Statement in response to the public consultation on potential candidates for substitution for

Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2) (MBO) for PT's 2, 6, 11, 12 and 13

AND

Reaction product of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1) (HPT) for PT's 2, 6, 11 and 13

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Content

1. Introduction

General comments:
As outlined in the guidance "Submission of information in the public consultation on potential candidates for substitution under the Biocidal Products Regulation" the purpose of the public consultation is to gather relevant information, especially information on available substitutes or alternatives. The information on the availability of possible alternatives is of high importance at the product authorization stage when a comparative assessment needs to be performed.

We would like to provide you with further information on possible alternatives for the active substances MBO and HPT. From our point of view the comparative assessment is a very complex process which needs to be established by authorities. We would like to emphasize, that the information given is mostly based on the intrinsic properties and risk of the substance. In order to have a workable outcome of such a comparative assessment much more information should be taken into account like for instance the impact of C&L of the products as well as the consequences for downstream users.

While collecting this data we discovered that a few basic questions are still unclear to us:

1) MBO and HPT are classified as carcinogen Cat 1B and fulfil therefore the exclusion criteria of the BPR due to the fact that they release formaldehyde. This is true for the pure active substances. In the max. final use concentration of 1500 ppm (= 0.15%) (and less depending on the application) both actives do not need to be classified as carcinogen according to CLP and hence don't fulfil the exclusion criteria and the intended uses are considered to be safe.

   Limit of labelling carcinogen Cat 1B:

   MBO concentration ≥ 0.222%
   HPT concentration ≥ 0.357%

   Question: How to deal with carcinogen substances which have a proven safe level under the scope of the BPR when the final use is safe?

2) When collecting the relevant data it became clear that we are comparing different chemical substance which have widely varying hazards with different adverse endpoints for human health and the environment. All of these active biocidal substances are supported because they have technical advantages for different applications often within the same PT.

   Question: What is the agreed methodology to carry out and evaluate the right viable substitutes? This question is linked to toxicological and also to technological aspects.

   Even though industry is not actively involved in the process of comparative assessment, the parameters of decision-making by authorities are of great interest to industry. If there is no precise information with respect to the methodology, it will be almost impossible to invest in the development of new active biocidal substances as no prediction regarding possible marketing in the future can be made.

We compared the actives MBO and HPT with biocidal actives which are already approved for certain PT's as well as with biocidal actives which are still in the registration process (without final BPC and RAC evaluation):

The intended uses of the biocidal active MBO/HPT (HPT not PT12) are:

- as microbiocidal system cleaner of metal working systems (disinfection of the inner surface of vessels and tubes) (PT 2)
- as in-can preservative in fuels and water based fluids, (PT 6),
- as preservative for closed recirculating cooling water systems (PT 11),
- as slimicide in the oil industry (offshore) for the preservation of drilling muds (PT 12),
- as preservative for water based metal working or cutting fluids (PT 13)

MBO and HPT belong to a category of biocidal actives known as formaldehyde-releasers (or formaldehyde-donors). These substances control microbial growth in a water-containing product or equipment by the slow release of formaldehyde directly into the matrix.
There are at least ten other formaldehyde-releasers being considered for authorisation under BPR for several different product types.

Based on the decision by the Risk Assessment Committee (RAC) to classify MBO/HPT as carcinogen category 1B, due to the amount of releasable formaldehyde, we would assume that all formaldehyde-releasers will be classified as carcinogen category 1B. Since formaldehyde is the initiator that MBO/HPT are subjected to a comparative assessment we will only compare MBO/HPT with active biocidal substances which follow another mode of action than the release of formaldehyde.

That is the rational why formaldehyde-releasers will not be discussed in this paper as alternatives for substitution of MBO/HPT.

2. PT 2/PT13

General issue with respect to the assigned PT: PT2/PT13 dilemma

Furthermore we like to draw attention to a problem concerning the PT2 listing of MBO/HPT:
Actually we only applied for PT 2 due to one use. This is the use in so called system cleaners for metalworking fluids and circulation systems. It is still unclear to us in which of the two possible PTs (PT 2 or PT 13) the use is to be classified.

The use description and the exposure scenarios of these two PTs are identical and both are covered by PT 13. The only difference is the claim “cleaning and disinfecting” of the metal working fluid circulation systems. Due to the claim “disinfection” some EU-Member states believe that the right PT is PT 2. Within the manual of decisions of the BPD the use of an antimicrobial system cleaner has been assigned to PT 13. Due to the non-binding character of this decision still some countries insist on PT 2 while others agree with PT 13.

As far as we are concerned there had not been a final decision by authorities regarding the correct PT for this use. This uncertainty is the only reason why MBO as well as HPT have been assigned to both PT’s (2 and 13).

To demonstrate the dilemma a brief description of the use is given below:

In general, the purpose of system cleaners is to reduce the risk caused by permanent microbiological contamination (biofilms) from infected surfaces and materials (mainly tubes and tanks) in metalworking machines.
Primarily the intention is to clean the system at areas that are difficult to access, before new metal working fluids will be inserted in the single or the central system. Therefore, the system cleaner contains emulsifier

and surfactants, and biocides. After the soaking time, the system cleaner containing used metal working fluid will be dumped and the system will be rinsed with additional water. Overall, the intention of system cleaning is to clean and to reduce micro-organisms in the system before filling with new fluids, to avoid having a negative set-up of the fresh metal working fluid at the beginning.

System cleaners are liquids and added by applicant in a diluted form to the metalworking fluid to clean and sanitize (or disinfect) contaminated surfaces, such as vessels, pipes, filters, etc. which can't be reached by standard cleaning operations.
Common system cleaners typically consist of antimicrobial substances in combination with cleaning & wetting agents. System cleaners are used to attack biofilms and to remove dirt and residues from surfaces in the entire plant. Especially in so called dead ends which can't be reached by standard cleaning processes.
Therefore a system cleaner will be added to a used metalworking fluid 6h -24h before the exchange of the complete liquid.

<u>Crucial property of formaldehyde releasers for PT 2/PT13:</u>

As mentioned above MBO/HPT belong to the group of formaldehyde releasing biocidal actives. Therefore a comparison with other formaldehyde releasing chemicals is not appropriate. Considering the chemical behaviour, MBO/HPT can only be compared with other biocidal actives with aldehyde functionality within the PT 2: glutaraldehyde.

The pH of a system cleaner for metalworking fluid installations is in 9.5 to 12 to guarantee a good corrosion protection against steel. Only formaldehyde releasing biocidal actives are stable and <u>active</u> under these pH conditions in a matrix of a metalworking fluid and which is supported under PT 2 and PT 13.

Due to its composition and the high pH a system cleaner is able to break potential biofilms in the system. The removed parts of the biofilm will be flushed by the metalworking fluid into the filtration system. Micro-organisms released out of biofilms will be destroyed by the biocides. By this treatment it is guaranteed that even the dead spaces of the tank and tubing system of the machines are disinfected and the risk of an immediate microbial recontamination by remaining biofilms after refilling with fresh metalworking fluid is eliminated.

Conclusion: MBO/HPT as bactericides are due to their unique* stability at high pH values not replaceable by other bactericidal actives supported under PT 2 and PT 13 for the use in antimicrobial system cleaners.

*(as other amine based formaldehyde releasing compounds).

3. PT 6, Description

Biocides are used to preserve fuels against microbial contamination in storage tanks as well as in vehicles, emergency energy generators and heating oil to prevent degradation of fuel which causes blockage of pumps and engine corrosion. Already contaminated diesel can also be disinfected.

Table 1: Comparison of MBO/HPT with alternative CMI/MI for fuel preservation in PT 6

Active	MBO	HPT	CMI/MI
Identity & Properties			
a) Identity (CAS Number)			55965-84-9
b) Candidate for substitution	Yes	Yes	No
c) Health risks	Carc. 1B Muta. 2 Acute Tox. 4 Acute Tox. 3 Acute Tox. 4	Carc. 1B Muta. 2 Acute Tox. 4 Acute Tox. 4 STOT RE 2	Acute Tox. 3 for acute oral hazard Acute Tox 2 for acute dermal hazard Acute Tox 2 for acute inhalation hazard Skin Corr. 1B Skin Sens. 1A

	STOT RE 2 Skin Corr. 1B Eye Dam. 1 Skin Sens. 1A	Skin Corr. 1C Eye Dam. 1 Skin Sens. 1A	
d) Environmental risks	Aquatic Chronic 2	Aquatic Chronic 2	Aquatic Acute 1 Aquatic Chronic 1;
e) Physical hazards and classification	Danger! H350 : May cause cancer H341: Suspected of causing genetic defects H332: Harmful if inhaled H311: Toxic in contact with skin H302: Harmful if swallowed H373 (gastrointestinal tract, respiratory tract): May cause damage to organs through prolonged or repeated exposure H314: Causes severe skin burns and eye damage H318: Causes serious eye damage H317: May cause an allergic skin reaction H411: Toxic to aquatic life with long-lasting effects	Danger! H350 : May cause cancer H341: Suspected of causing genetic defects H332: Harmful if inhaled H302: Harmful if swallowed H373 (gastrointestinal tract, respiratory tract): May cause damage to organs through prolonged or repeated exposure H314: Causes severe skin burns and eye damage H318: Causes serious eye damage H317: May cause an allergic skin reaction H411: Toxic to aquatic life with long-lasting effects	Danger! H331: Toxic if inhaled H311: Toxic in contact with skin H301: Toxic if swallowed H314: Causes severe skin burns and eye damage H317: May cause an allergic skin reaction H410: Very toxic to aquatic life with long lasting effects.
f) Effectiveness against target organisms	Yes	Yes	Yes
Technical Feasibility			
a) mode of action	Reaction with sulphur containing proteins	Reaction with sulphur containing proteins	Reaction with amine and sulphur containing proteins
b) stability and compatibility of use concentration for requested pH and application	Yes	Yes	Yes
c) impact on corrosion	Corrosion protection on mild steel by 90%	Corrosion protection on mild steel by 90%	Does not avoid corrosion
d) Suitability at low temperatures	water free, freezing point < -39°C, low viscosity	Approx. 20% water. freezing point -10°C, low viscosity	Contains water, must be blended with methanol or glycol to avoid freezing
Other aspects			
Oil solubility:	Yes	Yes	No
Contains AOX (org. halogens)	No	No	Yes
Permission according German Clean Air act	Yes	Yes	No
Contains Sulfur	No	No	Yes
Effective against anaerobe bacteria (SRB)	Yes	Yes	No
Ashless additive for fuel	Yes	Yes	No
Conclusion			
For PT 6 there is no significantly beneficial alternative for MBO/HPT in place because the alternative (CMI/MI) is not soluble in fuel and contains halogen which is not allowed according to German Clean Air Act.			

Currently MBO is the <u>only</u> fuel biocide on the market which fulfils the key requirements for the automotive industry. It forms no residues when burned in an engine (ashless additive), has no negative impact on the catalyst systems (free of sulfur and halogens), no formation of dioxins (free of halogens) and complete combustion to CO_2, NO_2 and H_2O. Therefore diesel fuels preserved with MBO do fulfil the requirement of the EN 590 (Automotive fuels - Diesel - Requirements and test methods).

This is the reason why MBO is today approved by nearly all leading European Companies in the Oil Industry (Shell, Exxon/Mobile; BP, Lotos, Orlen, etc.) , the Automotive Industry (Mercedes Benz, MAN, Renault, Volvo, etc).; Transport Organisations (Major Truck & Bus fleets, Marine shipping fleets etc.) and other organisations holding strategic fuel reserves (NATO, German armed forces, Dutch armed forces, etc.). In this highly regulated application biocidal active can’t be used without all these approvals as a fuel additive/biocide.

Additionally it has to be pointed out that MBO and HPT are very effective against anaerobe bacteria (espec. Sulfate reducing bacteria = SRB) which produce the very toxic gas hydrogen sulphide (H_2S) which decomposes very fast and completely other actives like e.g. the whole group of isothiazolinones.

Today no non-chemical alternatives are available to give diesel fuels a long lasting preservation effect (0.5 – 3 years).

Approx. 10% - 15% of the diesel fuels used in Europe are preserved with a fuel biocide!

It has to be considered that Diesel Fuel itself is already labeled as a carcinogen category 1b (H350 = May cause cancer). The addition of 50ppm – 500 ppm (v/v) of MBO or HPT to a diesel fuel has <u>no</u> influence on the labelling and safe-handling of diesel fuels!

In addition to this schülke has generated workplace exposure data for the use as fuel biocide that demonstrate typical occupational exposure of workers in respect to the critical hydrolysis product formaldehyde. It could be shown that human exposer to formaldehyde is very low for this application.

Reference values Formaldehyde	
Occupational exposure SCOEL (2016)	0.3ppm (8h)
Occupational exposure SCOEL (2016)	0.6ppm (STEL)
OEL air level (WHO)	0.4ppm
AEC-Formaldehyde core dossier	0.12 mg/m^3 = 0.1ppm

Experiment: MBO_Eposure_in-fuel_refilling

Within this experiment the formaldehyde exposition in ambient air of employees was simulated by means of adding MBO to a vehicle tank that was filled with diesel and locating it in a factory room. Here MBO was transferred from 0.5l respectively 10l bottles into a 20l canister, which was used to simulate a fuel tank. This study can be regarded as worst case scenario as the measurement took place in a closed room without ventilation. During the refilling of MBO into a fuel tank no formaldehyde release to ambient air (values were below the detection limit of 0.01 mg/m^3) could be measured.

These values are far below the OEL air level of 0.4 ppm Formaldehyde (derived by WHO), below the occupational SCOEL limits (0.6 respectively 0.3 ppm) and also even below the discussed safe level air of 0.1 ppm Formaldehyde (AEC-Formaldehyde Core Dossier). No significant amount of formaldehyde can be found in the air and thus no significant amount of formaldehyde can have contact with human tissue.

With this experimental series it could be shown that, if handling and filling of MBO into a fuel tank is carried out in accordance with appropriate dosing devices and spilling could be avoided, the exposure value will be below 100 ppb (0.1 ppm; 0,00001%).

<u>4. PT 11, Description</u>

Biocides are used to control biofouling in (closed) liquid cooling systems and in in oil production processes. From the reservoir a mixture of gas, crude oil and water has to be separated from each other.
The water circulation system has to be protected against biofouling and Microbial Induced Corrosion (MIC) mainly caused by the H2S produced by anaerobe, sulphide reducing bacteria (SRB).

All biocidal actives with a positive BPC-Opinion for PT 11 are not stable at pH-values above pH 8. The typical pH-value for cooling liquids in closed circulation systems is in the pH range between 8.0 – 10.0. The reason is corrosion protection within the piping and heat exchanger system. These systems are from the technical point of view comparable with water based metalworking fluids therefore the actives MIT and CMI/MI will be discussed in more detail in chapter 6 (PT 13).

As clearly shown in the table below MBO and HPT are currently the only biocidal actives with a proven safe use at pH values above 8.

Again it has to be pointed out that MBO and HPT are very effective against anaerobe bacteria (espec. Sulfate reducing bacteria = SRB) and that MBO and HPT are currently the only biocidal actives with a positive BPC-opinion with a proven efficacy against SRB's (even if the pH value is above 8).

Table 2: approved biocidal actives for PT 11

Substance Name	EC -Number	CAS-Number	PT	Status	potential Alternative to MBO?
2-methyl-2H-isothiazol-3-one (MIT)	220-239-6	2682-20-4	11	Approved	No = not stable at pH > 8 Decomposition in the presence of sulfide
Glutaral (Glutaraldehyde)	203-856-5	111-30-8	11	Approved	No = not stable at pH > 8
Mixture of 5-chloro-2-methyl-2H- isothiazol-3-one (EINECS 247-500-7) and 2-methyl-2H-isothiazol-3-one (EINECS 220-239-6) (Mixture of CMIT/MIT)		55965-84-9	11	Approved	No = not stable at pH > 8 Decomposition in the presence of sulfide
Peracetic acid	201-186-8	79-21-0	11	Approved	No = not stable at pH > 8
PHMB (1600; 1.8) (polyhexamethylene biguanide hydrochloride with a mean number-average molecular weight (Mn) of 1600 and a mean polydispersity (PDI) of 1.8)		27083-27-8	11	Approved	No = not stable at pH > 8 Not effective against SRB at pH values >8
THPS	259-709-0	55566-30-8	11	Under review	No = not stable at pH > 8

A brief comparison of the toxicological properties of the different biocidal actives is given in Table 4.

5. PT 12, Description

Biocides are used in drilling muds to prevent the degradation of the drilling mud and also to prevent the introduction of harmful bacteria into the formation. Microorganisms can degrade the polymers resulting in loss of viscosity and adverse rheological effects.

A typical problem in all oil-exploration activities worldwide is the presence of H2S and/or its salts in every oil reservoir. The sources of H2S could be the formation by SRB's in the oil reservoir or it is trapped in the stone formation as a result the decomposition of the organic material millions of years ago.

All biocidal actives with a positive BPC-Opinion for PT 12 are not stable at pH-values above pH 8. The typical pH-value for water based drilling muds is in the pH range between 8.0 – 10.0. The reason for the high pH is the corrosion (rust) of piping and drilling equipment (steel).
MBO and HPT are currently the only biocidal actives with a proven safe use at pH values above 8 even in the presence of sulphides.

Table 3: approved biocidal actives for PT 12

Substance Name	EC -Number	CAS-Number	PT	Status	potential Alternative to MBO?
Acrolein	203-453-4	107-02-8	12	Approved	No = not stable at pH > 8
Glutaral (Glutaraldehyde)	203-856-5	111-30-8	12	Approved	No = not stable at pH > 8
Mixture of 5-chloro-2-methyl-2H-isothiazol-3-one (EINECS 247-500-7) and 2-methyl-2H-isothiazol-3-one (EINECS 220-239-6) (Mixture of CMIT/MIT)		55965-84-9	12	Approved	No = not stable at pH > 8 Decomposition in the presence of sulfide

Peracetic acid	201-186-8	79-21-0	12	Approved	No = not stable at pH > 8

A brief comparison of the toxicological properties of the different biocidal actives is given in Table4.

Table 4: Comparison of MBO/HPT with market standards for PT 11 and 12 for oilfield applications

Active	MBO	HPT (PT11 only)	Glutaraldehyde	THPS	Acrolein
Identity & Properties					
a) Identity (CAS Number)			111-30-8	55566-30-8	107-02-8
b) Candidate for substitution	Yes	Yes	Yes	Not yet decided	No
c) Health risks	Carc. 1B Muta. 2 Acute Tox. 4 Acute Tox. 3 Acute Tox. 4 STOT RE 2 Skin Corr. 1B Eye Dam. 1 Skin Sens. 1A	Carc. 1B Muta. 2 Acute Tox. 4 Acute Tox. 4 STOT RE 2 Skin Corr. 1C Eye Dam. 1 Skin Sens. 1A	Acute Tox. 3 STOT RE 2 Skin Corr. 1B Skin Sens. 1 Resp. Sens. 1	Acute Tox. 3 Skin Sens. 1A Eye Dam. 1 Repr. 2	Acute Tox. 1 Acute Tox. 2 Acute Tox. 3 Skin Corr. 1B Eye Dam. 1
d) Environmental risks	Aquatic Chronic 2	Aquatic Chronic 2	Aquatic Acute 1	Aquatic Acute 1 Aquatic Chronic 2	Aquatic Acute 1 Aquatic Chronic 1
e) Physical hazards and classification	Danger! H350 : May cause cancer H341: Suspected of causing genetic defects H332: Harmful if inhaled H311: Toxic in contact with skin H302: Harmful if swallowed H373 (gastrointestinal tract, respiratory tract): May cause damage to organs through prolonged or repeated exposure H314: Causes severe skin burns and eye damage H318: Causes serious eye damage H317: May cause an allergic skin reaction H411: Toxic to aquatic life with long-lasting effects	Danger! H350 : May cause cancer H341: Suspected of causing genetic defects H332: Harmful if inhaled H302: Harmful if swallowed H373 (gastrointestinal tract, respiratory tract): May cause damage to organs through prolonged or repeated exposure H314: Causes severe skin burns and eye damage H318: Causes serious eye damage H317: May cause an allergic skin reaction H411: Toxic to aquatic life with long-lasting effects	Danger! According to the harmonised classification and labelling (CLP00) approved by the European Union, this substance is toxic if swallowed, causes severe skin burns and eye damage, is toxic if inhaled, is very toxic to aquatic life, may cause an allergic skin reaction and may cause allergy or asthma symptoms or breathing difficulties if inhaled.	Danger! According to the classification provided by companies to ECHA in REACH registrations this substance is toxic if inhaled, is very toxic to aquatic life, is toxic to aquatic life with long lasting effects, is harmful if swallowed, causes serious eye damage, is suspected of damaging fertility or the unborn child and may cause an allergic skin reaction	Danger! Highly flammable liquid and vapour Fatal if swallowed Toxic in contact with skin Fatal if inhaled Corrosive to the respiratory tract Causes severe burns and eye damage Very toxic to aquatic life Very toxic to aquatic life with long lasting effects.
f) Effectiveness against target organisms	Yes	Yes	Yes	Yes	Yes
b) stability and compatibility of use concentration for requested pH and application	Yes	yes	Yes	No	Only for water injection
c) impact on corrosion	Corrosion protection on mild steel by 90%	Reaction with sulphur containing proteins	No effect	Very corrosive on mild steel	
d) Suitability at low temperatures	water free, freezing point < -39°C, low viscosity	Yes	Contains water, must be blended with methanol or glycol to avoid freezing	Contains water, must be blended with methanol or glycol to avoid freezing	Contains water, must be blended with methanol or glycol to avoid freezing
Conclusion	For PT 11 /12 there is no significantly beneficial alternative for MBO in place. Glutaraldehyde is also candidate for substitution due to sensitizing and toxic properties whereas THPS is also releasing formaldehyde and has a worse acute aquatic tox. profile and worse stability for the applications. For PT 11 there is no significantly beneficial alternative for HPT in place. Glutaraldehyde is also candidate for substitution due to sensitizing and toxic properties whereas THPS is also releasing formaldehyde and has a worse acute aquatic tox. profile and worse stability for the applications.				

6. PT 13 Description

In PT 13 application biocides are used to avoid a microbiological contamination of water based metal working fluids in circulation systems. The pH-value of these circulation systems is usually between pH 8.5 and pH 9.5. The typical microorganisms in such systems are bacteria, fungi and yeasts.
The lifetime of a metalworking fluid is between 6 weeks and 18 months (depending on several external factors). This shows clearly that biocides with a long lasting preservation effect are mandatory for PT 13 applications.

7. Comparison of MBO/HPT with market standards for PT 2 and 13 for metal working applications

MBO/HPT will be classified as carc. Cat. 1B. due to the fact that the amount of theoretically releasable formaldehyde is above 1000 ppm. It should be noted that:

1) As mentioned before 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.
2) A study by the DGUV Fachbereich Holz und Metall (special field wood and metal)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).
3) The content of free formaldehyde in 100% MBO/HPT is below 500 ppm (detected by NMR-technology)!
4) In the maximum recommended use concentration (end-dilution = 1500 ppm MBO) it is not possible to exceed the value of 750 ppm of releasable formaldehyde in a metalworking fluid circulation system = non carcinogen in the max. final use concentration.
5) No labelling of the metalworking fluid circulation system with H 350 risk phrase will be required even in the highest recommended use concentration in PT 13.
6) Stable at high pH values (up to pH13)
7) MBO is in any concentration water soluble (from 0% up to 100%)!
8) The high partition coefficient from mineral oil-water: 40. This means that in oil in water emulsions, MBO will move very fast from the oil phase into the water phase. Approx. 80% of all water mixed metalworking fluids in the EU are oil in water emulsions.
9) MBO is compatible with all types of metalworking fluids.

For the applications in PT 13 (Metal Working Fluids) it is important to know that we have two types of preservatives which are both essential for the successful preservation of a water-based metal working fluid in the circulation system. Therefore all metalworking fluids contain at least one active out of each group:

- Bactericides
- Fungicides

MBO is in use in metalworking fluid circulation system (PT13) mainly as a bactericide and today the market standard for amine based metalworking fluids in the European Union.

Currently there are still 27 biocidal actives in the registration process of the BPR. Ten (10) of these actives are formaldehyde releasing actives which will become candidates for substitution following the logic of the RAC decision for MBO, HPT and MBM.
Therefore we will not discuss the essential uses within the group of different formaldehyde releasing actives[1].

A similar situation we have for the group of pure fungicidal actives:

- BBIT (2-butyl-benzo [d]isothazol-3-one)
- OIT (2-octyl-2H-isothiazol-3-one)
- IPBC (3-iodo-2propynylbutylcarbamate)
- Biphenyl-2-ol
- Chlorocresol
- Sodium Pyrithione (pyridine-2-thiol-1-oxide, sodium salt)

The primary function of these actives is as a fungicide. Their bactericidal activity is limited or at least has major gaps. As these substances cannot be used without a bactericide, we will not further focus on this group of actives.

We focus on the remaining anti bactericidal actives (see table of PT 13 approved actives and the discussion on actives in the PT 13 registration process):

<u>CMI/MIT:</u> (CAS-Number: 55965-84-9):

For 3-4 decades CMI/MIT is a well-known biocide in metalworking fluid applications. It has a fast and very effective mode of action and the broad spectrum of activity against nearly all microorganisms which occur in metalworking fluids. However, CMI/MIT is only in use as a fire-fighting product. Which means that it is only in use in cases of a severe microbiological contamination of the circulation system and the standard preservatives don't work anymore. CMI/MIT is not in use as biostatic preservative in metalworking fluid industry!
The main limitations of CMI/MIT are:

- CMI/MIT is known as a very strong skin sensitizer (15 ppm = limit of labelling with H317: May cause an allergic skin reaction)
- pH of the biocidal product: 1-3 (decreasing pH of a metalworking fluid = metal corrosion, steel)
- Not stable at pH values > pH 8 (complete decomposition within 24 hours espc. In presence amines and/or alkanol-amines)
- Necessary use concentration of active substance (= 14% solution; ratio CMI/MIT = 3/1) in metalworking fluids: 30 ppm – 50ppm (= ca. 2-4 times above limit of labelling H 317)
- Dangerous to the environment; very toxic to aquatic life (acute 1 M-factor = 100 and chronic 1 M-factor = 100)

In case of a comparative assessment of MBO/HPT and CMI/MI in the recommended highest use concentrations we can state that both actives are essential for good housekeeping of water mixed metalworking fluids. MBO/HPT as a standard preservative (bactericide) with good long lasting effect (see description advantages MBO) and acceptable toxicological profile and CMI/MI as a very effective biocidal active in case of heavy microbiological contaminations. This represents the state of the art of housekeeping of metalworking fluids in the last two decades.

<u>Conclusion:</u>

We want to emphasize that currently the only practical choice of bactericides for PT 13 for downstream users are either products containing FARs or isothiazolinone products, in particular CMIT/MIT. 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 <u>at high concentrations</u>. The two FARs MBO and HPT are now automatically considered as candidates for substitution under the BPR solely as a result of their harmonized hazard classification due to read across to formaldehyde (i.e. as Carcinogenic Category 1B). For this reason, the group of isothiazolinones, and in particular CMI / MIT, are not considered to be candidates for substitution despite having the intrinsic hazard of being a strong skin sensitizer, with an elicitation concentration considered by RAC experts to be below the effective dose. Even without performing a formal comparative assessment it should be obvious that the only practical alternative to using FARs in PT13 to protect against bacteria have their own deficiencies with regard to the potential for significant and potentially career-threatening adverse effects on worker health. As the label triggers a lot of further regulations this will be the key indicator if the substance will be used by downstream users or not. In the case that the substance as well as the complete metal working system needs to be labelled as a skin sensitizer, nobody in industry would work with CMI / MIT, even if the substance is not a candidate for substitution and the use is considered to be safe.
The worst outcome of a comparative assessment would be that some substances will be banned and the remaining substances will not be used anymore due to in house chemical compliance rules.
This should illustrate that the comparative assessment might not be straight forward or be able to demonstrate using hazard and that one option is more desirable than another in terms of risk to worker safety and/or environmental harm.

MIT: (EC-Number: 220-239-6):

MIT is a relatively young biocidal active in PT 13 applications. It has been introduced approx. 15-20 years ago. The main advantage of MIT is better stability in a high alkaline metalworking fluid than CMI/MIT but the limitations are more or less the same:

- MIT is known as a very strong skin sensitizer (15 ppm = limit of labelling with H317: May cause an allergic skin reaction)
- pH of the biocidal product: 3-6
- Not stable at pH values > pH 9 (complete decomposition in presence of primary amines and/or alkanol-amines within 168 hours)
- Necessary use concentration of active substance in metalworking fluids: 150 ppm – 200ppm (>10 times above limit of labelling H 317)
- Dangerous to the environment; very toxic to aquatic life (acute 1 M-factor = 10 and chronic 1 M-factor = 1)
- An increase of allergic reactions on MIT in the public have been reported in the last 5 - 10 years.

Conclusion:
In case of a comparative assessment of MBO/HPT and MIT at the highest recommended use concentration of each active we can state that MBO/HPT is the better choice as bactericide the main reasons are:

- Better stability of MBO/HPT in alkaline environment
- MBO/HPT is less skin sensitizing than MIT in the maximum use-concentration.

BIT (EC-Number: 220-120-9):

BIT is an active which is stable at high pH values (8-12) and compatible with most metalworking fluid compounds.
BIT has two disadvantages which limit the use in metalworking fluids:

- BIT (like all other BIT-derivatives: BBIT and MBIT) has a well-known gap of efficacy against pseudomonas species (Paulus p. 664-667). Pseudomonas species are the most common bacteria in metalworking fluids. Therefore the use of BIT as bactericide in metalworking fluids is limited.
- BIT is a very strong skin sensitizer (like all isothiazolinone derivatives). Especially in high use concentrations (>300 ppm) which are necessary to control pseudomonas species skin irritations at workers have been observed in the last two decades (see product safety assessment 1,2-Benzisothiazol-3(2)-one (BIT) by The DOW Chemical Company).

Conclusion:
BIT is a potential alternative for formaldehyde releasing biocides but due to the gap of efficiency against pseudomonas species it can’t be used as single bactericide in metal working fluids. A combination with MBO/HPT or another bactericidal active (e.g. MIT) of both is preferred and necessary.

Diamine (EC-Number: 220-120-9):

Diamine is like BIT a bactericidal active which is stable at high pH levels (pH: 8-12) with a very broad spectrum of efficacy against bacteria. From the technical point of view this active has two main limitations which are the reason why diamine is nearly not present in the EU metalworking fluid industry:

- The amine reacts even under alkaline conditions like a cationic active (Paulus p. 724-725).
- Therefore Diamine is not compatible with the standard anionic emulsifiers (e.g. Na-laurylether sulfonate) in metalworking fluids. Most anionic surfactants inhibit the antimicrobial efficiency of Diamine completely.

- Due to its strong surface activity Diamine is causing severe foaming problems in metalworking fluid applications.

Today Diamine is only used in PT 13 niche applications where no anionic emulsifiers or surfactants are used (e.g. in selected antimicrobial system cleaner).

Conclusion:
Diamine is not a full alternative for MBO/HPT as market standard because of its incompatibility with anionic surfactants which are essential for all metalworking operations on iron alloys (stability at high pH values, corrosion protection, no foaming etc.). Diamine is an alternative for MBO/HPT in PT 13 niche applications only.

<u>Phenoxyethanol = PE</u> (EC-Number: 204-589-7):

PE has been known as a bactericide for three decades in metalworking fluid industry. PE is mainly in use in metalworking fluids (only emulsions) for metalworking operations on aluminium (and other non-iron-metal) alloys which are sensitive against amines and pH values above 9.5.

The main limitation of PE in metalworking fluids are:

- The limited solubility in water (max. 2,5%)
- The very high use concentration (1% - 2%)
- The low partition coefficient of 0,3% in mineral-oil to water.

Due to the arguments above PE is today only in use in metalworking fluids for special applications.

Conclusion:
Due to the low tendency of PE to move from the oil phase into the water phase (low partition coefficient) the use in oil in water emulsions is limited. MBO/HPT with a very high partition coefficient and by factor 10 lower use concentration is the preferred bactericidal active. The high partition coefficient of nearly 40 means in practice that MBO/HPT is fully and immediately available in the water phase after the preparation of the water mixed metalworking fluid.

<u>MBIT</u> (EC-Number: 2527-66-4):

MBIT belongs to the group of isothiazolinones. It is a new substance which has been in an approval process for years. As far as we are informed this substance has not been able to get authorized for PT13, even though it is a newly designed substance. This is a good indicator that is might get even more unlikely that industry will launch new molecules for use in metal working fluids. Besides this non-approval for MBIT, it shows that it is imperative to refer to already approved substances within a comparative assessment.

<u>DBNPA</u> <u>(EC-Number: 233-539-7)</u>

For more than 40 years DBNPA is a well-known biocidal active. It is successfully in use in many applications where the pH is <7. Under such conditions DBNPA is an excellent, fast acting bactericide. But DBNPA is also known for its extremely fast decomposition at pH-values > 7. On top of that it is well known that nucleophilic compounds like anionic emulsifiers (=standard in the metalworking industry; see CMI/MIT) will block the antimicrobial activity of DBNPA. That is why the use of DBNPA in the EU is very limited, or even negligible.

From the USA the concept of DBNPA-tablets (40% active ingredient) which release the active continuously over a long period of time at higher pH-values is known from the beginning of 2000. This concept can only be used in metalworking fluids free of anionic surfactants, which is by far the minority of applications (see. Diamine).

Conclusion:
Due to its technical limitations DBNPA (fast decomposition at pH>7 and in presence of nucleophilic compounds) is not an alternative to replace MBO in PT 13 applications.

8. Summary

This discussion shows that for all applications several biocidal actives are available. They all have advantages and disadvantages depending on the intended uses.
MBO and HPT are safe in their final use concentrations and provide several advantages in the intended applications.
The only limitation of MBO and HPT as typical amine based formaldehyde releasers is that they have to be labelled as concentrate with carc. Cat 1B and therefore fulfil the exclusion criteria.

9. References:

- Directory of Microbicides for the Protection of Materials edited by Wilfried Paulus (2005)
- Production Chemicals for the Oil and Gas Industry, Second Edition by Malcolm A. Kelland (2014)
- Quantification of Hydrogen Sulfide and Methanethiol and the Study of Their Scavenging by Biocides of the Isothiazolone Family, Eric Ferrot, Alain Bagnoud and Esmeralda Cicchetti; ChemPlusChem 2014, 79 77-82