Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

N,N-Methylenebismorpholine

Product type: 13

ECHA/BPC/028/2014

Adopted

3 October 2014

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Opinion of the Biocidal Products Committee

on the application for approval of the active substance N,N-Methylenebismorpholine for product type 13

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 13 of the following active substance:

Common name:	**N,N-Methylenebismorpholine;**
	4,4'-Methylenedimorpholine;
	Dimorpholinomethane
Chemical name(s):	**N,N-Methylenebismorpholine**
EC No.:	**227-062-3**
CAS No.:	**5625-90-1**
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 Lubrizol Deutschland GmbH, Metalworking Additives on 1st August 2007, the evaluating Competent Authority Austria submitted an assessment report and the conclusions of its evaluation to the Commission on 25 July 2013. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC and its Working Groups. 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/addressing-chemicals-of-concern/biocidal-products-regulation/potential-candidates-for-substitution-previous-consultations* on 10 February 2014, 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 11 April 2014.

Adoption of the BPC opinion

Rapporteur: BPC member for Austria

The BPC opinion on the approval of the active substance N,N-Methylenebismorpholine (MBM) in product type 13 was adopted on 3 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 N,N-Methylenebismorpholine (MBM) 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 MBM in product type 13. 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 and materials suitable for storage and transport of the active substance and biocidal product.

Validated analytical methods are available for the active substance as manufactured and for the relevant and significant impurities.

Classification of active substance: no harmonised classification is available. A CLH dossier was submitted to ECHA and the discussion in RAC is scheduled for June 2015.

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

Proposed classification according to the CLP Regulation	
Hazard Class and Category Codes	Skin Corr. 1B, H314 Skin Sens. 1, H317 Carc. 1B, H350 Muta 2, H341
Labelling	
Pictograms	GHS05, GHS07, GHS08
Signal Word	Danger
Hazard Statement Codes	H314: Causes severe skin burns and eye damage H317: May cause an allergic skin reaction H350: May cause cancer H341: Suspected of causing genetic defects
Specific Concentration limits, M-Factors	M = not applicable
Justification for the proposal	
MBM hydrolyses to formaldehyde and morpholine upon contact with biological tissues. Morpholine is classified only for skin corrosion and acute toxicity due to local effects. The toxicity of MBM is related to the toxicity of formaldehyde: local skin (and eye) corrosive effects, skin sensitization, local genotoxicity and local carcinogenicity. Toxicological data for carcinogenicity are read across from formaldehyde to MBM. For environmental effects C&L according to Regulation (EC) No 1272/2008, Annex VI, Table 3.1 and Regulation (EU) No 286/2011 is not necessary, since neither the active substance (MBM), nor the hydrolysis products (formaldehyde and morpholine) fulfil the classification and labelling criteria.	

b) Intended use, target species and effectiveness

N,N'-Methylenebismorpholine containing biocidal products are used as bactericides for the preservation of metal working fluids (PT13) which are prone to bacterial decay. The product is intended to be incorporated by professional users into water based emulsifiable metalworking fluids (MWF) to act as a preservative with bactericidal activity. The lubricant concentrate, intended for the preparation of water based emulsifiable metal working fluids, contains the active substance at a concentration of 3% w/w. The use concentration of the active substance in metalworking fluids is typically 0.15% w/w. The active substance has to be regularly or occasionally re-dosed if the concentration is below the effective concentration of 0.15% w/w.

The assessment of the biocidal activity of the active substance demonstrates that it has a sufficient level of efficacy against gram negative bacteria such as *Citrobacter freundii*, *Alcaligenes faecalis*, *Pseudomonas aeruginosa* and *Enterobacter aerogenes*.

The active substance is a formaldehyde-releaser. The biocidal activity of the active substance is due to the interaction of the released formaldehyde with protein, DNA and RNA. The interaction with protein results from a combination with the primary amide and the amino groups. It reacts with carboxyl, sulfhydryl and hydroxyl groups.

As formaldehyde is not specific for one cellular target, the development of resistance is unlikely, if sufficiently high formaldehyde concentrations are guaranteed that exceed the capacity of the innate detoxification systems. For this reason, sublethal and accordingly subinhibitory formaldehyde concentrations – which may originate through dilution effects particularly in consumer products – must be avoided.

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

A common core dossier was developed for formaldehyde, which was agreed at a Biocides Technical Meeting. This core dossier forms the basis of the hazard assessment of formaldehyde for all formaldehyde releasing active substances.

Human health

AEC and AEL estimates were based on threshold assumption in line with the conclusion of the formaldehyde core dossier.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios		
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**
Formulation of lubricant concentrate	primary: inhalation and dermal exposures*	professional
Use in metal working processes	Secondary: inhalation and dermal exposures*	professional

*inhalation: RMMs (Risk Mitigation Measure) are considered to be efficient enough that concentrations in air do not exceed the AEC (Acceptable Exposure Concentration) of formaldehyde or MBM.

Formulation of lubricant concentrate

The substance as manufactured can be used to prepare lubricant concentrates (3% w/w N,N'-Methylenebismorpholine), which are used for the preparation of metal working fluids.

These tasks were considered for the formulation of lubricant concentrates:

- Mixing of single components of lubricant concentrate by workers;
- Sampling for surveillance of the formulation;
- Filling and bottling of lubricant concentrate for resale;
- Cleaning of vessels.

The given tasks contain processes in closed, automated systems, handling of small amounts (sampling) or highly diluted solutions (cleaning with water, dilutions of 1:100 or more seem to be likely, company statement). Following the safety sheet, protective goggles/safety glasses, safety shoes, overalls and protection aprons are required during work in the production hall. As the scenario "use in metal working processes" covers handling of the pure substance (100% w/w)- preparation of a dilution like in this case, contains aerosol formation and direct dermal contact without gloves, the formulation of lubricant concentrate is considered to be covered by the following scenario.

Use in metal working processes

N,N'-Methylenebismorpholine is used to preserve metal working fluids in a concentration of 0.15% w/w. This can be done either by direct addition of the biocidal product to the metal working fluid or by adding a lubricant concentrate containing 3% w/w N,N'-Methylenebismorpholine.

The following description is based on information provided by the applicant:

Addition of lubricant concentrate to metal working fluids and appropriate dilution may occur automatically in a closed pipeline system or in a reservoir of metal working fluids in a separate room.

The metal working processes like drilling, milling, cutting, grinding, turning etc. are carried out in closed chambers or even in production streets with several closed chambers along one production process (large production sites). Contact with contaminated areas in the production hall as well as exposure to formed aerosols and gaseous releases by inhalation during metal working processes are forseeable.

The following tasks were considered and assessed. They reveal potential contact of workers with N,N'-Methylenebismorpholine/formaldehyde. Use of gloves was not considered for these uses and this sector of use except for the ES "mixing and loading of biocidal product and/or lubricant concentrate". Gloves are required for this task.

- mixing and loading of biocidal product and/or lubricant concentrate;
- machine work (drilling grinding etc; tool setting and dismantling, operator near to machine);
- control and cleaning of work pieces;
- fluid monitoring: control of pH, formaldehyde concentrations etc.;
- gathering shavings/chippings/turnings (swarf removal) for recycling before mwf is going to the ultrafiltration system;
- discharging of system (and sump maintenance).

Risk assessment

Exposure estimates were lower than the local AEC and systemic AEL (Acceptable Exposure Level) estimates and consequently the risk was considered acceptable. Also the qualitative risk assessment for local effects was considered acceptable. Respiratory exposure estimates for metal working fluid (treated with MBM) were based on measured data in plants using closed chambers and local exhaust ventilation systems. However exposure to MBM as such, has to be completely excluded by the use of appropriate piping technology due to its corrosive and skin sensitizing properties. Manual handling of MBM appears unacceptable.

Environment

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios	
Scenario	**Description of scenario including environmental compartments**
Preservative for water based emulsifiable metal working fluids	According to the ESD relevant emissions only take place during the life cycle stage waste treatment to the wastewater and not during industrial use.

No degradation of the biocidal product or losses of the fluid due to adsorption to treated surfaces are considered and the metal working fluid still contains 0.15% N,N'-Methylenebismorpholine at the end of service life.

Despite following this conservative approach no unacceptable risk is detected in a higher tier calculation for any environmental compartment.

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)	Cat 1B
	Mutagenicity (M)	Cat 2
	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)	T
Endocrine disrupting properties	not considered to have endocrine disrupting properties	

Consequently, the following is concluded:

N,N-Methylenebismorpholine does meet the exclusion criteria laid down in Article 5(1) of Regulation (EU) No 528/2012 by the released formaldehyde being a carcinogen Cat 1B.

N,N-Methylenebismorpholine does meet the conditions laid down in Article 10(1)(a) of Regulation (EU) No 528/2012, and is therefore considered as a candidate for substitution by meeting the exclusion criteria.

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 a position paper was submitted by the EU formaldehyde-releaser producers (Formaldehyde Biocide Interest Group, FABI) supported by 4 other comments. In addition, 2 comments were received from third parties. These comments included information on the availability of alternative active substances and information claiming the essentiality of formaldehyde releasers, like MBM, for the use of preservation of products during storage. In the comments similar and simultaneous regulatory decision making for similar formaldehyde releasers is requested, control options based on voluntary labelling instead of classification are proposed by industry and considerations with regard to risk as well as technical arguments (along the classification rules) against the classification proposal for Carcinogenicity Category 1B are presented by industry. It is noted that the technical arguments supporting the classification are listed in the assessment report and in the CLH report.

2.2.2. POP criteria

A PBT assessment was performed for N,N'-Methylenebismorpholine and its hydrolysis products. Based on the available data MBM, morpholine and formaldehyde are neither vPvB, nor PBT substances. Furthermore, none of the 3 substances meets two of the PBT criteria. Therefore, neither the parent nor its hydrolysis products meet the criteria for POPs either.

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

In view of the conclusions of the evaluation, it is proposed that MBM 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: 92.1% w/w.
2. Relevant impurity: max. 0.005% w/w (=50 ppm) formaldehyde.
3. MBM is considered a candidate for substitution in accordance with Article 10(1)(a) of Regulation (EU) No 528/2012.
4. 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
5. For professional users, safe operational procedures, appropriate organisational

[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)

and technical risk mitigation 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.

6. Mixing and loading of MBM to formulation vessels shall be automated, unless at product authorization excluding potential exposure to skin, eye and respiratory tract to MBM can be demonstrated by other means.

The active substance does not fulfil the criteria according to Article 28(2)(a) and 28(2)(b) to enable inclusion in Annex I of Regulation (EU) 528/2012.

2.4. Elements to be taken into account when authorising products

1. Whilst the efficacy data provided is sufficient to recommend approval of the substance, data demonstrating the efficacy of the product at the minimum application rate against the range of proposed target organisms using the recommended application equipment must be provided at the product authorisation stage.

   Metal working processes are required to be performed in closed chambers during these processes preventing exposure of workers to aerosols. In addition local exhaust ventilation is required at the work place,.

2. The active substance MBM 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.

3. The environmental exposure assessment for PT 13 as described in the Emission Scenario Document (ESD) is being revised currently. The exposure for MBM was estimated based on an intermediate revision of the ESD agreed at the Environment Working Group, which is described in the Assessment Report. At product authorisation, if available, the revised ESD has to be considered. The revised ESD will also contain on-site treatment of waste which was not considered in the current evaluation.

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 MBM.

However, further data shall be required as detailed below:

1. No chronic toxicity study with Daphnia for formaldehyde has been provided. Therefore a new long-term Daphnia study or a letter of access to the already available study (Formaldehyde Core Dossier) shall be provided as soon as possible but at the latest 6 months before the date of approval to the evaluating Competent Authority (Austria).

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