Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

MBIT

Product type: 13

ECHA/BPC/140/2016

Adopted

16 December 2016

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

Opinion of the Biocidal Products Committee

on the application for approval of the active substance MBIT 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 non-approval in product type 13 of the following active substance:

Common name:	MBIT
Chemical name:	2-Methyl-1,2-benzisothiazol-3(2H)-one
EC No.:	-
CAS No.:	2527-66-4
New 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 Rohm and Haas Europe Trading ApS on 26 November 2009, the evaluating Competent Authority Poland submitted an assessment report and the conclusions of its evaluation to ECHA on 24 March 2016. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-18) and its Working Groups (WG-IV-2016). Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

Adoption of the BPC opinion

Rapporteur: Poland

The BPC opinion on the non-approval of the active substance MBIT in product type 13 was adopted on 16 December 2016.

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 MBIT in product type 13 may not 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 MBIT in product type 13. MBIT (chemical class isothiazolinones) acts by a two step mechanism, which involves rapid inhibition of microbial growth and metabolism followed by irreversible cell damage resulting in loss of cell viability. Growth inhibition is the result of rapid disruption of respiration (oxygen uptake) and enzyme activity (alcohol dehydrogenase). The dehydrogenase class of enzymes plays a critical role in metabolic pathways, which provide key precursor substrates for the Krebs cycle. Certain isothiazolinones (CMIT and BIT) were shown to inhibit ATP synthesis and produce free radicals within cells after contact with the biocide. Although ATP and free radicals were not directly tested versus MBIT, given the similarity of mechanism of action of the various isothiazolinones tested, it is reasonable to assume MBIT also impacts ATP pools in microorganisms and generates cidal intracellular radicals. This feature of its mode of action would thereby significantly affect the potential of the cells to maintain the energy balance required for growth, nutrient metabolism, biosynthesis and repair of excess damage.

The active substance is obtained by chemical synthesis. 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 product.

Analytical methods are available for the active substance as manufactured, for the relevant and significant impurities and the relevant matrices soil, water and air.

A harmonised classification for MBIT is not available and the active substance is not listed in Annex VI of the Regulation (EC) No 1272/2008. A CLH dossier will be submitted to ECHA at the beginning of 2017.

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

Proposedclassification according to the CLP Regulation	
Hazard Class and Category Codes	Acute Tox. 3, H301 Acute Tox. 4, H332 Acute Tox. 4, H312 Skin Corr. 1B, H314 Eye Dam. 1, H318 Skin Sens. 1A, H317 Aquatic Acute 1, H400 Aquatic chronic 2, H411
Labelling	
Pictogram codes	GHS05 GHS06 GHS09

Signal Word	Danger
Hazard Statement Codes	H301: Toxic if swallowed H332: Harmful if inhaled H312: Harmful in contact with skin H314: Causes severe skin burns and eyes damage H317: May cause an allergic skin reaction H410 Very toxic to aquatic life with long lasting effects
Specific Concentration limits, M-Factors	M = 1 (Aquatic acute)
Justification for the proposal	
H301: Based on oral LD_{50} in female rats = 175 mg/kg body weight H332: Due to the absence of mortality and complete lack of clinical findings observed in the acute inhalation study at 2.22 mg/L of product (0.53 mg/l of MBIT). H312: 1000 mg/kg/d < LD_{50} for MBIT <2000 mg/kg/d. H314: Based on skin irritation study where at one of rabbits' skin necrosis was observed. H317: Based on skin sensitisation study where MBIT is a skin sensitizer at 1800 ppm a.s.; EC_3 = 10455 ppm and 6900 ppm. H400: Based the 48 hours ErC50 of 0.24 mg/l from the *Pseudokierchneriella subcapiata* study and 96h LC_{50} of 0.24 mg/L for *Oncorhynchus mykiss.* H411: Based the 48 hours NOErC of 0.012 mg/l from the *Pseudokierchneriella subcapiata* and the substance being rapidly biodegradable. Taking into account that the simulation tests show rapid primary biodegradation of MBIT in the environment and the degradation products N-Methyl-2-(methylthio)-benzamide, 2-(methylcarbamoyl)- benzene sulfonic acid and 2-carbamoyl- benzene sulfonic acid are not classified as hazardous to the environment it can be concluded that MBIT is rapidly degradable for the purposes of aquatic hazard classification.	

b) Intended use, target species and effectiveness

MBIT biocide is active against a wide variety of microorganisms (bacteria, fungi) over a broad range of environmental conditions that occur within metalworking fluid systems. These systems include but are not limited to the metalworking fluids and metal cleaning fluids. MBIT biocidal products in PT 13 are used exclusively by professionals or industrial users. A single dose of biocides containing MBIT preserves metalworking fluids up to about 5-6 weeks. Products containing MBIT should be added to the diluted fluids or concentrate prior to dilution fluids.

The action of MBIT against target organisms is based on a two step mechanism, which involves rapid inhibition of growth and metabolism followed by irreversible cell damage resulting in loss of viability. Its mode of action significantly affect the potential of the cells to maintain the energy balance required for growth, nutrient metabolism, biosynthesis, and repair of excess damage (from overproduction of radicals). All these processes are essential in bacteria and fungi, which explains why MBIT is such a broad-spectrum biocide.

The data on MBIT and the representative biocidal products have demonstrated sufficient efficacy against bacteria and fungi. The efficacy of MBIT against bacteria and fungi has been proven for application rates between 75 to 300 ppm of active ingredient, related to target organism.

The mechanism of action of MBIT involves rapid inhibition of growth, respiration, and thiol-containing dehydrogenase 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 MBIT 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 MBIT. Using MBIT in combination or rotation with other biocides may help to avoid the potential risk of developing resistance.

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

Human health

MBIT is corrosive to the skin and eyes. Data from studies in animals show that MBIT is also a skin sensitiser. The critical endpoints for MBIT are driven by its local toxicity, therefore a local risk assessment was carried out. The apparent systemic effects of MBIT, are considered secondary to local effects. Nonetheless, a systemic risk assessment was performed to supplement the local risk assessments.

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**
Manual mixing and loading	**Primary exposure to biocidal product or MWF with concentrate:** metalworking fluid is preserved by either the direct addition of the biocide product (25 % of MBIT) itself or by the addition of a metalworking fluid concentrate containing the biocidal active substance. End-use concentration of MBIT in metalworking fluid is 75 to 300 ppm. Dermal and inhalation exposure. PPE: gloves and coated coveralls	Professionals	Acceptable with PPE
Application	**Primary exposure to preserved MWF:** the metalworking process includes machine set-up, machine operation and work piece removal operating the machines, handling objects wetted with MWF. Dermal and inhalation exposure. PPE: no PPE	Professionals	Acceptable
Post application – sump maintenance	**Primary exposure to preserved MWF:** the inspection of the sump fluid, removal of excess swarf and general machine maintenance. Dermal and inhalation exposure. PPE: at least gloves and coated coveralls	Professionals	Acceptable with PPE
Laundering contaminated clothing at home	**Secondary to biocidal product or MWF with concentrate:** adult laundering contaminated work clothing at home. Dermal exposure. PPE: no PPE	General public	Acceptable

Product specific data showed that the representative product containing 25% MBIT is damaging to the eyes, but is not a skin irritant or a skin sensitiser. All primary and secondary exposures of professionals are acceptable. During mixing and loading and post-application (sump maintenance) phases appropriate PPE (gloves and coated coveralls) are necessary to reduce exposure via the dermal route.

General public may be exposed to the product during laundering contaminated work clothing at home. This exposure scenario is considered acceptable.

Based on assessment of the scenarios listed above, it is concluded that exposure levels of professionals and general public are acceptable.

Environment

The main emission route of MBIT through its use in the representative biocidal product is via wastewater to sewage treatment water plants (STP) and subsequent release via effluents to surface water and sediment, and then via sludge application to soil and groundwater. There are no direct emissions to surface water or sediment.

Exposure of the environment via the atmosphere is considered to be neglible. In addition secondary poisoning is not assessed due to the low bioaccumulative potential of the substance.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
On-site wastewater treatment scenario 300 ppm of MBIT Fconc =0.05*	Emission to sewage treatment plant (STP). Release via STP to surface water and sediment. Release via application of sludge from STP to soil and groundwater.	Acceptable risk for STP and soil Unacceptable risk for surface water (MBIT) and groundwater (metabolites)
On-site wastewater treatment scenario 300 ppm of MBIT Fconc =0.2*		Acceptable risk for STP and soil Unacceptable risk for surface water (MBIT) and groundwater (metabolites)
External wastewater treatment scenario 300 ppm of MBIT Fconc =0.05*		Acceptable risk for STP and soil Unacceptable risk for surface water (MBIT) and groundwater (metabolites)
External wastewater treatment scenario 300 ppm of MBIT Fconc =0.2*		Acceptable risk for STP, surface water and soil Unacceptable risk for groundwater (metabolites)
On-site wastewater treatment scenario 75 ppm of MBIT Fconc =0.05*		Acceptable risk for STP and soil Unacceptable risk for surface water (MBIT) and groundwater (metabolites)
On-site wastewater treatment scenario 75 ppm of MBIT Fconc =0.2*		Acceptable risk for STP, surface water and soil Unacceptable risk for groundwater (metabolites)
External wastewater treatment scenario 75 ppm of MBIT Fconc =0.05*		Acceptable risk for STP, surface water and soil Unacceptable risk for groundwater (metabolites)
External wastewater treatment scenario 75 ppm of MBIT Fconc =0.2*		Acceptable risk for STP, surface water and soil Unacceptable risk for groundwater (metabolites)

* Water fraction of concentrate in diluted metalworking fluid for dilution rate 1:5 (Fconc = 0.2) and 1:20 (Fconc = 0.05).

MBIT and its metabolites do not pose unacceptable risks for STP micro-organisms and soil.

In all scenarios with the highest (300 ppm) concentration of MBIT an unacceptable risk to surface water is identified, except for "External treatment scenario with F_{conc} of 0.2". In the lowest, but still efficaceous concentration of MBIT (75 ppm), the risk related to MBIT in surface water is in all scenarios acceptable with one exception: "On-site treatment scenario with F_{conc} of 0.05", where PEC/PNEC is slightly above 1.

MBIT metabolites do not pose an unacceptable risk for surface water.

Due to behaviour and physico-chemical properties of MBIT and its metabolites, sediment is an irrelevant environmental compartment for these substances.

No unacceptable risk is identified for MBIT in groundwater. In general, leaching of this active substance to groundwater is not to be expected because of its rapid biodegradation in soil. However, an unacceptable risk is identified in all scenarios for three metabolites (Metabolite #1, #2 and #3) as the estimated groundwater concentrations exceed the limit of 0.1 µg/L. These risks are identified for application of sludge on arable lands as well as grassland.

Overall conclusion

Acceptable risks were identified for human health provided adequate PPE is worn for mixing and loading and post-application for professionals. However, for the environment unacceptable risks were identified for all scenarios for groundwater.

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:

<table>
<tr><th colspan="2">Property</th><th colspan="2">Conclusions</th></tr>
<tr><td rowspan="3">CMR properties</td><td>Carcinogenicity (C)</td><td>No classification required</td><td rowspan="3">MBIT does not fulfil criterion (a), (b) and (c) of Article 5(1)</td></tr>
<tr><td>Mutagenicity (M)</td><td>No classification required</td></tr>
<tr><td>Toxic for reproduction (R)</td><td>No classification required</td></tr>
<tr><td rowspan="3">PBT and vPvB properties</td><td>Persistent (P) or very Persistent (vP)</td><td>not P or vP</td><td rowspan="3">MBIT does not fulfil criterion (e) of Article 5(1) and does not fulfil criterion (d) of Article 10(1)]</td></tr>
<tr><td>Bioaccumulative (B) or very Bioaccumulative (vB)</td><td>not B or vB</td></tr>
<tr><td>Toxic (T)</td><td>not T</td></tr>
<tr><td>Endocrine disrupting properties</td><td colspan="3">MBIT is not considered to have endocrine disrupting properties. MBIT does not fulfil criterion (d) of Artcile 5(1).</td></tr>
<tr><td>Respiratory sensitisation properties</td><td colspan="3">No classification required. MBIT does not fulfil criterion (b) of Article 10(1).</td></tr>
<tr><td>Concerns linked to critical effects</td><td colspan="3">MBIT does not fulfil criterion (e) of Article 10(1).</td></tr>
<tr><td>Proportion of non-active isomers or impurities</td><td colspan="3">MBIT does not fulfil criterion (f) of Article 10(1).</td></tr>
</table>

Based on ecotoxicological data the metabolites of MBIT are not toxic or bioaccumulative. Metabolite #2 and Metablite #3 are also not persistent. Metabolite #1 should be considered as potentially persistent or very persistent, however as it can consequently meet only 1 out of the 3 PBT criteria, a further clarification of it's P status is not required.

Consequently, the following is concluded:

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

MBIT 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"[1] and in line with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[2] agreed at the 54th and 58th 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).

2.2.2. POP criteria

MBIT and its metabolites do not meet the criteria for being persistent organic pollutants.

2.3. BPC opinion on the application for approval of the active substance MBIT in product type 13

In view of the conclusions of the evaluation, it is proposed that MBIT shall not be approved as no safe use could be demonstrated: an unacceptable risk is identified for groundwater as the concentrations of several metabolites (Metabolite #1, #2 and #3) exceed the limit of 0.1 µg/L. The BPC considered if further data could be requested to refine the risk assessment for groundwater for the metabolites. However, as a safe use needs to be demonstated based on the data available in the application this was not considered an option by the BPC noting the possibilities for the submission of additional information during the evaluation and during the peer review after the submission of the assessment report and the conclusions of its evaluation by the evaluating Competent Authority[3]. It is therefore concluded that biocidal products containing MBIT as an active substance may not be expected to meet the criteria laid down in point (b) of Article 19(1)(b)(iv). Consequently, it is proposed that MBIT in product-type 13 shall not be approved and included in the Union list of approved active substances.

MBIT does not fulfil the criteria according to Article 28(2)(a) to enable inclusion in Annex I

[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] Reference is made to the document "Introducing new information during the peer review process of active substance approval" agreed at BPC-13 and published at https://echa.europa.eu/documents/10162/4221979/peer_review_info_jan2016_en.pdf/7fbb63d5-b7e8-472b-b166-5ced176af87d.

of Regulation (EU) 528/2012 as MBIT gives rise to the following concerns: it is classified as skin sensitizer (Skin Sens. 1A), corrosive (Skin Corr. 1B, Eye Dam. 1), and toxic to aquatic life (Aquatic Acute 1, Aquatic Chronic 2).

o0o