Comments on the ECHA public consultations for 3,3'-methylene-bis[5-methyloxazolidine] (Oxazolidin/MBO) and α,α',α''-trimethyl-1,3,5-triazine-1,3,5(2H,4H,6H)-triethanol (HPT)

The two active substances "Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)" (MBO) and "Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1)" (HPT) belong to a category of biocidal actives known as formaldehyde-releasers (or formaldehyde-donors or FARs). These substances control microbial growth in a water-containing product or in equipment by the slow release of formaldehyde directly into the matrix. There are at least ten other formaldehyde-releasers being considered for authorisation under the Biocidal Products Regulation (BPR) for several different product types including PT6 (in can preservatives) and PT13 (metalworking fluids).

Both these FARs and another (MBM) have recently been included in the 10th ATP to CLP and are the first of this category to be classified as Category 1B CMR substances based on read across to formaldehyde. It follows that the RAC will assign the same harmonised classification to the remaining FARs when they are assessed by this committee in the future because they all function by the same mechanism, namely release of formaldehyde into an aqueous matrix. It can therefore be assumed that all FARs will eventually be classified as Category 1B carcinogens under the CLP and will be candidates for substitution. This means that any decision taken concerning the substitution of any of these FARs will also eventually apply to the remaining members of this category.

The objective of the substitution provision of the BPR is to identify substances of particular concern to public health or the environment and to ensure that these substances are phased-out and replaced by more suitable alternatives over time. The criteria are based on the intrinsic hazardous properties in combination with its use. If the active substance meets one or more exclusion criteria the legislation makes it clear that it will only be approved for five years. The inevitable outcome of this regulatory activity will therefore be the eventual elimination from the market of an entire, important category of bactericidal active substances. This means that once all the FARs in the Review Programme have been similarly assessed, there will be a significantly restricted palette of bactericidal products available to downstream users for many applications. This will be especially acute for PT13 (metalworking fluids) where the choice of bactericides available to downstream users will be reduced by almost 70% (as illustrated by Table 1a). Industry experts predict that this will have potentially serious consequences such as, for example, the ability to have a sufficient spectrum of activity to control the wide range of deleterious organisms encountered in the production and use of the preserved products. Additionally, it is known that aldehyde-based bactericides are the only type considered to be

effective against endotoxins, which in the past have been implicated in large scale industrial adverse health incidents. Such limitations on the type of available bactericidal actives will undoubtedly present major practical problems for downstream users who need to control microbial activity in their products and/or end uses as described below. This is likely to affect SMEs disproportionately because these companies do not have access to the same level of in-house expertise often available to larger companies to effectively manage biocidal contamination using a reduced palette of bactericidal products, with the inevitable result that costs for SMEs will also increase disproportionately.

When an active substance is identified as a candidate for substitution, products containing that active substance would be subject to a comparative assessment at the time of authorisation and will only be authorised for use if there are no better alternatives. In terms of the comparative assessment of safety to workers it is worthwhile highlighting that exposure of EU workers to formaldehyde itself is already extremely well controlled. This is in contrast to human exposures to other active substances that do not rely on release of formaldehyde for their biocidal activity but are also part of the Review Programme. This is because a significant number of EU Member States have an Occupational Exposure Limit in place for formaldehyde and an EU-wide Indicative Occupational Exposure Level Value for formaldehyde has now been agreed and published by the Scientific Committee on Occupational Exposure Limits (SCOEL). The SCOEL recommendation for formaldehyde confirms a safe exposure limit at 0.3 ppm (8h-TWA) and 0.6 ppm (STEL). This recommendation is expected to further limit short-term and long-term exposure to formaldehyde in the workplace to a level significantly below that considered by RAC to trigger nasopharyngeal carcinogenicity in humans (i.e. 2 ppm) without additional measures being necessary. Other national/EU-wide schemes that concern specific applications already include additional controls that minimise or eliminate products containing formaldehyde-releasing biocides.

Additionally, and perhaps more significantly, a recent study by the DGUV Fachbereich Holz und Metall and involving other stakeholders including the association of German Lubricant Manufacturers (Verbraucherkreis Industrie Schmierstoffe; VKIS) has demonstrated that measured airborne levels of formaldehyde were found to be below the national occupational exposure limit (safe working limit) in all but one metalworking machining location examined. Further investigation of the circumstances leading to the anomalous measurement is needed before taking any regulatory action that would lead to the loss of an entire category of biocidal products. This independent study strongly indicates that, at least for this application, there is no justification to institute additional regulatory measures for MBO/HPT (and by analogy all other formaldehyde-releasers) such as substitution under the BPR in order to protect EU workers from adverse effects associated with potential exposure to formaldehyde. In house measurements by the producers confirm that workers are not exposed to levels of formaldehyde that are greater than the current national occupational exposure limits under normal use conditions. Furthermore, the study findings agree with the theoretical calculation that at their effective

dose, formaldehyde-releasers would never generate a level of released formaldehyde in an aqueous solution that was greater than the regulatory threshold for classifying mixtures as potentially carcinogenic (i.e. 1000 ppm), even under the unrealistic scenario where all available formaldehyde was released instantaneously.

It is widely accepted that biocides are an essential part of the sustainability of aqueous-based products. The general trend from solvent-containing systems towards water-containing systems for some applications is seen as a more environmentally-beneficial option but demands increased biocidal protection during production, storage and use. It therefore follows that in the absence of effective preservation there would be considerably greater spoilage of water-based products, requiring higher disposal levels and the greater consumption of resources to produce replacement stocks. Consequently the use of effective biocides is an essential, not optional, element in aqueous formulations.

The range of biocidal active substances available to downstream users for particular end-use applications has been unchanged for at least a decade. This is due in part to their effectiveness, their cost-effectiveness, their ease of incorporation into products and the apparent lack of harm to workers at typical use levels and/or when handled according to the manufacturer's recommendation (based on the absence of significant levels of reportable worker health problems in the supply chain being attributed to specific substances). Currently downstream users have the option to use different chemical types in combination to achieve effective biocidal control. Such combinations are essential as any preservative system needs to address a wide range of different microbial threats, which on the simplest level includes bactericides and fungicides.

A probable unintended outcome of the harmonised classification of MBO and HPT (and by analogy all formaldehyde-releasers) as Category 1B carcinogens is that they immediately become candidates for substitution. The likely outcome of this regulatory action is to reduce the chemical diversity of available bactericides, especially for metalworking fluids (PT13) where only a limited number of biocidal actives and associated chemical types undergoing formal BPR review, with no probability of new active ingredients being developed.

Typically, where the range of microbial control chemistries is limited, there is a greater risk and frequency of bacterial contamination developing in the products that need protecting. All biocidal actives have a limited spectrum of efficacy against microorganisms and therefore removal of an entire class of active substances such as formaldehyde-releasers from the EU market will make it more difficult to provide protection from bacterial contamination and spoilage. The concern of FARs being eliminated from the EU marketplace has already been

raised with the Member States' Competent Authorities for PT6 by the downstream user organisation CEPE.[1]

As well as the likely increased frequency with which contaminated metalworking fluid or spoiled product would have to be discarded the reduced spectrum of biocidal active substances that are available to downstream users is also expected to cause fluid maintenance to require greater and more frequent attention, which will almost certainly significantly increase costs for the various industries that currently rely on FAR biocides and could impact SMEs disproportionately. There is also a greater risk, in particular to metalworkers, due to the possibility of colonies of harmful human pathogens contaminating end use fluids and equipment that would result from the probable elimination of a proven effective control mechanism for such organisms. This is because out of the current spectrum of biocidal active ingredients in the BPR Review Programme only FARs have been demonstrated to render endotoxins less harmful.

It is also important to recognise that we are not aware of any company who is actively engaged in or even planning to bring a new biocidal active ingredient to market for PT6 or PT13. This means that there is no new technology that will be developed in future to fill the void left by the potential disappearance of an entire category of biocidal active substances. The reason for this is the relatively high up-front costs and unattractive return on investment associated with developing novel biocidal actives, an increasing regulatory complexity and the uncertainty of commercial success of bringing new active substances to market under the BPR (and its predecessor legislation). In this context it is also relevant that any 'new' biocidal active substances brought to market with a complete set of supporting toxicity data would not have the benefit of the long-term, in-use experience that exists with FARs. As a result, there is a possibility that such products may introduce different, unexpected and unacceptable risks for specific end uses.

As well as the absence of any new concepts or active substances for antimicrobial protection of PT13 there is also the obligation for a comparative assessment for products containing active substances which are candidates for substitution, where potential chemical alternatives are compared with the substitution candidate with regard to any risks they pose and the potential benefits from their use. Again we want to emphasize that currently the only practical choice of bactericides for PT 13 for downstream users are either products containing FARs or isothiazolinones. As both substance types are very efficient bactericides both share the potential of being unavoidably hazardous to human health when tested in laboratory animal models at high concentrations. And therein lies a practical problem with the concept of 'comparative assessment' and the replacement of a candidate for substitution with a nominally

[1] CEPE, „The need for a holistic approach on in-can preservatives", 2014. https://circabc.europa.eu/sd/a/146478a1-64b3-4f44-a579-08410f857c49/CA-May14-Doc.4.4%20-%20Approvals%20of%20PT6.pdf

'less hazardous' substance. Industry has long emphasized that comparative assessments are difficult to implement and there is currently a lack of an agreed methodology that could be used to evaluate viable substitutions.[2] In particular, it is still unclear how such decisions are to be made and according to which criteria, especially in those circumstances when the only credible alternatives for certain biocidal product types have very different hazard profiles, related to different endpoints, and when the alternatives can potentially have a negative impact on human health and/or the environment themselves if misused. It therefore follows that a comparative assessment based on hazard alone might not be straight forward to perform or be able to demonstrate beyond reasonable doubt that one option of bactericidal control is more desirable than another in terms of risk to worker safety and/or environmental harm.

Furthermore, since the stated purpose of the BPR is a level playing field across all Member States in terms of free movement of products within the Union as well as a high level of protection of humans and/or the environment, of equal importance is the question whether it is proportionate (and legal) to remove a sub-section of FARs from the EU market whilst allowing other FARs that operate by the same mechanism of action to remain in commerce. In our opinion it is inconceivable that any regulatory action leading to a situation where products containing these two active substances are eliminated whilst products containing other FARs remain on the market in the EU for a substantial period of time would be pursued, based only on the arbitrary timing of review by an evaluating Member State. The fact that a product containing one of these substances could be replaced by a different substance functioning by exactly the same mechanism of action appears to contradict the purpose of the BPR. The only sensible and proportionate option therefore would be to delay any consideration by the Commission of the elimination and /or substitution of these two FARs until all members of this category could be considered for substitution/elimination at the same time.

It follows, therefore, that if all FARs are eventually recommended for substitution or are subject to time-limited authorisation and are subsequently eliminated from commerce then end users can expect that no new types of active substance will be developed and/or brought to market as an alternative way of controlling microbial activity for many end uses, especially the industrial applications described above. This lack of innovation, together with the observation that FARs are the predominant means of controlling bactericidal activity in the end-use fluid for applications such as PT13 (where they are currently used in more than 50% of biocidal products to control deterioration of water-containing products by bacteria) means that any recommendation to substitute MBO and HPT (and by analogy all formaldehyde-releasers) would create new and significant fluid management problems among those downstream users who

[2] European Commission 'Technical Guidance Note on comparative assessment of biocidal products' Note for discussion with competent authorities for biocidal products

currently use these products in full knowledge of their mechanism of action in controlling microbial activity (i.e. by releasing formaldehyde into the product matrix).

Table 1a: List of bactericidal active substances included in the Review Programme for Product Type 13 (Metalworking fluid preservatives)

Substance	EC number	CAS number	Type	Category
2-Phenoxyethanol	204-589-7	122-99-6	Bactericide/ Fungicide	Phenolic
Diamine	219-145-8	2372-82-9	Bactericide	Amine
BIT	220-120-9	2634-33-5	Bactericide	Isothiazolinone
MIT	220-239-6	2682-20-4	Bactericide	Isothiazolinone
C(M)IT/MIT 3:1	Reaction mass	55965-84-9	Bactericide	Isothiazolinone
Reaction products of ethylene glycol with paraformaldehyde (EGForm)	222-720-6	3586-55-8	Bactericide	Formaldehyde-releaser
HHT	225-208-0	4719-04-4	Bactericide	Formaldehyde-releaser
MBM	227-062-3	5625-90-1	Bactericide	Formaldehyde-releaser
DMDMH	229-222-8	6440-58-0	Bactericide	Formaldehyde-releaser
Oxazolidin/MBO	266-235-8	66204-44-2	Bactericide	Formaldehyde-releaser
CTAC	223-805-0	4080-31-3	Bactericide	Formaldehyde-releaser
Cis CTAC	426-020-3	51229-78-8	Bactericide	Formaldehyde-releaser
TMAD	226-408-0	5395-50-6	Bactericide	Formaldehyde-releaser

EDHO	231-810-4	7747-35-5	Bactericide	Formaldehyde-releaser
(benzyloxy)methanol	238-588-8	14548-60-8	Bactericide	Formaldehyde-releaser
HPT	246-764-0	25254-50-6	Bactericide	Formaldehyde-releaser
DBNPA (note 1)	233-539-7	10222-01-2	Bactericide	Electrophilic

Note 1 = the substance is unstable in metalworking fluids; its use is confined to situations where user desires short or no delay/quick kill of microbes.

Table 1b: List of fungicidal active substances included in the Review Programme for Product Type 13 (Metalworking fluid preservatives)

Substance	**EC number**	**CAS number**	**Type**	**Category**
Chlorocresol	200-431-6	59-50-7	Fungicide	Phenolic
Biphenyl-2-ol	201-993-5	90-43-7	Fungicide	Phenolic
2-Phenoxyethanol	204-589-7	122-99-6	Bactericide/ Fungicide	Phenolic
OIT	247-761-7	26530-20-1	Fungicide	Isothiazolinone
BBIT	420-590-7	4299-07-4	Fungicide	Isothiazolinone
Sodium pyrithione	223-296-5	3811-73-2	Fungicide	Pyrithione
IPBC	259-627-5	55406-53-6	Fungicide	Carbamate

For more information please contact:
Guy Parker
+32 2.676.73.67 or gpa@cefic.be

About FABI

The Formaldehyde Biocides Interest Group (FABI) is a registration group of Cefic, composed of 20 European producers of formaldehyde and formaldehyde releasers. Its aim is the continued support of a Common Hazard Dossier on Formaldehyde intended to support the approval of Formaldehyde or Formaldehyde Releasers as active substances under the Biocidal Products Regulation (EU) 528/2012.