Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

1,2-BENZISOTHIAZOL-3-(2H)-ONE (BIT)

Product type: 13

ECHA/BPC/287/2021

Adopted

5 October 2021

Opinion of the Biocidal Products Committee

on the application for approval of the active substance 1,2-BENZISOTHIAZOL-3-(2H)-ONE (BIT) for product type 13

In accordance with Article 90(2) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products (BPR), the Biocidal Products Committee (BPC) has adopted this opinion on the approval in product type 13 of the following active substance:

Common name:	**BIT (Benzisothiazolinone)**
Chemical name:	**1,2-Benzisothiazolin-3-one**
EC No.:	**220-120-9**
CAS No.:	**2634-33-5**

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 applications by Lanxess, Troy Chemical Company BV, Rohm and Haas (currently Nutrition & Bioscience (Switzerland) GmbH) and the Task Force (Arch&Clariant&Thor), currently EBITTF (THOR GmbH, Laboratorios Miret, S.A. and Lonza Cologne GmbH) on 12 July 2007, the evaluating Competent Authority Spain submitted an assessment report and the conclusions of its evaluation to the Commission in March 2012. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC Working Groups (WG-V-2015 and WG-II-2021). Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Adoption of the BPC opinion

Rapporteur: Spain

The BPC opinion on the application for approval of the active substance 1,2-Benzisothiazolin-3-one in product type 13 was adopted on 5 October 2021.

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 1,2-Benzisothiazol-3-(2H)-one (BIT) EC No. 220-120-9; CAS No. 2634-33-5 in product type 13 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 1,2-Benzisothiazol-3-(2H)-one (BIT)in product type 13. BIT belongs to the chemical class of isothiazolinones and 1is used against a wide range of microbes. BIT belongs to the chemical class of isothiazolinones.

Specifications for the reference source are established.

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

Validated analytical methods are available for the active substance as manufactured and for the relevant and significant impurities. Validated analytical methods are available for soil, air, water, and sediment.

Harmonised classification for 1,2-Benzisothiazolin-3-one is available. A proposal has been submitted to ECHA to change this classification, as indicated below.

The current entry for 1,2-Benzisothiazolin-3-one according in Annex VI of Regulation (EC) No 1272/2008 (CLP Regulation) is:

Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 4 Skin Irrit. 2 Eye Dam. 1 Skin Sens. 1 Aquatic Acute 1
Labelling	
Pictogram codes	GHS07 GSH05 GHS09
Signal Word	Dgr
Hazard Statement Codes	H302 Harmful if swallowed H315 Causes skin irritation H318 Causes serious eye damage H317 May cause an allergic skin reaction H400 Very toxic to aquatic life

Specific Concentration limits, M-Factors	Skin Sens. 1; H317: C ≥ 0,05 %

The proposed classification and labelling for 1,2-Benzisothiazolin-3-one according to CLP Regulation is:

Proposed Classification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 4 Acute Tox. 2 Eye Dam. 1 Skin Sens. 1B Aquatic Acute 1 Aquatic Chronic 1
Labelling	
Pictogram codes	GHS06 GHS05 GHS09
Signal Word	Dgr
Hazard Statement Codes	H302 Harmful if swallowed H330 Fatal if inhaled H318 Causes serious eye damage H317 May cause an allergic skin reaction H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting efects
Specific Concentration limits, M-Factors	Oral: ATE = 454 mg/kg Inhalation: ATE = 0.25 mg/L Skin Sens. 1B; H317: SCL ≥ 0.05 % M=1(Aquatic Acute 1) M=1 (Aquatic Chronic 1)
Justification for the proposal	
Although this biocidal active substance has a current entry in Annex VI of CLP regulation, it is necessary to update the current human health and environmental hazards due to differences in acute toxicity, skin irritation, skin sensitization and aquatic chronic hazards, as well as, its ATEs and M-Factors with the current harmonised classification.	

b) Intended use, target species and effectiveness

The active substance is intended to be used by professionals in the metal industry, in different working sectors, as follows:

- Blast furnaces: production of steel;
- Iron foundry: moulding of steel into half or end products;
- Rolling mills: rolling of steel to half products to be used by the steel production industry;

- Metal forming: forcing of metal products in the shape of the end product;
- Metal cutting: creation of products by cutting away chips of the product;
- Galvanic industry: application of protective metal coatings to metal products.

BIT is a broad spectrum antimicrobial biocide which exhibits rapid inhibition of growth at very low levels and biocidal effects at higher levels or for longer contact periods. Given this relationship between concentration and effect, BIT may function as a bactericide, bacteriostat, fungicide, and fungistat, depending on the dose level applied, system conditions, and the level of microbial control desired. BIT is most active as a bactericide, but does show antifungal activity at higher use levels.

The rates of the active ingredient for PT13 uses are: 1500-9000 ppm BIT for metal working fluid concentrate and 100-360 ppm BIT for metal working tank additive.

The mechanism of action of BIT involves reaction with protein-thiol targets, including specific dehydrogenase and phosphatase enzymes, affecting a variety of metabolic processes within the cell. Developing resistance to multiple targets simultaneously by microorganisms is very difficult and cells have to expend significant amounts of energy to repair and modify the various BIT targets and repair the damage from the radicals while their overall metabolic processes and energy systems are shut down. This explains why it is difficult for cells to become resistant to biocides like BIT. Nevertheless, as microbial resistance to BIT has been described in the literature, special attention should be given at the product authorization stage.

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

Human health

BIT is an isothiazolinone harmful if swallowed and toxic if inhaled. BIT may cause serious damage to the eye. Skin sensitization was observed in test animals and humans.

The critical endpoints for BIT are driven by its local toxicity: skin sensitisation for the dermal route, respiratory tract irritation for the inhalation route and stomach irritation for the oral route. A local risk assessment is therefore required for these effects. Unspecific systemic effects are also seen with BIT but at much higher dose levels. Systemic AELs have been derived and a systemic risk assessment performed to supplement the local risk assessments.

After evaluating the exposure and characterizing the risk to human health of the biocidal products and treated articles according to the pattern of use requested by the applicant, the conclusions for each scenario are:

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Loading	**Primary exposure** Automatic loading of the biocidal product to prepare the MWF-concentrate PPE: new gloves for each work shift, impermeable coverall and goggles/face mask RMM for medium hazard class chemicals (labelling, instructions for use, child proof closure, packaging minimising risk	Industrial / professional workers	Acceptable with PPE and RMM

Summary table: human health scenarios			
	for exposure)		
Loading	**Primary exposure** Manual loading of the biocidal product to prepare the MWF-concentrate PPE: protective gloves, impermeable coverall and goggles/face mask RMM for medium hazard class chemicals	Industrial / professional workers	Acceptable with PPE and RMM
Mixing/loading	**Primary exposure** Mixing/loading of the MWF-concentrate PPE: protective gloves, impermeable coverall and goggles/face mask RMM for medium hazard class chemicals (labelling, instructions for use, child proof closure, packaging minimising risks for use)	Industrial / professional workers	Acceptable with PPE and RMM
Application	**Primary exposure** Metal working fluids on turning machine PPE: impermeable coverall RMM for medium hazard class chemicals (labelling, instructions for use, child proof closure, packaging minimising risk for exposure)	Industrial / professional workers	Acceptable with PPE and RMM
Application	**Primary exposure** Handling of work pieces, tools outside the turning machine PPE: new gloves for each work shift and impermeable coverall RMM for medium hazard class chemicals (labelling, instructions for use, child proof closure, packaging minimising risk for exposure)	Industrial / professional workers	Acceptable with PPE and RMM
Maintenance	**Primary exposure** Machine/sump maintenance PPE: protective gloves and coated coverall RMM for medium hazard class chemicals (labelling, instructions for use, child proof closure, packaging minimising risk for exposure)	Industrial / professional workers	Acceptable with PPE and RMM

The population groups expected to be exposed to BIT PT13 are industrial and professional users.

Secondary exposure is not relevant for the industrial use of BIT in MWF as the metals are further used by professionals or in industry when the processed metals were cleaned and risk assessment for consumers via residues in food and animal health is not foreseen.

Concerning the systemic effects, acceptable risks were identified for industrial and for primary exposure, when PPE and RMM are used, as indicated in the Summary Table: Human health scenarios.

Concerning local effects, and with regard to primary exposure, a qualitative assessment for sensitization has been undertaken in accordance with current guidance. This identified acceptable risks for all scenarios as long as appropriate PPE (Substance/task appropriate gloves, Skin coverage with appropriate barrier material based on potential for contact with chemicals and Eye protection) are worn and appropriate engineering controls (fully automated processes, good ventilated areas) are in place for professionals

Concerning local effects, a qualitative assessment for sensitization has been undertaken in accordance with current guidance. This identified acceptable risks for all scenarios as long as technical and organizational RMM adequate for medium hazard chemicals (labelling, instructions for use, child proof closure, packaging minimising risk for exposure) and appropriate PPE (Substance/task appropriate gloves, Skin coverage with appropriate barrier material based on potential for contact with chemicals and Eye protection) are used.

All scenarios resulted in acceptable risk.

Environment

BIT shows rapid photolysis (DT50 of 2 hours) in the aquatic environment over a wide range of environmentally relevant pH values. It is stable to hydrolysis at pH 4, 7 and 9 with a half-life greater than 1 year. Given the low VP (3.02×10^{-3}– 6.3×10^{-5} Pa at 20ºC) and slight water solubility (ca. 1.2 g/L at 20ºC and pH 7), the concentration of BIT in the air is expected to be low. For biotic degradation, BIT was shown to be non ready biodegradable. Simulation tests show very short half-lives of BIT which transforms into several metabolites. In aquatic systems with estuarine and sea water, BIT can be degraded rapidly with half-lives at 12ºC of 0.95 and 1.24 days in estuarine water and 5-12 days in sea water. In soil BIT degrades very fast with DT50 < 1 day

BIT has a log K_{ow} = 0.7 and its potential for bioaccumulation is very low. The experimental (not normalised) BCF for fish of 6.9 L/Kg_{wwt} led to similar conclusions, even with a non-reliable test result. BIT koc = 196.87kg/L showing medium or moderate adsorption properties.

For acute toxicity algae were the most sensitive trophic level with a 24-hour ErC50 value = 0.108 mgBIT/L based on the geomean (four studies) of P.subcapitata endpoints. Again algae were demonstrated to be the most sensitive trophic level regarding long-term effects with a 24-hour ErC10 of 0.026 mg BIT/L (geomean *P. subcapitata*). Endocrine acticity could not be sufficiently investigated for the environment. Yet, it is unlikely that BIT accomplishes such properties although no conclusion can be reached.

The evaluation of the exposure and characterization of the risk to the environment of the biocidal products have been performed according to the pattern of use requested by the applicant.

Due to the physico-chemical properties of BIT and its rapid degradation in surface waters, it may be expected that this active substance will not partition into sediment to a significant extent and therefore the exposure to this compartment has not been included in the assessment, taking into account BPR Guidance Parts B+C, Vol IV, 2017, section 3.5.2.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Preservative for water miscible metalworking fluids by industrial users	Emission to sewage treatment plant and indirect emissions via STP to surface water, soil and groundwater.	Based on the risk assessment on STP and surface waters unacceptable risks were identified for BIT. Some RMMs are currently available and can be used, leading to acceptable risks.

As mentioned before, for STP and surface waters, unacceptable risks have been identified. Nevertheless, the approval could be possible if at least one biocidal product containing that active substance could meet the criteria laid down in point (b) of Article 19(1) of BPR No 528/2012, taking into account the factors set out in Article 19(2) and (5). This is to be expected as long as the MWF waste containing BIT can be processed in such a way that little or no exposure to the aquatic compartment is expected, with a BIT reduction in the water phase of such waste above 85%, by applying some risk mitigation measures and provided a RCR below 1 is obtained.

The applicants have submitted several documents that prove the possibility of establishing some risk mitigation measures to reduce BIT content in the MWF waste. These risk mitigation measures include the separation from the oil phase and the water phase from the emulsion. An external management company must treat the oil phase. Applying some treatments to the water phase could achieve a BIT deactivation/degradation above 85% in the water phase:

- Isothiazolinones can be deactivated by an organic thiol or by a neutralization/ inactivation agent such as sodium glycolate;
- Degradation of BIT by sodium thiosulphate or potassium mono persulphate and potassium peroxydisulphate has been analysed by one of the applicants with a BIT degradation above 85% in water;
- Photodegradation of BIT under UVC irradiation achieves more than 90% BIT degradation;
- BIT degraded rapidly due to the ozonation effects. Ozonation markedly decreased the toxic effects of BIT on zebrafish embryos due to less toxicity of oxidized products;
- The concentration of BIT in the waste of MWFs collected in a metalworking shop was below the limit of detection (0.67 mg/L) in all samples, from an initial BIT concentration of around 100 ppm.

Overall conclusion

All human health scenarios resulted in acceptable risk and secondary exposure is not relevant for the industrial use of BIT in MWF. Regarding environment, risk mitigation measures are available to reduce the identified risks to an acceptable level. Treatments to the water phase should achieve a BIT deactivation/degradation above 85% in the water phase to ensure a safe use. Therefore, it could be demonstrated that the evaluated use is safe.

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	1,2-Benzisothiazolin-3-one 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)	not P or vP	BIT 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	BIT does not fulfil criterion (d) of Article 5(1) No conclusion can be drawn whether BIT fulfils criterion (e) of Article 10(1)
	Section B of Regulation (EU) 2017/2100: ED properties with respect to non-target organisms	No conclusion can be drawn	
	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. BIT does not fulfil criterion (b) of Article 10(1)		
Concerns linked to critical effects other than those related to endocrine disrupting properties	BIT does not fulfil criterion (e) of Article 10(1)		
Proportion of non-active isomers or impurities	BIT does not fulfil criterion (f) of Article 10(1)		

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], with "Further guidance on the application of the substitution criteria set out under Article 10(1) of the BPR"[2] and with "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).

Consequently, the following is concluded:

- 1,2-Benzisothiazolin-3-one does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012;
- 1,2-Benzisothiazolin-3-one 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.

According to the Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009, EATS-mediated adversity and endocrine activity have been sufficiently investigated for human health, but not for environment where additional information should be requested. Consequently, for the endocrine-disrupting properties as defined in Regulation (EU) No 2017/2100, no conclusion can be drawn for environment 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 BIT for PT 13 was submitted before 1 September 2013.

2.2.2. POP criteria

Regarding POPs criteria, due to its very low vapor pressure and Henry constant, the release of BIT to the atmosphere will be negligible.

2.3. BPC opinion on the application for approval of the active substance 1,2-Benzisothiazolin-3-one in product type 13

In view of the conclusions of the evaluation, it is proposed that 1,2-Benzisothiazolin-3-one 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:
   a. The active substance BIT, as manufactured, shall have a minimum purity of 965 g/kg (theoretical calculated dry weight).

2. The authorisations of biocidal products are subject to the following condition(s):

[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/ui/group/e947a950-8032-4df9-a3f0-f61eefd3d81b/library/48320db7-fc33-4a91-beec-3d93044190cc/details).

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. industrial or professional users.

   ii. Surface water, the sewage treatment plant (STP), and sediment.

BIT cannot be included in Annex I of Regulation (EU) No 528/2012 because it meets the criteria of Article 28(2) (a) as it is classified as H330 (Acute Tox. 2) and H317 (Skin Sens. 1B).

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. Some situations of resistance with BIT have been described in the literature and therefore before authorizing products, Member States should pay attention to possible occurrence of resistance.

   b. Biocidal products that trigger classification as skin sensitisers shall be used with appropriate personal protective equipment where exposure cannot be reduced to an acceptable level by other means.

   c. An unacceptable risk for surface water and STP has been identified. 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. Treatments to the water phase should achieve a BIT deactivation/degradation above 85% to ensure a safe use.

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 1,2-Benzisothiazolin-3-one (BIT).

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