derogation in Article 5(2) is met. The process related to the demonstration of whether the conditions for derogation set in Article 5(2) are met, is not in the remit of the BPC[1]. 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 Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1), furthermore addressed as RP 1:1 in product type 11. RP 1:1 was originally notified as α,α',α''-trimethyl-1,3,5-triazine-1,3,5(2H,4H,6H)-triethanol or HPT[2]. RP 1:1 is a formaldehyde-releaser. 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 and materials suitable for storage and transport of the active substance and biocidal product. Regarding the explosive properties the justification for non submission of data has not been accepted. An experimental test has to be conducted as the substance contains of unknown constituents and therefore the waiving cannot be justified by structural considerations.

Validated analytical methods are available for the active substance as manufactured and for the relevant and significant impurities. With regard to the methods submitted for determination of the hydroliysis product 2-hydroxypropylamin in water and soil the data has been considered as not sufficient.

The classification and labelling for RP 1:1 according to Regulation (EC) No 1272/2008 (CLP Regulation) as agreed by RAC-35 (December 2015) and published in Regulation (EC) No 2017/776 (10th adaption to technical progress):

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 4, H302 Acute Tox. 4, H332 Skin Corr. 1C, H314 Eye Dam. 1, H318 Skin Sens. 1A, H317 STOT RE 2, H373 Muta 2, H341* Carc. 1B, H350** Aquatic Chronic 2, H411
	* The classification as a mutagen need not apply if it can be shown that the maximum theoretical concentration of releasable formaldehyde, irrespective of the source, in the mixture as placed on the market is less than 1%.

[1] See document: Further guidance on the procedures related to the examination of the exclusion criteria and the conditions for derogation under Article 5(2) (CA-Nov14-Doc.4.5-Final).

[2] The renaming of α,α',α''-trimethyl-1,3,5-triazine-1,3,5(2H,4H,6H)-triethanol - HPT into Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1) is not regarded as a redefinition according to Article 11 of Regulation (EU) No 1062/2014.

	** The classification as a carcinogen need not apply if it can be shown that the maximum theoretical concentration of releasable formaldehyde, irrespective of the source, in the mixture as placed on the market is less than 0.1%.
Labelling	
Pictograms	GHS 05, GHS 07, GHS 08, GHS 09
Signal Word	Danger
Hazard Statement Codes	H302: Harmful if swallowed H332: Harmful if inhaled H314: Causes severe skin burns and eye damage H317: May cause an allergic skin reaction H373: May cause damage to organs (gastrointestinal tract and respiratory tract) H341: Suspected of causing genetic defects H350: May cause cancer 411: Toxic to aquatic life with long lasting effects
Suppl. Hazard Statement Code	EUH071: Corrosive to the respiratory tract
Specific Concentration limits, M-Factors	M = not applicable

b) Intended use, target species and effectiveness

RP 1:1 containing biocidal products can be used directly for preservation of liquid cooling systems. For this application the biocidal product is applied as manufactured, i.e. it is mixed into the process solutions by users. The biocidal products containing "reaction product from paraformaldehyde and 2 hydroxypropylamine (ratio of 1:1)" are used only in closed systems. They are not intended to be applied in once-through cooling systems or large open recirculating cooling systems.

The biocidal product tested inhibited growth of gram negative bacteria such as *Pseudomonas putida, Pseudomonas fluorescens*., *Pseudomonas aeruginosa, Escherichia coli*, *Klebsiella oxytoca, Legionella longbeachea,* gram positive bacteria such as *Staphylococcus aureus* and *Mycobacterium avium*, fungi such as *Fusarium spec.* and yeasts such as *Candida albicans.*

The studies showed that the growth inhibition concentration is 0.05% (v/v) (only for bacteria and only valid for closed cooling water systems) and 0.2% (v/v) if growth of fungi should be prohibited also. It has to be noted that risk assessment has been carried out with the concentration of 0.05% (v/v) (= 500 ppm), therefore fungicidal claim for PT11 is not supported by this CAR.

The active substance is a formaldehyde-releaser. The biocidal activity of the active substance is due to the interaction of the released formaldehyde with protein, DNA and RNA. The interaction with protein results from a combination with the primary amide and the amino groups. It reacts with carboxyl, sulfhydryl and hydroxyl groups.

As formaldehyde is not specific for one cellular target, the development of resistance is unlikely, if sufficiently high formaldehyde concentrations are guaranteed that exceed the capacity of the innate detoxification systems.

c) Overall conclusion of the evaluation including need for risk management measures

A common core dossier was developed for formaldehyde, which was agreed at a Biocides Technical Meeting and a final BPC opinion has been endorsed in December 2015. This core dossier forms the basis of the hazard assessment of formaldehyde for all formaldehyde releasing active substances.

Human health

The toxicity of the active substances is dominated by skin sensitization and local irritation and local (in vitro) genotoxicity (but negative systemic in vivo genotoxicity) and the hydrolysis study and efficacy mode of action support that the equilibrium within the RP 1:1 quickly shifts towards formaldehyde and 2-hydroxypropylamine by dilution and by the reaction of formaldehyde with biological media. This is essentially the basis for reading across the classification of formaldehyde for germ cell mutagenicity category 2 and carcinogenicity category 1B. However the risk assessment provided below for local and for systemic effects includes also the potential for carcinogenic effects.

The risk from the application of RP 1:1 as PT 11 within liquid cooling systems within industrial processes is characterised in the evaluation. 100% RP 1:1 as manufactured is loaded to cooling liquids with a final concentration of typically 0.05%. Exposure to RP 1:1 has to be completely excluded due to the corrosive and sensitizing hazard. Exposure to treated cooling liquids may happen. Due to the high dilution of RP 1:1 in cooling liquids full hydrolysis to formaldehyde and 2-hydroxypropylamin is expected. Therefore risk estimates are provided just for the situation of full hydrolysis. However risk estimates are provided only for formaldehyde, not for 2-hydroxypropylamin, since for the latter the AEL is much higher and the vapour pressure, i.e. exposure potential, is much lower compared to formaldehyde. Risk for loading of RP 1:1 to liquid cooling systems, sampling of cooling liquid, cleaning of containers and maintenance of the system is considered.

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**
PT 11: Use of b.p. in closed liquid cooling systems	Primary exposure covering the following tasks: loading, dosing, sampling, cleaning, maintenance of the system Exposure to active substance and treatment solution Acceptable with automatic dosing system, technical and organisational RMM and PPE (like gloves, coveralls, masks) for high local hazard category (loading, dosing) and RMM for standard industrial workplace for other tasks.	Industrial workers	Acceptable with RMM and PPE

For the loading of the corrosive and sensitizing RP 1:1 to liquid cooling systems closed systems have to be used in order to allow concluding that the risk for local respiratory and local dermal effects is acceptable. Exposure to the cooling liquid containing just 0.05% of RP

1:1 (~0.017% formaldehyde, below classification limits for formaldehyde) results in an acceptable risk with standard industrial organisational and technical RMM. In this case also risk for systemic effects is acceptable.

Considering that local irritation is a condition for the development of tumours and applying a deterministic threshold AEC and AEL, also the risk for potential carcinogenic effects appears acceptable.

No exposure of general public, no exposure of pets and no dietary exposure is expected due to the intended PT 11 use. Dermal contact against dried concentrates in dirty clothes in home laundry of working clothes is assumed to be not relevant as RP 1:1 residues will quickly hydrolyse and generate gaseous formaldehyde, which is transferred to the gaseous phase and will not remain on the clothes.

Environment

The risk characterisation was based on the hydrolysis products 2-hydroxypropylamine and formaldehyde as during the disinfection and use of the metal working system RP 1:1 has almost completely hydrolysed. The parent compound itself is therefore not expected to reach any environmental compartment. 2-Hydroxypropylamine and formaldehyde are expected to be readily biodegradable in the environment and are unlikely to bioaccumulate in biota. For acute toxicity algae is the most sensitive species with a 72h-E_rC50 of 5.7 mg/L (geometric mean, *Desmodesmus subspicatus*) for formaldehyde and a 96h-E_bC50 of 118.4 mg/L (nominal, buffered, *Pseudokirchneriella subcapitata*) for 2-hydroxypropylamine. Both compounds are not classifiable towards environmental hazards based on the available data.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
PT 11: Release from complete system drainage from the closed recirculating system (Tier 1a)	This scenario considers complete drainage of the cooling system for maintenance or in case of uncontrolled microbial growth, resulting from lack of a routine monitoring programme. Emissions are discharged during complete drainage without any pre-treatment into the municipal STP, which represent a rather unrealistic worst case situation (Tier 1a). Consequently, there is exposure of the aquatic (surface water and sediment) compartment and the terrestrial (soil and groundwater) compartments, the latter as a result of contaminated sewage sludge spreading on land.	Acceptable for 2-hydroxypropylamine. Acceptable for formaldehyde if the cooling system is completely disposed of as hazardous waste, otherwise not acceptable for STP, freshwater and soil.
PT 11: Release from design and dosing losses (Tier 1b)	For the cumulative release from design and dosing losses were taken into account. The emissions are discharged into the municipal STP without any pre-treatment. **Affected environmental compartments:** STP, surface water, sediment, soil, groundwater.	Acceptable
PT 11: Release from complete system drainage from the closed recirculating system with pre-treatment (Tier 2)	Tier 2 is provided as realistic scenario for the case that according to national laws the drainage will not be disposed as hazardous waste, but will be treated by a specialised waste treatment company. This scenario considers complete drainage of the cooling system for maintenance or in case of uncontrolled microbial growth, resulting from lack of a routine monitoring programme. The releases during complete drainage are pre-treated in either an on-site STP or an STP of a specialized waste treatment company before the discharge enters into the municipal STP, which represent a realistic scenario (Tier 2: two STPs in a row trigger that the emissions calculated in Tier 1a were reduced by the fraction degraded in the STP). Tier 2 is based on the assumption that the waste water is e.g. purified microbial prior to final discharge to a municipal STP. **Affected environmental compartments:** STP, surface water, sediment, soil, groundwater. Depending on the national legislation and in line with the Urban Waste Water Treatment Directive 91/271/EEC sludge from an industrial STP may not be spread on soil in agriculture, horticulture and grassland; this exposure pathway has not been assessed.	Acceptable

The risk assessment was calculated for the life cycle stage "waste treatment after refreshment, design and dosing losses".

For closed liquid cooling systems, releases to the environment are likely during dosing, leakages (design losses, Tier 1b) and during the periodical refreshment (complete drainage, Tier 1a, Tier 2).

When considering the phase of complete drainage of the closed recirculating system with direct release to a municipal STP (Tier 1a):

- the risk is acceptable for groundwater;

- the risk is acceptable for STP, freshwater and soil only when the cooling system is completely disposed of as hazardous waste (for example draining by specialized companies that disposes the drain liquid via high-temperature incineration).

The risk is acceptable for all compartments when considering the release from dosing events and from design losses (Tier 1b) as well as from release from complete system drainage from the closed recirculating system with pre-treatment (Tier 2). Tier 2 covers potential national situation at product authorisation stage.

Surface water intended for the abstraction of drinking water exceeded the parametric value of 0.1 µg/L of the Drinking Water Directive 98/83/EC. This may be considered by the relevant national authorities when issuing permits for recovery plants.

Overall conclusion

Overall a safe use has been identified for the use of RP 1:1 in closed liquid cooling systems in PT11 provided adequate RMM and PPE are considered for human health and environment.

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)	Cat 1B	RP 1:1 does fulfil criterion (a) of Article 5(1)
	Mutagenicity (M)	Cat 2	
	Toxic for reproduction (R)	no classification required	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	not P or vP	RP 1:1 does not fulfil criterion (e) of Article 5(1) and does not fulfil criterion (d) of Article 10(1)
	Bioaccumulative (B) or very Bioaccumulative (vB)	not B or vB	
	Toxic (T)	T	
Endocrine disrupting	RP 3:2 is not considered to have endocrine disrupting properties. RP		

properties	3:2 does not fulfil criterion (d) of Article 5(1).
Respiratory sensitisation properties	No classification required. RP 3:2 does not fulfil criterion (b) of Article 10(1).
Concerns linked to critical effects	RP 3:2 does not fulfil criterion (e) of Article 10(1).
Proportion of non-active isomers or impurities	The substance does not contain a significant proportion of non-active isomers or impurities. RP 3:2 does not fulfil criterion (f) of Article 10(1).

Consequently, the following is concluded:

Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1) does meet the exclusion criteria laid down in Article 5(1) of Regulation (EU) No 528/2012 by the released formaldehyde being a carcinogen Cat 1B.

Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1) does meet the conditions laid down in Article 10(1)(a) of Regulation (EU) No 528/2012, and is therefore considered as a candidate for substitution by meeting the exclusion 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"[3] and in line with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[4] 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

A PBT assessment was performed for RP 1:1 and its hydrolysis products. Based on the available data RP 1:1, 2-hydroxypropylamine and formaldehyde are neither vPvB, nor PBT substances. Furthermore, none of the three substances meets two of the PBT criteria. Therefore, neither the parent nor its hydrolysis products meet the criteria for POPs either.

2.2.3. Public consultation for potential candidates for substitution and alternative substances or technologies

As RP 1:1 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 4 November 2016 to 3 January 2017. Four contributions were submitted: one by an industry stakeholder association, two by individual companies and one by a member state. The same contributions were submitted in the consultation on the structurally and toxicologically related substance RP 3:2.

In the member state contribution it is stated that no information on alternatives is available as the product types are not covered by their national authorisation scheme. This may be the case for more member states.

[3] 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)
4 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)

In the three industry contributions information is submitted on the importance of formaldehyde releasers in the control of microbial growth in water-containing products or equipment. In addition, information on alternatives is submitted for all product types.

Three general observations are made in the industry contributions:

- First, it is stated that other formaldehyde releasers are not considered as alternatives as it can be foreseen that these will also be classified as carcinogen category 1B and subsequently meet the exclusion criteria. In total 10 other formaldehyde releasers are under evaluation and one (formaldehyde released from N,N-Methylenebismorpholine or MBM for PT 6 and 13) is already approved.
- Second, it is stated that for an effective preservation of many water-based products a bactericide and fungicide is needed. Subsequently, fungicide active substances cannot be regarded as suitable alternatives.
- Last, it is stated that another class of bactericides are the isothiazolinones. Although these are not meeting the substitution criteria it should be considered that these are all classified as strong skin sensitisers. This triggers several obligations for the user making this class of active substances not suitable alternatives.

For PT11 in the industry contributions glutaraldehyde, THPS and acrolein are indicated as possible alternatives in oilfield applications. Glutaraldehyde is also candidate for substitution. THPS is also a formaldehyde releaser, has a more severe classification for acute aquatic toxicity compared to RP 1:1 and its stability prevents its application for the same use as RP 1:1. Acrolein also has a more severe aquatic toxicity compared to RP 1:1.

The following active substances are already approved for PT11: C(M)IT/MIT, glutaraldehyde, peracetic acid and PHMB (1600; 1.8). C(M)IT/MIT belongs to the class of isothiazolinones, while PHMB (1600; 1.8) is also a candidate for substitution meeting two out of the three PBT criteria. Glutaraldehyde is also a candidate for substitution as it is a respiratory sensitiser.

The limited information available is insufficient to conclude on the availability of suitable alternatives for the intended uses assessed.

2.3. BPC opinion on the application for approval of the active substance RP 1:1 in product type 11

As the exclusion criteria are met, RP 1:1 should normally not be approved unless one of the conditions for derogation set in Article 5(2) of Regulation (EU) No 528/2012 is met.

If RP 1:1 is approved and included in the Union list of approved active substances, the approval shall be subject to the following specific conditions:

1. Specification: the active substance has to be considered as substance of Unknown or Variable composition or Complex reaction products (UVC). Therefore the minimum purity is 1000 g/kg (100% by wt).

2. RP 1:1 is considered a candidate for substitution in accordance with Article 10(1)(a) of Regulation (EU) No 528/2012.

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

    a. Products shall only be authorised for use in Member States where at least one of the conditions set in Article 5(2) of Regulation (EU) No 528/2012 is met.

    b. 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. In addition, pursuant to point 10 of Annex VI to Regulation (EU) No 528/2012, the product assessment shall include an evaluation as to whether the conditions of Article 5(2) of Regulation (EU) No 528/2012 can be satisfied.

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

   i. Industrial workers and professionals;

   ii. Sewage Treatment Plant, surface water and the terrestrial compartment.

4. The placing on the market of treated articles is subject to the following condition:

   a. The person responsible for the placing on the market of a treated article treated with or incorporating RP 1:1 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.

RP 1:1 does not fulfil the criteria according to Article 28(1) to enable inclusion in Annex I of Regulation (EU) 528/2012 as it is classified as Skin Corr. 1C, Skin Sens. 1A, STOT RE 2, Muta 2, Carc. 1B.

2.4. Elements to be taken into account when authorising products

1. The active substance RP 1:1 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 national 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 for professional users is identified for the product, safe operational procedures and appropriate organisational measures shall be established. Where exposure cannot be reduced to an acceptable level by other means, products should be used with appropriate personal protective equipment.

   b. Surface water intended for the abstraction of drinking water exceeded the parametric value of 0.1 µg/L of the Drinking Water Directive 98/83/EC. This may be considered by the relevant national authorities when issuing permits for recovery plants.

   c. Unacceptable risks have been identified for the release from complete system drainage from the closed recirculating system for the sewage treatment plant, surface water and the terrestrial compartment. Labels and, where provided, safety data sheets, shall indicate that disposal following drainage of the closed recirculating system shall be handled as hazardous waste, unless it can be demonstrated at product authorisation that risks to the environment can be reduced to an acceptable level by other means.

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 RP 1:1. However, further data shall be required as detailed below. Data must be provided as soon as possible but not later than 6 months before the date of approval to the evaluating Competent Authority (Austria):

a. Regarding the explosive properties of the active substance an experimental test has to be conducted as the substance contains unknown constituents and therefore the waiving cannot be justified by structural considerations.

b. A specific or highly specific and fully validated analytical method for the determination of the hydrolysis product 2-hydroxypropylamin in water.

o0o