Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Glutaraldehyde

Product type: 11

ECHA/BPC/023/2014

Adopted

1 October 2014

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Opinion of the Biocidal Products Committee

on the application for approval of the active substance glutaraldehyde for product type 11

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 11 of the following active substance:

Common name(s):	**Glutaraldehyde**
	Glutaral
Chemical name(s):	**1,5-pentanedial**
EC No.:	**203-856-5**
CAS No.:	**111-30-8**
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 BASF SE on 27 October 2008 and Dow Benelux B.V. on 30 October 2008, the evaluating Competent Authority Finnish Safety and Chemicals Agency submitted an assessment report and the conclusions of its evaluation to the Commission on 30 March 2011 and 31 January 2013. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC and the Commission via the Biocides Technical Meetings (TM). 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 http://echa.europa.eu/fi/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations on 17 December 2013, 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 15 February 2014.

Adoption of the BPC opinion

Rapporteur: BPC Member for Finland.

The BPC opinion on the approval of the active substance glutaraldehyde in product type 11 was adopted on 1 October 2014.

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.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that the glutaraldehyde in product type 11 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

Glutaraldehyde is a linear five carbon dialdehyde which is produced and sold as an aqueous solution containing 48.5-52.5 % glutaraldehyde by weight. Glutaraldehyde as manufactured is a technical concentrate (TK), and the theoretical dry weight specification of glutaraldehyde covering both reference sources is a minimum purity of 95.0 % (wt), 950 g/kg. Specifications for the reference sources are established. The representative product in the evaluation is identical to the active substance.

This evaluation covers the use of glutaraldehyde in product type 11. Glutaraldehyde acts by reacting with the free amino groups of some proteins that are located in the cell walls and membranes of micro-organisms. This reaction leads to cross-linking. Cross-linked microbial cells cannot transport nutrients or perform any critical metabolic functions. Glutaraldehyde also deactivates various membrane-bound enzymes. The kinetics of the cross-linking mechanism is influenced by the pH, the contact time, the glutaraldehyde concentration and the temperature. In viruses, the main targets for glutaraldehyde are nucleic acid, proteins and envelope constituents. The established reactivity of glutaraldehyde with proteins suggests that the viral capsid or viral-specific enzymes are vulnerable to glutaraldehyde treatment.

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 the biocidal product.

Validated analytical methods are required and available for the relevant matrices water, soil and blood. Analytical methods for the determination of residues in food and feed stuffs are not deemed necessary, because for the assessed use residues are not expected due to chemical nature of glutarladehyde, which reacts rapidly with proteins and other organic matter contained in the food and feed stuffs. Certain analytical methods are required as further information (see 2.5 Requirement for further information).

The current harmonised classification and labelling for glutaraldehyde according to Regulation (EC) No 1272/2008 (CLP Regulation) is presented below. In addition, an opinion on the revised harmonised classification was formed on 2-6 June 2014 by the Risk Assessment Committee (RAC). The opinion of RAC 29 is also presented.

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

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 3 * H331 Acute Tox. 3 * H301 Skin Corr. 1B H314 Resp. Sens. 1 H334

	Skin Sens. 1 H317 Aquatic Acute 1 H400
Labelling	
Pictograms	GHS06, GHS05, GHS08, GHS09
Signal Word	Danger
Hazard Statement Codes	H331: Toxic if inhaled H301: Toxic if swallowed H314: Causes severe skin burns and eye damage H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled H317: May cause an allergic skin reaction H400: Very toxic to aquatic life
Specific Concentration limits, M-Factors	C ≥ 10 % Skin Corr. 1B; H314 0,5 % ≤ C < 10 % Skin Irrit. 2; H315 2 % ≤ C < 10 % Eye Dam. ; H318 0,5 % ≤ C < 2 % Eye Irrit. 2; H319 C ≥ 0,5 % STOT SE; H335 C ≥ 0,5 % Skin Sens. 1; H317

[1] Note: Annex VI of Regulation 1272/2008 lists glutaraldehyde as the pure (100%) substance.

The RAC 29 opinion (2-6 June 2014) on the classification and labelling for glutaraldehyde according to the CLP Regulation is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 3 H301 Acute Tox. 2 H330 Skin Corr. 1B H314 Resp. Sens. 1 H334 Skin Sens. 1A H317 STOT SE H335 Aquatic Acute 1 H400 Aquatic Chronic 2 H411
Labelling	
Pictograms	GHS06, GHS05, GHS08, GHS09
Signal Word	Danger
Hazard Statement Codes	H301: Toxic if swallowed H330: Fatal if inhaled H314: Causes severe skin burns and eye damage H334: May cause allergy or asthma symptoms or breathing difficulties if inhaled H317: May cause an allergic skin reaction H335: May cause respiratory irritation H410: Very toxic to aquatic life with long lasting effects
Supplementary Hazard Statement Code(s)	EUH071
Specific Concentration limits, M-Factors	STOT SE 3; H335: C ≥ 0,5% M = 1 for Aquatic Acute

b) Intended use, target species and effectiveness

Glutaraldehyde has been applied and evaluated as a preservative for closed and open recirculating cooling systems and as a preservative in injection and hydrotest water in oil extraction industry in PT 11. All uses are professional uses. Prevention of microbial proliferation is needed in the water used to for injections into the rock formation in order to keep up or increase the pressure on the oil producing zone. Prevention of microbial proliferation is also needed in the water used for hydrotesting (often long term pressure or integrity testing of transit lines or other equipement).

Glutaraldehyde is potentially effective against a wide variety of micro-organisms including gram positive and negative bacteria, sulphate reducing bacteria, fungi (yeasts and moulds), algae and biofilms,. The microbes are killed faster at higher concentrations, higher temperatures and higher pH. The efficacy is also enhanced by longer contact time. Sufficient effectiveness against bacteria was demonstrated, but further studies are needed to demonstrate the effectiveness against fungi, bacterial spores and mycobacteria at the intended use concentrations for product authorisation. Similarly, efficacy against algae and biofilms was not demonstrated for the intended use concentrations and should be proven at product authorisation.

Resistance to glutaraldehyde in certain mycobacteria strains has been reported in hospitals for a use which is outside the scope of regulation (EU) No 528/2012. The cell surface of the resistant strains has been modified so that there are no or few sensitive reaction sites for glutaraldehyde. Resistance development may thus be theoretically possible, but despite of use for decades no observations of resistance development has been made in industrial applications.

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

Human health

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios		
Scenario	**Primary or secondary exposure and description of scenario, exposed group**	**Acceptable or unacceptable**
Mixing and loading closed recirculating system	**Primary exposure**: professionals, connecting/disconnecting drums	Acceptable with RPE, gloves, double coveralls
Draining a closed recirculating system	**Primary exposure**: professionals	Acceptable, gloves and coated coveralls required
Loading open recirculating system	**Primary exposure**: professionals, connecting/disconnecting drums	Acceptable with RPE, gloves, double coveralls
Bystander exposure, open recirculating system	**Secondary exposure:** adult and child, inhalation exposure to spray drift	Acceptable
Preservatives for mineral oil extraction (flooding and oil injection water) - mixing and loading	**Primary exposure:** professionals, adding of product to oilfield injection water or to the produced fluids (connecting/disconnecting of lines/hoses)	Acceptable with RPE, gloves, double coveralls
Slimicide in oilfield extraction fluids (flood and oil injection water) - mixing and loading semi automatically	**Primary exposure:** professionals, adding product to the header reservoir of oilfield injection water (connecting/disconnecting of lines/hoses)	Acceptable with RPE, gloves, double coveralls

For professional users exposure to glutaraldehyde was evaluated for the scenarios summarized in the table above. All evaluated use scenarios are identified as safe uses with appropriate PPE.For secondary exposure only inhalation was considered relevant. No concern was identified derived for dermal exposure.

According to the RAC 29 opinion glutaraldehyde is classified as Skin sens 1A. Due to skin sensitising property PPE (gloves, coverall) is required for professionals in the use of biocidal product.

Glutaraldehyde is classified as Resp sens 1 according to the CLP Regulation. No scientific concept is available to derive a threshold value for safe exposure on the basis of the existing data concerning respiratory sensitisation. The evidence does however support the general principle that sensitization occurs in workplaces where high exposure occurs either regularly or as high peak concentrations. The available data seem to suggest that where sensitization has occurred, exposure has occurred to at least 20-30 ppb, and often much higher. This should however not be understood as a proposal for a threshold value. Nevertheless, as the data indicate that sensitization has occurred at significantly higher concentrations than the $AEC_{inhalation}$, this is considered as a reference value that is likely to be protective for sensitization effects as well. Because respiratory sensitization has been linked with high peak exposure concentrations, $AEC_{acute\ inhalation}$ (122 ppb) should be regarded as a ceiling value that should never be exceeded.

Environment

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Acceptable or unacceptable**
Closed recirculating cooling systems	Defouling and maintenance treatment: Waste water emission to STP (sewage treatment plant). Emissions to surface water, soil and groundwater via STP.	Acceptable
Small open recirculation cooling systems • without STP	Defouling and maintenance treatment: Direct emission to soil from cooling tower and subsequent emission to groundwater. Direct waste water emission to surface water.	Unacceptable
Small open recirculation cooling systems • with STP	Defouling and maintenance treatment: Direct emission to soil from cooling towers and subsequent emission to groundwater. Waste water emission to STP. Emissions to surface water, soil and groundwater via STP.	Unacceptable
Preservative for oilfield injection water	Direct discharge water emission to seawater.	Acceptable
Preservative for hydrotest water	Direct discharge water emission to seawater.	Unacceptable

Closed recirculating cooling systems and preservation of oilfield injection water are identified as safe uses. Unacceptable risk was identified in the scenario small open recirculation cooling system with and without STP. Preservation of hydrotest water is considered safe when glutaraldehyde concentration decreases before hydrotest water is released to sea. Dissipation of glutaraldehyde can be demonstrated for the use applied for under product authorisation. If dissipation cannot be demonstrated risk mitigation measures should be applied.

Unacceptable risks are identified from the direct emissions of small open recirculation cooling towers to soil during maintenance treatment. In addition, unacceptable risks are identified from direct and indirect emissions to surface water during both defouling and maintenance treatment. The use in small open recirculating cooling systems is not allowed unless data is submitted for product authorisation to demonstrate that product will not present unacceptable risk.

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
	Mutagenicity (M)	No classification required
	Toxic for reproduction (R)	No classification required

PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Not P or vP
	Bioaccumulative (B) or very Bioaccumulative (vB)	Not B or vB
	Toxic (T)	Not T
Endocrine disrupting properties	Glutaraldehyde is not considered to have endocrine disrupting properties	
Respiratory sensitisation properties	Classified as respiratory sensitizer Cat. 1 H334	

Consequently, the following is concluded:

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

Glutaraldehyde does meet the conditions laid down in Article 10(1)(b) of Regulation (EU) No 528/2012, and is therefore considered as a candidate for substitution by being respiratory sensitizer.

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" agreed at the 54th meeting 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[1]. 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 and d).

During public consultation two confidential comment were received from third parties. The confidential comment included information on the availability of an alternative active substance for the product type 11. In addition, there are several other active substances intended for use in the same product type already approved or are currently being reviewed under Regulation (EU) No 528/2012b.

2.2.2. POP criteria

Glutaraldehyde does not fulfil criteria for being a persistent organic pollutant (POP). Glutaraldehyde does not have potential for long-range transboundary atmospheric transport.

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

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

1. Specification: minimum purity of the active substance evaluated: The active substance as manufactured is an aqueous solution of 485-525 g/kg (48.5-52.5 %, by wt) solution of glutaraldehyde. The theoretical (calculated) dry weight specification: minimum purity of glutaraldehyde is 950 g/kg (95.0 %, by wt).

[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. Glutaraldehyde is considered a candidate for substitution in accordance with Article 10(1)(b) of Regulation (EU) No 528/2012.

3. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any use covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.

4. For industrial or professional users, safe operational procedures and appropriate organisational measures shall be established. Where exposure cannot be reduced to an acceptable level by other means, products shall be used with appropriate personal protective equipment.

5. Products shall not be authorised for the use in small open recirculating cooling systems, as referred to in the exposure assessment, unless data is submitted for product authorisation to demonstrate that product will not present unacceptable risk to soil and surface water.

6. Products shall not be authorized for the preservation of hydrotesting water unless it can be demonstrated that the product will not lead to an unacceptable risk.

Glutaraldehyde gives rise to concern for both human health and environment, i.e. it is acutely toxic by oral and inhalation route, is corrosive and a skin sensitizer and is toxic to aquatic life of category 1 mentioned in Article 28(2) of the BPR. In addition glutaraldehyde fulfils the substitution criteria as it is a respiratory sensitizer. Therefore inclusion in Annex I of Regulation (EU) 528/2012 is not acceptable.

2.4. Elements to be taken into account when authorising products

The active substance glutaraldehyde 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.

1. Whilst sufficient efficacy has been demonstrated to recommend approval of the active substance, tests appropriate for the product type demonstrating sufficient efficacy of the product at the minimum in-use concentration against the proposed target organisms must be provided at product authorisation stage for each relevant application. In this context, the dependence of the efficacy on the respective type of soiling needs to be carefully evaluated as the efficacy of glutaraldehyde is strongly influenced by soiling.

2. To support the full label claim, further tests will be necessary. This especially refers to the label claims "fungicidal", "sporicidal", "mycobactericidal", "algicidal" and "against biofilms".

3. Resistance to glutaraldehyde in certain mycobacteria strains has been reported in hospitals. Resistance development may thus be theoretically possible also in industrial applications and therefore the resistance management strategy is required for the product authorisation. The resistance management measures could include (but should not be restricted to) the following factors: to vary the products used, to use more than one product simultaneously, to alternate treatment regimes and to monitor occurrence of resistance.

4. In some of the submitted tests for PT 11 the control without active substance did not show any growth, showed a reduction or was not tested. Further studies in which the control displays a clear growth during the test have to be submitted for product authorisation stage. Relevant tests (challenge test, field test) with focus on static action are required.

5. Where relevant, a dietary risk assessment will need to be performed at product authorisation.

The active substance glutaraldehyde 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.

2.5. Requirement for further information

Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of glutaraldehyde. However, further data shall be required as detailed below:

1. A new analytical method for the determination of glutaraldehyde in air should be submitted. Data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (eCA).

2. A confirmatory analytical method for the determination of glutaraldehyde in the technical material should be submitted for one of the applicants (BASF). The applicant should also submit an analytical method for determination of impurities in the technical material, or submit adequate validation data on the existing ones including recovery, repeatability, and LOQ. Data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (eCA).

3. Confirmatory methods should be submitted for one of the applicants (Dow) for determination of glutaraldehyde and the impurity in aqueous formulations of glutaraldehyde. Data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (eCA).

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