Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate

Product type: 2

ECHA/BPC/363/2022

Adopted

22 November 2022

Opinion of the Biocidal Products Committee

on the application for approval of the active substance "reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate" for product type 2

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:	**reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate**
Chemical name:	**reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate**
EC No.:	**-**
CAS No.:	**-**

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 the BPC opinion

Following the submission of an application by YOU Solutions Germany GmbH on 31 July 2007, the evaluating Competent Authority Italy submitted an assessment report and the conclusions of its evaluation to the Commission on 27 July 2010. To review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via BPC (BPC-45) and its Working Groups (WGIII2022). Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Adoption of the BPC opinion

Rapporteur: Italy

The BPC opinion on the application for approval of the active substance “reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate” in product type 2 was adopted on 22 November 2022.

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 “reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate” 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 “reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate”, in product type 2. The active substance is already approved for product type 8 (Regulation EU 2016/1093).

At the Working Group meeting for analytical methods and physico-chemical properties (APCP WG III in 2022), the need to redefine the active substance was discussed. It was concluded that the substance composition and reference specification was consistent with the active substance assessed and approved under product type 8, but that the name in the list of Annex II to Regulation (EU) No 1062/2014 and in Regulation (EU) 2016/1093 (didecylmethylpoly(oxyethyl)ammonium propionate) was not appropriate. The active substance is redefined as “reaction mass of N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate and N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate” to reflect that it consists of a reaction mass of the following active constituents:

n = 0	N,N-didecyl-N-(2-hydroxyethyl)-N-methylammonium propionate	C3H5O2.C23H50NO (CAS 107879-22-1)	77.5-86.4% w/w dry weight
n = 1	N,N-didecyl-N-(2-(2-hydroxyethoxy)ethyl)-N-methylammonium propionate	C3H5O2.C25H54NO2 (CAS not available)	4.7-9.0% w/w dry weight
n = 2	N,N-didecyl-N-(2-(2-(2-hydroxyethoxy)ethoxy)ethyl)-N-methylammonium propionate	C3H5O2.C27H58NO3 (CAS not available)	≤0.20% w/w dry weight
n: degree of ethoxylation			

The active substance is abbreviated as DMPAP (an abbreviation related to the name previously used for this substance). DMPAP is a cationic surfactant-type active substance.

DMPAP is not manufactured solvent-free, but as a technical concentrate, i.e. ca. 60% DMPAP in ethylene glycol, diethylene glycol and water. Specifications for the reference sources 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 are available for the active substance as manufactured and for the significant impurities. Validated analytical methods are available for the relevant matrices soil and water (both drinking and surface water).

A harmonised classification does not exist for DMPAP under CLP regulation. The evaluating Competent Authority (eCA) intends to submit the following harmonised classification proposal to ECHA.

The proposed classification and labelling for DMPAP according to Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute toxicity 4 Skin Corrosion 1B Eye Dam. 1 STOT SE 3 Aquatic Acute 1 Aquatic Chronic 1
Hazard Statement Code	H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H318: Causes serious eye damage. H335: May cause respiratory irritation. H400: Very toxic to aquatic life. H410: Very toxic to aquatic life with long lasting effects.
Labelling	
Pictogram codes	GHS05, GHS07, GHS09
Signal Word	Danger
Hazard Statement Codes	H302: Harmful if swallowed. H314: Causes severe skin burns and eye damage. H335: May cause respiratory irritation. H410: Very toxic to aquatic life with long lasting effects.
Specific Concentration limits, M-Factors	M factor=10 (Acute) M factor=1 (Chronic)
Justification for the proposal	
NOTE: The classification as Eye Dam. 1 H318 and STOT SE 3 H335 was not discussed for the PT8 approved before. This additional classification has been assigned to DMPAP evaluated under PT2 according to the CLP Regulation.	

b) Intended use, target species and effectiveness

DMPAP is a broad spectrum biocide intended to be used in product type 2 for disinfection of hard surfaces in private and public health areas by professional users.

The requested use in PT 2.01b, for preventing infections in people manipulating instruments during the process of re-sterilization, was not included in the present assessment since the Regulation EU 528/2012 applies to biocidal products and includes disinfectants, but excludes products that are defined in, or within the scope of, the Medical Devices directive (Council

Directive 93/42/EEC of 14 June 1993), like products for pre-wash of instruments by immersion.

Since it is surface active, DMPAP has fair wetting properties and reacts strongly with cell walls of micro-organisms. The mode of action is via destruction of cell walls by sticking on the exterior structures and by entering and disintegrating the inner phospholipid-bilayer-based membrane structures. Due to this interaction, it severely alters the cell wall permeability, disturbs membrane-bound ion-translocation mechanisms, and may facilitate the uptake of other biocides.

Quaternary ammonium compounds, in general, are known to be effective against Gram+ bacteria and enveloped viruses, with limited efficacy against Gram-negative bacteria, non-enveloped viruses and bacterial spores. For the specific object of this dossier, aqueous dilutions of the active substance (a.s.) were tested according to EN test methods to show activity against bacteria and yeasts. The a.s. concentration demonstrated to be efficacious against both targets is 0.5 g/L.

Since the many years of use of quaternary ammonium compounds, there is no indication that their efficacy in use is diminishing over time. Nevertheless, as the possible occurrence of resistance should be monitored for all biocides, and as any situation might change, at product authorization stage strategies of resistance management will be reviewed if needed and/or further actions will be taken when a suitable guidance that appropriately predicts the occurrence of resistance to a given biocide becomes available.

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

Human health

The main critical effects associated with DMPAP are due to its corrosive properties. The active substance (a.s.) induces severe erythema, desquamation, and corrosive eschar in the rabbit skin, and therefore it is classified as corrosive to skin. No specific studies on a.s. toxicokinetics and metabolism are available, however, the read across from data on a structurally related compound, namely didecyldimethylammonium chloride (DDAC), has been accepted. Based on the available results, it was noted that the systemic toxic effects were secondary to the observed local toxicity. Therefore, only a local risk assessment was considered necessary for the use of DMPAP.

The endocrine-disrupting properties of the a.s. have been sufficiently investigated. Based on the available evidence DMPAP does not meet the ED criteria for human health according to the criteria laid down in Regulation (EU) No 2017/2100.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios			
Scenario	**Primary exposure and description of scenario**	**Exposed group**	**Conclusion**
Disinfection of hard surface by spraying (coarse spray)	Mixing and loading: dilution of concentrate biocidal product (containing 15% w/w of a.s.) to the in-use concentration (0.05% w/w). PPE for mixing and loading: gloves, goggles, protective coveralls. Spraying: Disinfection of tiles, floors, walls, i.e. hard surface by spraying (coarse and trigger spray) in the general sanitary sector.	Professional users	Acceptable with PPE (needed for mixing and loading, only)
Disinfection of hard surface by mopping	Mixing and loading: dilution of concentrate biocidal product (containing 15% w/w of a.s.) to the in-use concentration (0.05% w/w). PPE for mixing and loading: gloves, goggles, protective coveralls. Mopping: Disinfection of tiles, floors, walls, i.e., hard surface by mopping in the general sanitary sector.	Professional users	Acceptable with PPE (needed for mixing and loading, only)

When appropriate risk mitigation measures are in place, including appropriate exposure control measures like PPE, potential risks associated with local effects were acceptable for the assessed uses.

In-use concentrations do not trigger any classification for local effects. Therefore, no qualitative local risk assessment has been performed for inhalation and dermal route. Nevertheless, for primary exposure via dermal route a semi-quantitative local risk assessment has been conducted.

No exposure is expected via inhalation route due to the dimensions of the particle sizes generated during the coarse/trigger spray application. The assessed product is not volatile, and care should be taken that the application process does not result in the generation of and exposure to inhalable aerosols. In case of spraying, only coarse sprays (trigger spray) with big droplets are recommended. Coarse sprays with droplets > 100 µm are not inhaled (Guidance on BPR). Consequently, systemic effects do not occur, and exposure/local effect potential is controlled or eliminated based on application equipment (which produces non-respirable particles), use patterns, and/or PPE.

In conclusion, no unacceptable risk was identified due to the direct applications of the diluted solutions.

Since the in-use dilutions are of low concentration as well as the active substance has a low volatility, for secondary exposure dermal and inhalation exposure were considered negligible.

Environment

Studies with DMPAP have been submitted at different times during the evaluation process of this active substance, partly during PT8 evaluation and as post-approval data in PT8, to cover also the requirements for PT2.

DMPAP is not readily biodegradable, although it can be considered inherently biodegradable according to a high and constant removal rate measured as primary biodegradation and complete mineralization; the substance has been identified as persistent according to the guidance update (Technical agreements for Biocides Environment Nov 2021). DMPAP is hydrolytically and photolytically stable under environmentally relevant conditions, while it is neither volatile nor expected to be present in the air. DMPAP can be considered immobile in soil and a DT_{50} of 120.8 d (12°C) was derived by a soil degradation study (OECD 307) carried out on the active substance.

For the aquatic compartment, acute toxicity data showed the most sensitive group being invertebrates whilst according to chronic toxicity data the most sensitive group is fish.

For the terrestrial compartment, plants were concluded as the most sensitive organism group based on the available data with DMPAP on earthworms, soil microorganism and plants. The evaluation of secondary poisoning via aquatic food chain is based on read across with DDAC, with short-term dietary toxicity data on birds and from a 90-day oral repeated dose study with dog retrieved from the human health section and using the fish experimental bioconcentration factor (BCF). The potential for bioaccumulation is low according to the accepted read-across with DDAC. Given the low potential for bioaccumulation determined for the structurally related DDAC, it is considered that no further assessment is necessary for DMPAP.

For the endocrine-disrupting properties, with respect to non-target organisms, in relation to the criteria set out in section B of Regulation (EU) No 2017/2100, no conclusion can be drawn based on the available data, due to the lack of studies on reproduction/development and/or thyroid axis in aquatic vertebrates. However, for reports submitted before 1 September 2013 (as the present one), the eCA has to conclude based on the already available data and/or the data provided by the applicant and, in case the data is insufficient to reach a conclusion, the BPC may conclude in its opinion that no conclusion could be drawn.

Three major metabolites were detected in the degradation studies for STP sludge, soil and water-sediment system. The risk assessment for the aquatic and terrestrial compartment for metabolite M1a, as worst case, was carried out.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Disinfection for sanitary purposes	Releases of disinfectants used for sanitary purposes based on average consumption. Compartments assessed: sewage treatment plant (STP), surface water, sediment, soil, groundwater.	DMPAP (parent): Acceptable Metabolites: Unacceptable (groundwater)
Disinfection of industrial area small scale	Releases of disinfectants used in industrial area small scale. Compartments assessed: sewage treatment plant (STP), surface water, sediment, soil, groundwater.	DMPAP (parent): Acceptable Metabolites: Acceptable

Following the use of DMPAP, PEC/PNEC ratios are less than one for all compartments for small scale scenario demonstrating that the risks following the use of the active substance for this specific application are acceptable.

For DMPAP, metabolites were identified but not further characterized in relation to their environmental fate properties. Only QSAR predicitions are available, leading to estimated porewater concentrations higher than the reference value of 0.1 µg/L for groundwater in the Tier 1 assessment. As a refinement, the concentrations in groundwater were estimated using FOCUS PEARL modelling, performed for release of disinfectants used for industrial area small scale, demonstrating a safe use with PEC_{GW} values below the trigger value of 0.1 µg/L as laid down by the Drinking Water Directive 2006/118/EC.

Overall conclusion

For human health, acceptable risk was identified for the disinfection of hard surface by spraying (coarse spray) and by mopping in the general sanitary sector by professional users, when appropriate RMMs are in place for the mixing and loading phase to prevent local effects.

For the environment acceptable risk was identified for the scenario on disinfectants used in industrial area small scale. Given the necessary refinements applied in relation to metabolite risk assessment, it is proposed that at product authorization attention should be paid to appropriate RMMs to limit the emission to environment. Alternatively, a restriction of use to limited to small scale application (RTU) is proposed.

In conclusion, safe use of DMPAP was identified for industrial use small scale application.

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)	No classification required	DMPAP 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)	P	DMPAP does not fulfil criterion (e) of Article 5(1) and does not fulfil criterion (d) of Article 10(1). According to QSAR analysis information, DMPAP metabolites do not fulfil criterion (e) of Article 5(1) and do not fulfil criterion (d) of Article 10(1).
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B	
	Toxic (T)	Not T	
Endocrine disrupting properties	Section A of Regulation (EU) 2017/2100: ED properties with respect to humans	No	DMPAP does not fulfil criterion (d) of Article 5(1) for human health. About the environment no conclusion can be taken due to insufficient information. Therefore, it cannot be ascertained whether the substance fulfils criterion (e) of Article 10(1) for the environment.
	Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms	No conclusion can be drawn based on the available data	
	Article 57(f) and 59(1) of REACH	No	
	Intended mode of action that consists of controlling target organisms via their endocrine system(s)	No	
Respiratory sensitisation properties	No classification required. DMPAP does not fulfil criterion (b) of Article 10(1).		
Concerns linked to critical effects other than those related to endocrine disrupting properties	DMPAP does not fulfil criterion (e) of Article 10(1).		
Proportion of non-active isomers or impurities	As the proportion of impurities is below 20%, DMPAP does not fulfil criterion (f) of Article 10(1).		

Consequently, the following is concluded:

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

DMPAP does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012 and is therefore not considered as a candidate for substitution.

DMPAP does not meet the exclusion criteria laid down in criterion (d) of Article 5(1) for human health whereas data are insufficient to conclude on criterion (e) of Article 10(1) for the environment of Regulation (EU) 2017/2100.

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], "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[2] and "Implementation of scientific criteria to determine the endocrine–disrupting properties of active substances currently under assessment[3]" agreed at the 54th, 58th and 77th 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).

For the endocrine-disrupting properties as defined in Regulation (EU) No 2017/2100, properties of DMPAP have been sufficiently investigated and based on the available evidence, the substance does not meet the ED criteria for human health according to the criteria laid down in Regulation (EU) No 2017/2100. With respect to non-target organisms, in relation to the criteria set out in section B of Regulation (EU) No 2017/2100 no conclusion can be drawn based on the available data. For reports submitted before 1 September 2013, it is mentioned in the CA meeting note mentioned above that the evaluating Competent Authority has to conclude based on the already available data and/or the data provided by the applicant and, in case the data is insufficient to reach a conclusion, the BPC may conclude in its opinion that no conclusion could be drawn. It is noted that the evaluation of DMPAP for PT2 was submitted before 1 September 2013.

2.2.2. POP criteria

DMPAP meets the P criterium, but it is neither B nor T. No potential for long-range environmental transport is expected, either. Subsequently, it is concluded that DMPAP is not expected to meet the POP criteria.

2.3. BPC opinion on the application for approval of the active substance DMPAP in product type 2

In view of the conclusions of the evaluation, it is proposed that DMPAP shall be approved and be included in the Union list of approved active substances, subject to the following specific conditions:

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[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).

[3] See document: Implementation of scientific criteria to determine the endocrine –disrupting properties of active substances currently under assessment (available from https://circabc.europa.eu/sd/a/48320db7-fc33-4a91-beec-3d93044190cc/CA-March18-Doc.7.3a-final-%20EDs-%20active%20substances%20under%20assessment.docx).

1. Specification: minimum purity of the active substance evaluated: 86.1% w/w dry weight.

2. The authorisations of biocidal products are subject to the following conditions:

    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. Environment: groundwater.

DMPAP meets the criteria for classification according to Regulation (EC) 1272/2008 as skin corrosive of category 1B, specific target organ toxicity – single exposure (category 3) and aquatic acute category 1. Subsequently, the active substance does not fulfil the criteria according to Article 28(2)(a) to enable inclusion in Annex I of Regulation (EU) 528/2012.

2.4. Elements to be taken into account when authorising products

1. 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 assessment of the risk during spraying may be required at product authorisation where use of the product may lead to inhalable aerosol formation (droplets ≤ 100 µm).

    c. The concentration of metabolites in groundwater exceeded the threshold of 0.1 µg/L for disinfection for sanitary purposes. If these concentrations cannot be reduced to an acceptable level these uses may not be authorised.

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 DMPAP.

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