

Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Glutaraldehyde

Product type: 6

ECHA/BPC/022/2014

Adopted

1 October 2014

Opinion of the Biocidal Products Committee

on the application for approval of the active substance glutaraldehyde for product type 6

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 6 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 23 July 2007 and Dow Benelux B.V. on 27 July 2007, 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 6 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 6 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 6. 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 glutaraldehyde, 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 for preservation of detergents (washing and cleaning fluids) by consumers and professionals, for preservation of paper wet-end additives and paper coatings by professionals and for preservation of drilling and cementing fluids in oil extraction by professionals in product type 6. Glutaraldehyde is needed for microbial control in organic, mineral or pigment slurries during their storage before these slurries are used as fillers or colorants in the paper production. In drilling and cementing fluid glutaraldehyde is used for microbial control to ensure the stability during the storage. Drilling muds are used for the well drilling and cementing fluids are used for mechanical support to sub-surface structures of the well.

Glutaraldehyde is potentially effective against a wide variety of micro-organisms including gram positive and negative bacteria, sulphate reducing bacteria, fungi (yeasts and moulds) and algae. 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, mycobacteria and algae at the intended use concentrations for 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 observation 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 |
| Connecting drum to pump | Primary exposure: professionals, handling container during end-use product formulation | Acceptable with RPE, gloves, double coveralls |
| Loading laundry softener | Primary exposure*: professionals and non-professionals | Acceptable |
| Mixing and loading | Primary exposure*: professionals and non-professionals, mixing and loading liquid dish washing detergent | Acceptable |
| Applying liquid detergent | Primary exposure*: professionals and non-professionals | Acceptable |
| Applying wax emulsion | Primary exposure*: professionals and non-professionals, manual application | Acceptable |
| Applying car polish | Primary exposure*: professionals and non-professionals | Acceptable |
| Manual surface disinfection | Primary exposure*: professionals | Acceptable |
| Loading and unloading slurry tanks | Primary exposure*: professionals | Acceptable with RPE |
| Exposure to laundry softener | Secondary exposure: non-professionals, exposure to laundry softener in clothing contacting with skin | Acceptable |
| Exposure to liquid detergent | Secondary exposure: non-professionals, residues of liquid detergent present on crockery following washing | Acceptable |
| In can preservatives for intermediates used in oil drilling | Primary exposure*: professionals, adding concentrate: connecting/disconnecting feeder system | Acceptable with RPE, gloves, double coveralls |

* Primary exposure to the end-use product treated with glutaraldehyde

For professional and non-professional users exposure to glutaraldehyde was evaluated for the scenarios summarized in the table above. Safe uses were identified when wearing of appropriate personal protective equipment (PPE), including gloves, RPE and double coverall was assumed in most critical scenarios. The potential risk for respiratory sensitization or skin sensitization is covered by the generic concentration limit of 0.1%.

According to the RAC 29 opinion glutaraldehyde is classified as Skin sens. 1A. Several end-use products containing glutaraldehyde (concentration of 0.1%) as PT 6 substance (e.g. laundry detergent, car polish) are treated articles and can be used by the general public.

Products classified as skin sensitizers and containing skin sens 1A classified substance cannot be authorised for the general public (CA-Sept13-Doc6.2a-FinalRev1). Due to glutaraldehyde concentration (0.1 %) end-use products like detergents will be classified as skin sensitizing 1A according to the CLP Regulation. Dermal contact cannot be excluded during the use of these treated articles indicating a major concern for the

general public and thus glutaraldehyde containing biocidal products should not to be used in consumer products.

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 |
| Detergents: Formulation (tonnage) | Waste water emission to STP ¹ . Emissions to surface water, soil and groundwater via STP. | Acceptable |
| Detergents: service life (tonnage) | Waste water emission to STP. Emissions to surface water, soil and groundwater via STP. | Acceptable |
| Detergents: Emission scenario for PT 2 for sanitary purposes | Waste water emission to STP. Emissions to surface water, soil and groundwater via STP. | Acceptable |
| Detergents: Emission scenario for PT 2 for professional detergents | Waste water emission to STP. Emissions to surface water, soil and groundwater via STP. | Acceptable |
| Paper production: Formulation | Waste water emission to STP. Emissions to surface water, soil and groundwater via STP | Acceptable |
| Paper production: Emission scenario for paper wet-end additives and paper coatings | Newsprint: Waste water emission to WWTP ² . Emissions to surface water, soil and groundwater via WWTP. Printing and writing paper: Waste water emission to STP. Emissions to surface water, soil and groundwater via STP. | Acceptable |
| Preservative for drilling muds/fluids | Direct discharge water emission to seawater. | Unacceptable |
| Preservative for cementing fluids | Direct discharge water emission to sea water. | Unacceptable |

¹ STP is a municipal sewage treatment plant with capacity to treat 2000 m³ wastewater per day.

² WWTP is an industrial waste water treatment plant with capacity to treat 5000 m³ wastewater per day.

All evaluated scenarios on detergents and paper production are identified as safe uses. Oilfield uses are considered safe when glutaraldehyde concentrations decrease in drillings muds or cementing chemicals before they are released to water. 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.

Glutaraldehyde is used to preserve various washing and cleaning fluids such as liquid detergents, wax emulsions and car polish which are currently considered as treated articles.

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 products¹. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution

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>)

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 6. In addition, there are several two other active substances intended for use in the same product type already approved or are currently being reviewed under Regulation (EU) No 528/2012.

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 6

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).
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. Glutaraldehyde shall not be used in treated articles, or in biocidal products intended for non-professional users at a concentration equal to or higher than 0.1% unless safe use can be demonstrated by other means than PPE.
6. Where a treated article has been treated with or intentionally incorporates glutaraldehyde, and where necessary due to the possibility of skin contact as well as the release of glutaraldehyde under normal conditions of use, the person responsible for placing the treated article on the market shall ensure that the label provides information on the risk of skin sensitization, as well as the information referred to in the second subparagraph of Article 58(3) of Regulation (EU) No 528/2012.
7. Products shall not be authorized for the preservation of drilling and cementing fluids 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.

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

2. 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.
3. In some of the submitted tests for PT 6 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. Further studies on efficacy of washing and cleaning fluids and paper wet-end additives are required.
4. Where relevant, a dietary risk assessment will need to be performed at product 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.

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).