Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

N,N-Methylenebismorpholine

Product type: 6

ECHA/BPC/027/2014

Adopted

3 October 2014

Opinion of the Biocidal Products Committee

on the application for approval of the active substance N,N-Methylenebismorpholine 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:	**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 6 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 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

This evaluation covers the use of MBM in product type 6. MBM is a formaldehyde-releaser. 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 fuels (PT 6) which are prone to bacterial decay. The product is intended to be incorporated by industrial users into fuels during the formulation process, which is carried out automatically, to act as a preservative with bactericidal activity. Formulation is performed in closed systems with a high degree of automation resulting in a final concentration of the active substance ranging between 0.01 and 0.1%, corresponding to a maximum of 0.016% total releasable formaldehyde in the fuel.

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 fuels	Primary exposure to the fuel treated with MBM: inhalation and dermal exposures*	professional
refueling of engines	primary exposure to the fuel treated with MBM: inhalation and dermal exposures*	general public, professional
refuelling of engines	secondary: inhalation exposure	general public bystanders

*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 fuels

Fuels are charged in formulation vessels. Most formulation sites have closed systems using automatic dosage systems. The biocidal product for preservation is added under stirring. Manual addition of the biocidal product is not covered by the performed assessment and out of scope. Workers are expected to wear personal protective equipment for dermal protection, if contact is feasible (e.g. use of gloves). Fuel formulations are prepared in 2 to 3 batches per day (each one lasting up to 2 hours). Potential exposures of professionals have to be considered via the following tasks: exposure of workers during the addition of biocidal product to the dosage system/directly to fuels, sampling for formulation control and filling the fuels. Cleaning of vessels is not performed, due to the physico-chemical properties of fuel. Therefore, this task was not assessed.

Refueling of engines: primary and secondary exposure to the treated fuel

Primary exposure of professionals and members of the general public via the use of fuels is given considering the work of filling station attendants and non-professional persons, who fill up their cars/engines on their own.

Secondary exposure of the general public is possible considering professionals, non-professionals refuelling engines and bystanders, who find themselves at the fuel filling station and who do not refuel cars (e.g. fellow passengers, children, infants, etc.).

Regarding current regulations (e.g. vapour recovery systems, automatic shut off systems in the dispensers) for service stations and in general when the handling of fuels is concerned, inhalation exposure to the biocide can be considered to be covered; as fuels and fuel vapours themselves are known to be of concern for public health. Therefore, exposure is strongly regulated and as well the consumer's general awareness is raised by e.g. signs to handle fuels carefully. Direct dermal contact is constricted by technical possibilities as well. The performed calculations did not reveal an unacceptable risk. No gloves are necessary for non-professionals and professionals. The standard technology of fuel stations is sufficient.

Risk assessment

Exposure estimates were lower than the local AEC and systemic AEL (Acceptable Exposure Level) estimates and consequently the risk was considered acceptable. Respiratory exposure estimates for fuel (treated with MBM) during formulation of fuels and during refuelling of engines were based on Consexpo-models considering expected conservative ventilation for the assessed locations (industrial sites, outdoor). 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**
In-can preservative for fuels	No emissions to the environment are expected from the use of MBM as an in-can preservative for fuels during the life cycle stages application and use. Large storage tanks at the refinery's site may contain vast amounts of water including formaldehyde and morpholine which are eventually discharged to a Sewage Treatment Plant (STP). Currently no scenario for emission of fuel preservatives from large oil storage tanks along with the aqueous phase exists. However, the volumes discharged to the sewer are expected similar to those of the scenario assessed for PT 13. Therefore, the risk assessment for storage in large tanks is covered by the risk assessment for PT 13.

No emissions to the environment are expected from the use of MBM as an in-can preservative for fuels as MBM containing biocidal products are added to fuels in automated closed systems. For fuels ending up in an engine, it is assumed that 100% of the substance will be burnt, thus emissions should not be considered. Therefore no unacceptable risks are expected for any of the environmental compartments at any life cycle stage: application, use and for the emissions from storage tanks.

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 6

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. 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.
6. Where a treated article has been treated with or intentionally incorporates MBM releasing formaldehyde, and where necessary due to the possibility of skin contact as well as the release of formaldehyde 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

[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)

(EU) No 528/2012.

With respect to the carcinogenic properties of MBM releasing formaldehyde and the use in treated articles of biocidal products containing MBM the following options are proposed by the BPC to be considered in the decision making process under Article 9(1) of Regulation (EU) No 528/2012:

I) Restricting the use to the representative use in fuels;

II) Including a condition: “where a treated article has been treated with or intentionally incorporates MBM, and where necessary due to the possibility of exposure as well as the release of formaldehyde under conditions of use, the person responsible for placing the treated article on the market shall ensure that the label provides information on the carcinogenicity, as well as the information referred to in second subparagraph of Article 58(3) of Regulation (EU) No 528/2012”;

III) At product authorisation special attention shall be paid to the carcinogenic properties of MBM releasing formaldehyde;

IV) For biocidal products containing MBM intended to be used for the treatment of, or the incorporation in articles, the application for authorisation should show that all these treated articles are safe for use. In this respect the assessment of a reference article (leading article) should allow to conclude that all other treated articles with a comparable treatment and similar use are also without unacceptable risk.

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. 4) In order to assure negligible emissions to the environment it is required that the application of MBM to the fuel (industrial use) is performed in closed systems.

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.

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).