Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Glyoxal

Product type: 2

ECHA/BPC/239/2020

Adopted

4 March 2020

Opinion of the Biocidal Products Committee

on the application for approval of the active substance Glyoxal 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:	**Glyoxal**
Chemical name:	**1,2-Ethanedial**
EC No.:	**203-474-9**
CAS No.:	**107-22-2**

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 2009, the evaluating Competent Authority France submitted an assessment report and the conclusions of its evaluation to ECHA on June 2019. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-34) and its Working Groups (WG V 2019). Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Adoption of the BPC opinion

Rapporteur: France

The BPC opinion on the approval of the active substance Glyoxal in product type 2 was adopted on 4 March 2020.

The BPC opinion was adopted by simple majority of the members present having the right to vote. The opinion and the minority position including their grounds are 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 Glyoxal 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 Glyoxal in product type 2. Glyoxal acts by crosslinking proteins and nucleic acids essential to microbial life processes which culminate in the death of the cell when the repair mechanism is overwhelmed.

The active substance is manufactured as an aqueous solution of 40% w/w of Glyoxal which is an equilibrium between ethanedial and its di- and trimers with a range of purity of 38.8-40.6%. The di- and trimers are releasing ethanedial when used. Specifications for the reference source are established. There are no relevant impurities.

The physico-chemical properties of the active substance have been evaluated and are deemed acceptable for the appropriate use, storage and transportation.

Validated analytical methods are available for the active substance as manufactured and for the impurities. Analytical methods have been provided for water and air but not sufficiently validated. Validated analytical methods are required for the determination of Glyoxal in air and water. For food and feedstuff, a validated analytical methods is required with a LOQ as low as possible.

A harmonised classification is available according to Regulation (EC) No 1272/2008 (CLP Regulation) for Glyoxal:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox 4 Skin Irrit 2 Eye Irrit 2 Skin Sens 1 Muta 2
Labelling	
Pictogram codes	GHS08 GHS07
Signal Word	Warning
Hazard Statement Codes	H332: Harmful if inhaled H315: Causes skin irritation H319: Causes serious eye irritation H317: May cause an allergic reaction H341: Suspected of causing genetic defects
Specific Concentration limits, M-Factors	-

In addition to the harmonized classification according to Regulation (EC) No 1272/2008 (CLP Regulation), STOT SE 3; H335 (irritating to the respiratory system) is proposed. An

intention was sent to ECHA on 15 January 2020 with an expected date of submission of the CLH dossier in April 2020.

b) Intended use, target species and effectiveness

Glyoxal is used for the disinfection in product type 2. Claimed uses are only intended to be performed by professional users. Glyoxal, being a di-aldehyde, acts by crosslinking proteins and nucleic acids essential to microbial life processes such as membrane integrity, metabolism and replication. When the rate of cross-linking overwhelms the repair mechanisms, cell death occurs.

Basic bactericidal activity of Glyoxal is demonstrated at 20 °C with a contact time of 60 minutes, without interfering substances, at 25 % v/v of Glyoxal as manufactured (40 % Glyoxal in water) i.e 10 % Glyoxal (or 100000 ppm).

The efficacy data demonstrated that the representative product (40 % w/w Glyoxal in water) showed bactericidal activity at the application rate of 25 % v/v of Glyoxal as manufactured i.e 10% v/v Glyoxal in 60 minutes contact time under clean conditions (0.3 g/L BSA[1]) and showed a virucidal efficacy on enveloped virus at the application rate of 12,5 % v/v, i.e 5% v/v Glyoxal, within 120 minutes under clean condition (0.3 g/L BSA).

Another representative product (a formulation with 10 % w/w Glyoxal) was tested in 80 % v/v dilution (i.e. 8 % v/v Glyoxal in the test) and showed bactericidal activity under clean conditions (0.3 g/L) in 60 min contact time.

Microbial resistance to Glyoxal itself has not been reported despite of its use for decades. However, resistance to aldehyde-based active substances has been reported in the literature. The cell surface of the resistant strains has been modified so that there are no or few sensitive reaction sites for aldehyde-based active substances. Resistance development may thus be theoretically possible. This aspect should be reviewed at product authorisation stage if appropriate.

Intended uses

Regarding product type 2 uses, a risk assessment was conducted for the disinfection of small, pre-cleaned areas and equipment, not frequently touched in the following areas and for the following purposes:

- Disinfection of industrial and institutional areas,
- Disinfection for sanitary purposes (industrial/institutional, e.g. tiles),
- Disinfection of instruments (pharmaceutical, cosmetic industry etc.), e.g. by immersion,
- Medical sector: Disinfection of rooms, furniture and objects,
- Medical sector: Disinfection of instruments, e.g. by immersion.

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

Human health

Glyoxal is harmful by inhalation. It induces skin and eye irritation as well as skin sensitization. Glyoxal is suspected of causing genetic effects and classified Muta Cat 2 – H341 according to the CLP regulation. However, based on the available information, it is not possible to conclude on the carcinogenic potential of Glyoxal. These results are in

[1] Bovin serum albumin.

accordance with the harmonised classification presented in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation).

Endocrine disrupting (ED) properties of Glyoxal have been sufficiently investigated and Glyoxal is considered not to have ED properties.

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**
Formulation process Mixing/Loading	*Primary exposure* Dermal and inhalation exposure - Incorporation into end-use disinfectants during automated industrial formulation processes	Industrial workers	Acceptable (only with automated processes and PPE)
Mixing/Loading	*Primary exposure* Dermal and inhalation exposure - Dilution of concentrate for application by spraying (trigger spray), dipping (immersion bath)	Professionals	Acceptable (only with automated processes and PPE)
Application by wiping (RTU)	*Primary exposure* Dermal and inhalation exposure - Application to hard surfaces using single use wiping tissues	Professionals	Not acceptable
Application by spraying	*Primary exposure* Dermal and inhalation exposure - Application of diluted disinfectant using a hand-held trigger (non-aerosol) spray	Professionals	Not acceptable
Application by immersion	*Primary exposure* Dermal exposure - Disinfection of equipment using an immersion bath	Professionals	Acceptable (only with automated processes)
Indirect exposure to treated surfaces and equipment	*Secondary exposure* Dermal and oral exposure - Non-user's exposure when touching the disinfected surfaces considering hand to mouth transfer	General public (adult, toddlers)	Acceptable (only with a rinsing step)

Glyoxal is classified as a Muta Cat 2. Although it is likely that there is a threshold mechanism, the available information does not allow the identification of a threshold. Therefore a qualitative risk assessment has been performed in accordance with the BPR Guidance Volume III Human health parts B and C: Assessment and Evaluation.

Acceptable risk is considered only for uses where automated processes are possible in order to drastically decrease the exposure to the active substance. In this context, the risk related to primary exposure to Glyoxal is considered acceptable for professional users during the disinfection of equipment using an immersion bath.

Moreover, strict Risk Management Measures and Operational Conditions are required to use products containing the active substance as well as appropriate personal protective equipment (gloves, coverall, RPE and eye protection).

Regarding secondary exposure, the risk is considered acceptable for indirect exposure to treated surfaces and equipment by general public only when no contact with the treated surface occurs and when a rinsing step is applied after the use of the product to avoid direct contact with the active substance.

Environment

In water, Glyoxal does not degrade by hydrolysis and photodegradation processes are of less importance. Indeed, the main forms of Glyoxal in aqueous solution are the hydrated monomers which do not essentially adsorb light above 290 nm. In air, Glyoxal rapidly degrades but due to its low evaporation potential, this process is of low relevance for biocide applications. Glyoxal is readily biodegradable. No additional data on degradation is available. Glyoxal has a low potential for adsorption on soil and sediment. Bioaccumulation potential in aquatic and terrestrial organisms is low. Glyoxal is not classified for the environment.

Based on all available data on the potential endocrine disruption of Glyoxal, no EATS-mediated activity nor adverse effects were observed. Glyoxal does not present an endocrine disrupter potential and is not a PBT / vPvB substance.

The table below summarises the exposure scenarios assessed:

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Disinfection of surfaces used in institutional areas by professional users based on tonnage approach	It is likely that the active substance used in each of the use areas will ultimately be discharged to drain and will enter a Sewage Treatment Plant (STP). As a result of this, there will be potential for exposure of the aquatic and the terrestrial compartments, as well as for groundwater, through indirect emissions via contaminated STP sludge.	Acceptable
Disinfection of industrial areas (large scale) by professional users		Acceptable (5 FOCUS PEARL EU scenarios acceptable for groundwater)
Disinfection of industrial areas (small scale) by professional users		Acceptable

Disinfection of institutional areas by professional users		Acceptable
Disinfection of rooms, furniture and objects in medical sector		Acceptable
Disinfection of instruments other than endoscopes in medical sector by dipping		Acceptable (2 FOCUS PEARL EU scenarios acceptable for groundwater)

Uses of Glyoxal do not result in an unacceptable level of risk to the STP, aquatic and terrestrial compartments.

Risks for groundwater are acceptable regarding the disinfection of small scale areas in industry, the disinfection of institutional areas and the disinfection of rooms, furniture and objects in medical sector (concentrations do not exceed the 0.1 µg/L limit set by the EU Drinking Water Directive (98/83/EC) for all FOCUS PEARL EU scenarios).

The $PEC_{groundwater}$ does not exceed the 0.1 µg/L limit only for 2 FOCUS PEARL EU scenarios for the disinfection of medical instruments by dipping and for 5 FOCUS PEARL EU scenarios for the disinfection of large scale industrial areas.

Risks are acceptable with the tonnage based approach for all environmental compartments (STP, aquatic, terrestrial and groundwater).

Overall conclusion

No unacceptable risks for human health and environment are identified considering the disinfection by dipping of the equipment via immersion bath, only when automated processes are applied for the mixing and loading phase as well as for application; appropriate personal protective equipment (gloves, coverall, RPE and eye protection) are worn during mixing and loading; and when rinsing of the equipment after immersion is performed.

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[a]	Glyoxal does not fulfil criterion (a), (b) and (c) of Article 5(1).
	Mutagenicity (M)	Muta 2	
	Toxic for reproduction (R)	No classification required	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	Not P or vP	Glyoxal 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)	Not T	

Endocrine disrupting properties	Section A of Regulation (EU) 2017/2100: ED properties with respect to humans	No	Glyoxal does not fulfil criterion (d) of Article 5(1) and criterion (b) of Article 10(1).
	Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms	No	
	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. Glyoxal does not fulfil criterion (d) of Article 5(1).		
Concerns linked to critical effects other than those related to endocrine disrupting properties	Glyoxal does not fulfil criterion (e) of Article 10(1).		
Proportion of non-active isomers or impurities	Not relevant. Glyoxal does not fulfil criterion (f) of Article 10(1).		
[a] based on the available information it was not possible to conclude on the carcinogenic potential of Glyoxal. Consequently, the information presented in the assessment did not trigger classification for carcinogenicity.			

Consequently, the following is concluded:

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

Glyoxal 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.

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"[2], "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[3] and "Implementation of scientific criteria to determine the endocrine –disrupting properties of active substances currently under assessment[4]" 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).

[2] 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).

[3] 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).

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

2.2.2. POP criteria

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

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

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

1. The active substance as manufactured is an aqueous solution of 40% w/w of Glyoxal. The range of purity of the active substance evaluated is 38.8-40.6% w/w of Glyoxal (equilibrium between ethanedial and its di- and trimers) in the solution.
2. The authorisations of biocidal products are subject to the following condition(s):
    a. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.
    b. In view of the risks identified for the uses assessed, the product assessment shall pay particular attention to:
        i. professional users;
        ii. the general public;
        iii. environment: groundwater.
3. The person responsible for the placing on the market of a treated article treated with or incorporating the active substance Glyoxal 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.

The active substance does not fulfil the criteria according to Article 28(2) to enable inclusion in Annex I of Regulation (EU) 528/2012 as Glyoxal gives rise to the following concerns: it is classified as suspected of causing genetic defects (Muta Cat 2) skin irritant (Skin Irrit 2), skin sensitizer (Skin Sens 1), eyes irritant (Eye Irrit 2) and it shows an acute toxicity by inhalation (Acute Tox 4).

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 industrial and/or professional users, safe operational procedures and appropriate organizational measures shall be established. Products shall be used with appropriate personal protective equipment and automated processes where exposure cannot be reduced to an acceptable level by other means.
    b. An unacceptable risk for general public in contact with treated surfaces and equipment is identified. The risk can be mitigated if treated surfaces are rinsed after treatment and access is restricted to treated surfaces until the surface has

fully dried after rinsing. However, if the risk cannot be reduced to an acceptable level by appropriate risk mitigation or by other means, these uses should not be authorised. Efficacy of the rinsing step has to be demonstrated.

c. An unacceptable risk for groundwater is identified for certain scenarios. If the risk cannot be reduced to an acceptable level by appropriate risk mitigation measures or by other means, these uses should not be authorised.

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 Glyoxal. However, the following further data must be submitted to the evaluating Competent Authority (FR) as soon as possible but no later than 6 months before the date of approval of the active substance:

- Analytical methods have been provided for the determination of Glyoxal in water and air but not sufficiently validated. A fully validated analytical method for the determination of Glyoxal (equilibrium between ethanedial and its di- and trimers) in water and in air with an adequate LOQ should be provided. In addition, sufficient information should be submitted to determine the background concentration in water.
- As the exposure of food and/or feedstuffs cannot be excluded, a validated analytical method for the determination of Glyoxal in food and feedstuff is required with a LOQ as low as possible. In addition, sufficient information should be submitted to determine the background concentration in food and/or feedstuff.

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