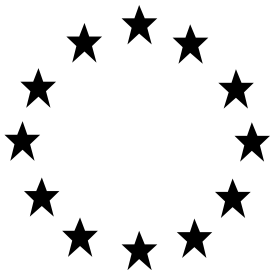
Regulation (EU) n°528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



Formaldehyde released from the reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)

[notified as 3,3'-methylene-bis(5-methyl¬oxazolidine) – MBO]

Product-type 2, 6, 11, 12 & 13

(disinfectant not intended for direct application to humans or animals, in-can preservative, preservative for liquid-cooling and processing systems, slimicide and working or cutting fluid preservative)

August 2017, revised July 2022 and April 2024

Austria

CONTENTS

1. STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1. Principle of evaluation

This assessment report has been established as a result of the evaluation of „Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)" (short: "RP 3:2") as product-type 2, 6, 11, 12 and 13 (disinfectant not intended for direct application to humans or animals, in-can preservative, preservative for liquid-cooling and processing systems and working or cutting fluid preservative), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market1, with the original view to the possible inclusion of this substance into Annex I or IA to that Directive.

The evaluation has therefore been conducted in the view to determine whether it may be expected, in light of the common principles laid down in Annex VI to Directive 98/8/EC, that there are products in product-type 2, 6, 11, 12 and 13 containing "RP 3:2" that will fulfil the requirements laid down in Article 5(1) b), c) and d) of that Directive.

1.2. Purpose of the assessment

The aim of the assessment report is to support a decision on the approval of "RP 3:2" for product-type 2, 6, 11, 12 and 13, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 2, 6, 11, 12 and 13 that contain "RP 3:2". In the evaluation of applications for product-authorisation, the provisions of Regulation (EU) No 528/2012 shall be applied, in particular the provisions of Chapter IV, as well as the common principles laid down in Annex VI.

The conclusions of this report were reached within the framework of the uses that were proposed and supported by the applicant (see Appendix II). Extension of the use pattern beyond those described will require an evaluation at product authorisation level in order to establish whether the proposed extensions of use will satisfy the requirements of Regulation (EU) No 528/2012.

For the implementation of the common principles of Annex VI, the content and conclusions of this assessment report shall be taken into account.

However, where conclusions of this assessment report are based on data protected under the provisions of Regulation (EU) No 528/2012, such conclusions may not be used to the benefit of another applicant, unless access to these data has been granted.

1 Directive 98/8/EC of the European Parliament and of the Council of 16 February 1998 concerning the placing biocidal products on the market. OJ L 123, 24.4.98, p.1

1.3. Procedure followed

This assessment report has been established as a result of the evaluation of "RP 3:2" as product-type 2, 6, 11, 12 and 13 (disinfectant not intended for direct application to humans or animals, preservative for liquid-cooling and processing systems and working or cutting fluid preservative), carried out in the context of the work programme for the review of existing active substances provided for in Article 16(2) of Directive 98/8/EC concerning the placing of biocidal products on the market.

"RP 3:2" (UVCB substance, no CAS no. attributed) was notified as an existing active substance, by Task Force Lubrizol Deutschland GmbH and Schülke & Mayr GmbH., hereafter referred to as the applicant, in product-type PT2, 6, 11, 12 and 13.

Commission Regulation (EC) No 1451/2007 of 4 December 2007[2] lays down the detailed rules for the evaluation of dossiers and for the decision-making process in order to include or not an existing active substance into Annex I or IA to the Directive.

In accordance with the provisions of Article 7(1) of that Regulation, AT was designated as Rapporteur Member State to carry out the assessment on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for "RP 3:2" as an active substance in product-type 2, 6 and 13 was 31 July 2007 and in Product Type 11 and 12 was 31 October 2008, in accordance with Article 9 (c) of Regulation (EC) No 1451/2007.

On 1 August 2007, AT competent authorities received from the applicant a dossier for product-type 2, 6 and 13, and on 31 October 2008 a dossier for product-type 11 and 12. The Rapporteur Member State accepted the dossier for product-type 2, 6 and 13 as complete for the purpose of the evaluation on 30 January 2008, and for product-type 11 and 12 on 30 January 2009. Due to data gaps the evaluation of the dossier for product-type 2 and 13 was suspended between 17 November 2008 and 31 March 2009. On 14 April 2009, the applicant submitted additional data as requested. With respect to still remaining data gaps the Austrian CA decided to prolong the suspension of the evaluation until 28 February 2010, to allow sufficient time for the applicant to finally close all data gaps.

On 18 February 2014, the Rapporteur Member State has sent, in accordance with Article 8 (2) of Regulation (EU) No 528/2012, to the applicant a copy of the evaluation report for comments on the conclusions of the evaluation within 30 days. On 13 March 2014, the Rapporteur Member State received the written comments from the applicant and revised the evaluation report where appropriate.

On 14 March 2014, the Rapporteur Member State has sent the draft evaluation report to ECHA. On 28 March 2014 the Rapporteur Member State received the result of the accordance check

2 Commission Regulation (EC) No 1451/2007 of 4 December 2007 on the second phase of the 10-year work programme referred to in Article 16(2) of Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. OJ L 325, 11.12.2007, p. 3

carried out by ECHA, which concluded that the draft evaluation report was not in accordance with the criteria as laid down in the Working procedure for the peer review of biocidal active substance evaluation. Subsequently the Rapporteur Member State has revised the draft evaluation report accordingly.

On 16 April 2014, the Rapporteur Member State has sent, in accordance with Article 8 (2) of Regulation (EU) No 528/2012, to the applicant a copy of the revised evaluation report for comments on the conclusions of the evaluation within 30 days. On 16 May 2014, the Rapporteur Member State received the written comments from the applicant and revised the evaluation report where appropriate.

On 20 May 2014, the Rapporteur Member State has sent the draft evaluation report to ECHA. On 4 June 2014 the Rapporteur Member State received the result of the accordance check carried out by ECHA, which concluded that the draft evaluation report was still not in accordance with the criteria as laid down in the Working procedure for the peer review of biocidal active substance evaluation. Subsequently the Rapporteur Member State has revised the draft evaluation report accordingly.

On 8 July 2014, the Rapporteur Member State has sent, in accordance with Article 8 (2) of Regulation (EU) No 528/2012, to the applicant a copy of the revised evaluation report for comments on the conclusions of the evaluation within 30 days. On 24 July 2014, the Rapporteur Member State received the written comments from the applicant and revised the evaluation report where appropriate.

On 20 August 2014, the Rapporteur Member State has sent the draft evaluation report to ECHA. On 9 September 2014 the Rapporteur Member State received the information from ECHA, that the dossier has been put on hold in order to wait for the finalisation of the RAC opinion on "RP 3:2".

On 4 August 2016, the Rapporteur Member State has sent, in accordance with Article 8 (2) of Regulation (EU) No 528/2012, to the applicant a copy of the revised evaluation report for comments on the conclusions of the evaluation within 30 days. On 2 September, the Rapporteur Member State received the written comments from the applicant and revised the evaluation report where appropriate.

On 29 September 2016, the Rapporteur Member State has sent the draft evaluation report to ECHA. On 21 October 2016 the Rapporteur Member State received the result of the accordance check carried out by ECHA concluding that the dossier will be further processed within process flow 17.

Following the peer review and commenting procedure of ECHA process flow 17 the evaluation was discussed in March 2017 in the Biocides Working Group Meeting II-2017.

Based on this, the assessment report and the opinions were originally adopted in BPC-21 in June 2017.

In the following discussions in SCBP-55 (November 2017) and SCBP-56 (January 2018), no conclusion on the approval/non-approval could be agreed as the argumentation for fulfilling the conditions for derogation according to BPR. Art 5(2) was considered not sufficient.

After the discussion in SCBP-56 also an ED-assessment according to the scientific criteria set out in Commission Delegated Regulation (EU) 2017/2100 was considered mandatory. A respective request from DG SANTE according to Article 75(1)(g) of Regulation (EU) No 528/2012 to the BPC was forwarded by ECHA to AT in May 2018. Therefore, the evaluation of "RP 3:2" was amended accordingly with an ED-assessment based on the available data.

In February 2020 ECHA has approved a change of participants in the applicant's consortium from Schülke & Mayr GmbH (who withdrew as applicant) to Vink Chemicals GmbH & Co. KG. Lubrizol Deutschland GmbH remained unchanged as applicant in the consortium

Before the submission of the revised documents in ECHA process flow 43 the ED assessment was subject to an e-consultation in March 2021 within the BPC WG HH and ENV experts. Furthermore, a written procedure of the ED expert group was conducted in May 2021, which was followed by an ED expert group ad hoc meeting on 24 June 2021. The advice of the experts was considered for the current version of the ED assessment.

Additionally, the ED assessment was sent to the applicants for commenting on 19 May 2021 in advance of the ED EG ad-hoc meeting.

On 12 August 2021, the Rapporteur Member State has sent, in accordance with Article 8 (1) of Regulation (EU) No 528/2012, to the applicant a copy of the revised evaluation report for comments on the conclusions of the evaluation within 30 days.

On 15 September 2021 the Rapporteur Member State has sent the revised evaluation report including the ED assessment to ECHA. On 14 October 2021 the Rapporteur Member State received the result of the accordance check carried out by ECHA (focussed on the ED assessment) concluding that the dossier will be further processed within ECHA process flow 43.

Following the peer review and commenting procedure of ECHA process flow 43 the ED evaluation was discussed in April 2022 in the Biocides Working Group Meeting I-2022.

In accordance to CA-March 15-Doc.5.1-Final the active substance was renamed in May 2023 to formaldehyde released from the reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2).

A request (Art. 75 (1) (g) of Regulation (EU) No 528/2012) by the Commission was received by ECHA on 17th February 2023 on the evaluation of the availability and suitability of alternatives to formaldehyde released from the reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 1:1) and (ratio 3:2) [in short: RP 1:1 and RP 3:2] for PT 2,6, 11, 12 (only RP 3:2) and 13. The BPC appointed AT as the rapporteur at its 46th meeting on 1 March 2023. The rapporteur presented the draft opinion to the BPC at its 48th and 49th meetings on 15 September and 23 November 2023, respectively. Following the adoption of the opinion at

the BPC meeting of 23 November 2023, the opinion was amended accordingly and delivered by ECHA to the Commission (final opinion: ECHA/BPC/405/2023).

In July 2023 the Commission requested the examination of efficacy tier 2 data on specific active substances acting as preservatives (PT 6-13) under Article 75(1)(g) of Regulation (EU) No 528/2012. The underlying mandate was forwarded by ECHA to the eCA. In order to address the necessity of requesting additional data, the eCA asked the member states (WG IV-2023) if the already available data can be considered as tier 2 and if further testing can be omitted. Based on the conclusions made in the EFF WG, the opinion was revised accordingly. The revised version was harmonised at WG-I-2024.

The previous version of this assessment report has been already published after BPC-21 in 2017. The revision from July 2022 is solely referring to the newly introduced ED-assessment. All other parts of the report remained unchanged. Additionally, only the change of participants was reflected in the relevant sections. The report was revised again in April 2024 due to the Article 75 (1) (g) mandate regarding Tier 2 efficacy studies. The conclusion of the respective BPC-WG discussions is included in this updated assessment report.

2. OVERALL SUMMARY AND CONCLUSIONS

2.1. Presentation of the Active Substance

2.1.1. Identity, Physico-Chemical Properties & Methods of Analysis

The biocidal active substance notified as "3,3'-methylene-bis(5-methyl¬oxazolidine" is a complex mixture prepared by reaction of paraformaldehyde and 2-hydroxy-propylamine at the ratio of 3:2.

The active substance is intended to release formaldehyde in aqueous solutions and therefore belongs to the substance class of formaldehyde releasers.

The active substance cannot be uniquely specified with the IUPAC name of the constituents, as not all the constituents could be identified. In addition the exact composition of the reaction mixture cannot be defined because of its variability depending on the concentration in aqueous systems, pH value and temperature. Therefore the active substance has to be considered as UVCB substance.

The most appropriate name for the active substance, which has to be considered as UVCB substance, should be "reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)" (short: "RP 3:2"). At its 35th meeting in December 2015 RAC adopted this naming of the active substance, as suggested by the eCA. It should be noted that CA-Document "CA-March 15-Doc.5.1-Final" dealing with the management of in situ generated substances in the context of the BPR lists the active substance as "Formaldehyde released from "3,3'-methylene-bis(5-methyl¬oxazolidine (MBO)". In May 2023 the active substance was renamed to formaldehyde released from the reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2).

Due to the evolving process of assigning the correct name to the active substance the following synonyms may be used throughout this CAR:

3,3'-methylene-bis(5-methyl¬oxazolidine (MBO)

N,N'-methylene-bis(5-methyloxazolidine)

Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)

"RP 3:2"

MBO

Since the active substance has to be considered as UVCB the specification is derived from the following identifiers:

- Starting materials paraformaldehyde and 2-hydroxypropylamine

[redacted]

[redacted]

[redacted]

Physico-Chemical Properties of "RP 3:2"

The composition of "RP 3:2" has been characterised by IR-, NMR-, UV/VIS- and MS-spectra.

"RP 3:2" is a colourless to yellowish liquid, has an amine like smell. The relative density is 1.05 at 20°C.

Since "RP 3:2" is considered as is a UVCB substance only a range of endothermic effects up to195°C (boiling) and an exothermal effect starting at 186 °C (decomposition) could be determined. The determination of vapour pressure has been considered as not relevant since the exposure assessment is based on formaldehyde. Therefore, the vapour pressure of formaldehyde was used for further calculations and not the value of the active substance or one of its constituents. The same reasoning applies for the Henry's law constant. The test item is completely miscible in water at room temperature. "RP 3:2" is completely miscible in DMSO, ethanol, n-Octanol, acetone and the solubility in n-heptane is 500 – 1000 mg/L at 20.5°C. "RP 3:2" is highly soluble in standard fat (HB 307) at 37°C.

The substance and the biocidal products are solely handled and marketed as aqueous solution which contains no organic solvents. The partition coefficient octanol-water is -0.043. The substance is regarded not to be surface active (surface tension is 68.1 mN/m at 20°C.) The viscosity is 21 mPa·s at 20°C.

The determination of the Dissociation Constant (pKa) is not possible; because the test substance is hydrolysable. No data for explosive properties have been submitted, which has been considered as not acceptable. Therefore a respective test has to be submitted to the eCA six months before the date of approval of the active substance. Its flash point is 73°C and its Auto-ignition temperature is 237°C. It is not considered to be reactive to container material (LDPE containers or in steel barrels or containers coated with LDPE).

Physico-Chemical Properties of Formaldehyde

For the physico-chemical properties of the hydrolysis product formaldehyde reference is made to the "Formaldehyde Core Dossier".

Physico-Chemical Properties of the hydrolysis product: 2-Hydroxypropylamine

2-Hydroxypropylamine is a hydrolysis product of the two active substances "reaction products from paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" notified as 3,3'-methylenebis(5-methyloxazolidine) and "reaction products from paraformaldehyde and 2-

hydroxypropylamine (ratio of 1:1)" notified as α, α′, α″-Trimethyl-1,3,5-triazine-1,3,5(2H,4H,6H)-triethanol.

Selected literature data on physico–chemical properties were provided by the applicant:

2-Hydroxypropylamine is a colourless to yellowish liquid and has a slight ammonia smell. Its melting point is 1.7°C and the boiling point is 160°C. The density is 0.9611 g/cm^3 at 20°C. The structure of 2-hydroxypropylamine is confirmed by IR- spectrum; 13C NMR-spectrum; 1H NMR-spectrum and MS-spectrum. The water solubility is 37 g/L at 11°C.

Vapour pressure of the hydrolysis product is 0.63 hPa at 25°C. 2-Hydroxypropylamine is soluble in all proportions in ethanol, diethyl ether, acetone, benzene and carbon tetrachloride and completely miscible with water. The viscosity is 23 mPas at 25°C.

With its low Henry's law constant, $4.94 \cdot 10^{-5}$ Pa m^3 mol^{-1} at 25°C, the substance is not expected to volatilize from aqueous solutions. The partition coefficient Octanol-Water log P_{OW} is -0.96.Because of the pKa of 9.94 at 10°C, the compound always protonated at environmental relevant pH values.

The hydrolysis product 2-hydroxypropylamine displays neither explosive nor oxidizing properties. Its flash point is 67°C.

The "Classification & Labelling Inventory" run by ECHA, which contains classification and labelling information on notified and registered substances received from manufacturers and importers, gives information that 2- hydroxypropylamine has metal corrosive properties. A database query dated February 2014 gave the information that 471 notifies out of 889 classified 2- hydroxypropylamine as Met. Corr. 1 (H290 May be corrosive to metals). However, it has to be noted, that the group of REACH registrants do not classify 2-hydroxypropylamine as metal corrosive.

Therefore further data/justification has to be submitted about metal corrosion property of the biocidal product, at the product authorisation stage.

The active substance as manufactured is a complex reaction product (UVCB substance) which forms a dynamic equilibrium in aqueous systems. The content of all constituents depends on the concentration of the active substance, the temperature and the pH-value. Because of the dynamic nature of the equilibrium analytical standard methods like HPLC/UV, LC/MS, GC/MS, photometry are difficult to use for characterisation of the composition and the determination of the active-ingredient-content or the impurities. NMR is supposed to be the only non-invasive method which does not change the equilibrium of the reaction mixture during analysis. Therefore, characterization by NMR has been provided additionally to get more information about the nature of the further constituents. However, this method is not suitable to monitor the composition of the active substance as manufactured (batch control, certificate of analysis) or the concentration in formulations of technical products and lubricants.

In conclusion, the active substance is specified by the maximally releasable formaldehyde which will be measured to control the produced batches. Hydroxylammonium chloride reacts with aldehydes under forming aldoximes and hydrochloric acid which will be determined by titration. Using this method the amount of releasable formaldehyde in the sample can be

characterised with sufficient precision. The method has been validated and shown to be sufficiently specific, accurate and sensitive.

The active substance is expected to hydrolyse completely under environmental conditions. Therefore, in the environment only the hydrolysis products formaldehyde and 2-hydroxypropylamine have to be considered. Regarding soil direct exposure to soil is not expected therefore no analytical method for soil is considered necessary. Regarding air analytical methods for the hydrolysis products formaldehyde and 2 hydroxypropylamine have been provided in Appendix "Formaldehyde Core-Dossier" as well as Appendix HPA. Regarding water, formaldehyde is the substance of concern with regard to ecotoxicity compared to 2-hydroxypropylamine. Respective methods are given for formaldehyde and 2-hydroxypropylamin in Appendix "Formaldehyde Core-Dossier" and in Appendix HPA. The method for determination of HPA in water has been considered as not sufficient. Therefore a respective validated method for HPA in water has to be submitted at product authorisation stage.

With regard to animal and human body fluids and tissues the active substance is expected to hydrolyse completely once the substance has entered human or animal bodies. In this respect formaldehyde is the substance of concern with regard to toxicity compared to 2 hydroxypropylamine. Respective analytical methods have been provided with the "Formaldehyde Core-Dossier".

2.1.2. Intended Uses and Efficacy

This dossier is to support the use of "RP 3:2" as Disinfectant system cleaner for metal working (PT2), as in can preservative exclusively in fuels (PT6), as preservative for closed recirculating cooling water systems (PT11), as slimicide in offshore drilling muds (PT12), as well as preservative for water based metal working fluids (MWF), only when directly dosed into the metal working system (PT13).

The effectiveness of the active substance in biocidal products against the intended target organisms (obligate or facultative pathogenic bacteria and fungi which might contaminate and spoil materials or subjects) has been demonstrated in basic experimental studies. These studies demonstrate that this formaldehyde-releaser is effective in inhibiting and irreversibly inactivating Gram negative and Gram positive bacteria (including mycobacteria) and fungi.

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.

The representative product for PT2 is a 10% aqueous solution of the active substance and the representative products for PT6, 11, 12 and 13 are the active substance as manufactured.

For use of the active substance in **PT2** products (disinfectant system cleaners) test reports according to EN 1040 and EN 1275 were submitted to determine the basic microbicidal effect of "RP 3:2". In these quantitative suspension tests the biocidal product tested exhibited sufficient bactericidal (*S. aureus*, *P. aeruginosa*; RF>5) and fungicidal (*C. albicans*, *A. niger*; RF>4) activity at a concentration of 2% at 1 h, 0.5% at 3 h and 0.25% at 6 h exposure (bactericidal) and 0.5% at 1 h and 0.25% at 3 h exposure (fungicidal). Overall, a microbicidal effect of the biocidal product was demonstrated with concentrations ranging from 0.25% (=2500 ppm) up to 2% (20000 ppm) depending on the exposure time.

The microbistatic effects were demonstrated by different growth inhibition test. The overall MIC is 0.05% (v/v) (bacteria), 0.15% (v/v) (mycobacteria, fungi).

For use of the active substance in **PT11** growth inhibition for some bacteria and fungi was determined in accordance to DGHM-standard methods. The biocidal product tested completely inhibited growth of 2 bacterial species (*Proteus sp.*, *Pseudomonas sp*.,) and one bacterial strain (*Pseudomonas putida*) at a concentration of 0.025% within 3 days and inhibited growth of the 2 fungal strains (*Acremonium spec*., *Fusarium spec.*) tested at a concentration 0.15% within 5 days. The overall MIC and or growth inhibition concentration is 0.025% (v/v) (only for bacteria and only valid for closed cooling water systems) and 0.15% (v/v) if growth of fungi should be prohibited also.

The main field of use for "RP 3:2" is preservation of water based processing liquids, such as metal working fluids (MWF) which belong to PT13. Machinery used for metal working processes, such as high speed CNC machines, need cooling too to ensure constant operating temperature for precision manufacturing. Therefore this equipment is attached to closed recirculating cooling systems using water based cooling liquids. Those water based cooling liquids need to cope with the same typical requirements of water based metal working fluids, such as corrosion protection, wetting agents, defoamers and biocides. Therefore the applicant has chosen the approach to use MWF isolates also for PT11 testing by arguing that the cooling liquid itself will be comparable to the composition of the MWF, with the exception of the lubricant which is only necessary for the MWF. In addition the cooling liquid and MWF are expected to face a similar microbial load, because they are used in the same metal working environment. Therefore testing a MWF isolate (tested Gram negative bacteria: Pseudomonas sp, Pseudomonas putida and Proteus sp.) for PT 11 has been considered as a valid approach.

Growth inhibition for some bacteria and fungi was determined in accordance to DGHM-standard methods. The biocidal product tested completely inhibited growth of 2 bacterial species (*Proteus sp., Pseudomonas sp.,*) and one bacterial strain (*Pseudomonas putida*) at a concentration of 0.025% within 3 days (Doc IIIB5.10.2/07) and inhibited growth of the 2 fungal strains (*Acremonium spec., Fusarium spec*.) tested at a concentration 0.15% within 5 days (Doc IIIB5.10.2/08).

The overall MIC and or growth inhibition concentration is 0.025% (v/v) (only for bacteria and only valid for closed cooling water systems) and 0.15% (v/v) if growth of fungi should be prohibited also.

The active substance also shows innate efficacy against *L. pneumophila*. The test (Doc IIIB5.10.2/16) showed a log 5 reduction of *L. pneumophila*, at concentrations of 0.25%, 0.15% and 0.1% of the active substance. No dose response could be seen at these concentrations. Although the lowest tested concentration at 0.1% is 4 times higher than the use conc. of 0.025% which has been derived from studies Doc IIIB5.10.2/07 and Doc IIIB5.10.2/08. a read across to "RP 1:1" could be established where a valid test against *Legionella longbeachae* has been submitted, showing a MIC at 0.025% (v/v). (Doc IIIB5.10.2/17).

To conclude the active substance is considered as sufficiently efficacious at an in use concentration of 0.025% (v/v) which is only valid for efficacy against bacteria and strictly limited for use in closed cooling water systems in metal working environments.

At product authorisation stage the efficacy of PT11 products (cooling water) based on "RP 3:2" should be tested in real or synthetic cooling water.

For use of the active substance in **PT13** tests showed that the biocide completely inhibited growth of the tested bacterial (including *Mycobacterium sp.)*, yeasts and fungal strains at ≥ 0.15 % w/w**.** The available data can be considered to include tier 2 data sufficiently simulating the anticipated service life of the MWF only when the product is directly applied into the MWF directly dosed in the metal working system. Thus, the efficacy of the representative product in such use has been sufficiently demonstrated. At the same time, it has to be noted that the available data cannot be considered tier 2 data when the product is dosed in the concentrated MWF. Therefore, the efficacy of the representative product in this use has not been demonstrated.

For use of the active substance in **PT6 t**he effectiveness of "RP 3:2" in biocidal products against the intended target organisms (bacteria such as *P. aeruginosa, Acinetobacter spec.,* and *E. aerogenes*) has been demonstrated in the preservation of a diesel-water fuel emulsion (Doc IIIB 5.10.2/11) at concentrations of 50 ppm and 250 ppm.. This study demonstrates that this formaldehyde-releaser is effective in inactivating Gram negative bacteria which are representative for the organisms in the intended field of use. In addition a screening study (Doc IIIB 5.10.2/10) has been submitted, testing the efficacy of "RP 3:2" against *Pseudomonas aeruginosa, Yarrowia tropicalis* (yeast) and *Hormoconis resinae* (fungus). However for deficiencies in the control samples this study can be considered as supportive for the bacteria testing. The available data can be considered as tier 2, due to the short-term nature of the use aging can be omitted as the test duration simulates the anticipated service life. Efficacy was demonstrated only in fuels and not in other matrices.

For use of the active substance in **PT12 t**he effectiveness of "RP 3:2" in biocidal products against target organisms representative for bacteria in oil-drilling muds such as sessile general heterotrophic bacteria (GHB), acid-producing general heterotrophic bacteria (APB) and sulphate reducing bacteria (SRB) has been shown (Doc IIIB 5.10.2/15). In addition two screening tests (Doc IIIB 5.10.2/13 and Doc IIIB 5.10.2/14) showed efficacy of "RP 3:2" against SRBs using an iron sulphide blackening method. "RP 3:2" showed efficacy at 800 ppm against sessile bacteria in laboratory testing. At product authorisation stage further studies under field conditions will be necessary to substantiate the current in-use concentrations of up to 1500 ppm, as reported by the applicant.

2.1.3. Classification and Labelling for the active substance

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonized classification and labelling (CLH) of "RP 3:2" (RAC, 2015)3 that is shown in Table 2.1.3-3.

Table 2.1.3-1 Classification and labelling of "RP 3:2" according to Reg. 1272/2008/EC agreed by RAC (December 2015)

Classification		**Justification**
Classification	Acute Tox. 4, H302 Acute Tox. 3, H311 Acute Tox. 4, H332 Skin Corr. 1B, H314 Skin Sens. 1A, H317 Eye Dam. 1, H318 STOT RE 2, H373 Muta 2, H341 Carc. 1B, H350 Aquatic Chronic 2, H411	See below
Hazard statements	H302: Harmful if swallowed	Animal testing results for "RP 3:2" and read across data from formaldehyde

3 https://echa.europa.eu/documents/10162/96051139-f376-4da3-b25a-130668d6db45

Classification		Justification
	H311: Toxic in contact with skin	Animal testing results for "RP 3:2" and read across data from formaldehyde
	H332: Harmful if inhaled	Animal testing results read across data from formaldehyde
	H314: Causes severe skin burns and eye damage	rabbit test results
	H317: May cause an allergic skin reaction	Positive GPMT with the active substance and consideration of use phase of substance: FA* release by contact with biological media and dilution
	H318: Causes serious eye damage	See RAC (2015); classification for skin corrosion includes classification for eye damage, but RAC decided that nevertheless additional classification for eye damage is needed, but additional H statement is necessary for labelling.
	H373: May cause damage to organs (gastrointestinal tract and respiratory tract)	Local effects in GIT observed with "RP 3:2" and local effects in respiratory tract expected from formaldehyde release (read across) at doses corresponding to the guidance value range and below doses triggering acute toxicity.
	H341: Suspected of causing genetic defects	consideration of use phase of substance: FA* release contact with biological media and dilution
	H350: May cause cancer	consideration of use phase of substance: FA* release contact with biological media and dilution
	H411: Toxic to aquatic life with long lasting effects	cf RAC (2015)

Classification		Justification
Specific classification limits	-	-

*FA= Formaldehyde

Labelling		
GHS Pictograms		
Signal words		Danger
Hazard statements		H302: Harmful if swallowed
		H311: Toxic in contact with skin
		H332: Harmful if inhaled
		H314: Causes severe skin burns and eye damage
		H317: May cause an allergic skin reaction
		H318: Causes serious eye damage
		H373: May cause damage to organs (gastrointestinal tract and respiratory tract)
		H341: Suspected of causing genetic defects
		H350: May cause cancer
		H411: Toxic to aquatic life with long lasting effects
Supplemental hazard statement code		EUH071: Corrosive to the respiratory tract
Precautionary Statements	**General**	-
	Prevention	P202: Do not handle until all safety precautions have been read and understood. P260: Do not breath dust/fume/ gas/mist/vapours/spray. P264: Wash … thoroughly after handling. P270: Do not eat, drink or smoke when using this product.

		P271: Use only outdoors or in a well-ventilated area. P280: Wear protective gloves/protective clothing/eye protection/face protection. P273: Avoid release to the environment
	Response	P301 + P330 + P331: IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. P303 + P361 + P353: IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water/ shower. P304 + P340: IF INHALED: Remove person to fresh air and keep comfortable for breathing. P305 + P351 + P338: IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. P362 + P364: Take off contaminated clothing and wash it before reuse. P308 + P313: IF exposed or concerned: Get medical advice/attention. P391: Collect spillage
	Storage	P405: Store locked up.
	Disposal	P501: Dispose of contents/container in accordance with local/regional/national/ international regulations (to be specified).

RAC (December 2015) concluded on classification for carcinogenicity category 1B.

2.1.4. Classification and labelling for the biocidal products

For the PT2 representative product

The PT2 representative product is a model formulation (dummy product) and represents a 10% aqueous solution of the active substance. Considering the general classification limits this dummy product has to be classified like the active substance, except for acute oral and acute inhalation toxicity. The latter is not required for the model formulation.

For the PT 6, 12 11 and PT 13 representative product

The PT6, PT11, PT12 and PT13 representative products are identical to the active substance, i.e. Grotan®OX, GrotaMar 71® and Contram™ MBO (a.s. as manufactured) and are marketed for further use as in-can preservative in water based technical products.

Therefore for classification and labelling of the biocidal product according to Regulation (EC) No 1272/2008, Annex VI reference is made to the classification and labelling of the active substance above.

2.2. Summary of the Risk Assessment

2.2.1. Risk arising from physico-chemical properties

None identified.

2.2.2. Human Health Risk Assessment

2.2.2.1. Hazard identification

No toxicokinetic or metabolism studies can be provided for the active substances "RP 1:1" and "RP 3:2", since they are produced by a 1:1 or 3:2 mixture of 2-hydroxypropylamine with paraformaldehyde resulting in various reaction products that are in equilibrium with each other, the equilibrium depending on dilution, pH and temperature. However from knowledge of the chemical reaction kinetics, the water hydrolysis study and the presumed biocidal mode of action it can be reliably assumed that in qualitative terms "RP 1:1" and "RP 3:2" hydrolyse to formaldehyde and 2-hydroxypropylamine upon contact with biological tissues and dilution in aqueous media. The intermediate reaction products that are in equilibrium with each other and the ultimate hydrolysis products are the same for "RP 1:1" and "RP3:2". Therefore, in order to get a better understanding of the toxicity of the overall mixtures, hazard data on both of the active substances ("RP 1:1" and "RP 3:2") have been assessed in parallel and for the risk assessment also the toxicology of the hydrolysis products Formaldehyde and 2-Hydroxypropylamine was considered.

Within the toxicological studies the active substances induced dominant local effects. The substances are corrosive to skin (and eye), according to the eCA acute (oral) toxicity seems to be due to the corrosive properties. However following the fact that acute toxicity data are available RAC nevertheless classified "RP 1:1" also for acute systemic toxicity category 4 for the oral and the inhalation route and "RP 3:2" for acute systemic toxicity category 4 for the oral, the dermal and the inhalation route..

In the 90 day repeated dose gavage studies in rats with "RP 1:1" and "RP 3:2" dominant local effects were detected in the GI tract, for "RP 1:1" with a LOAEC/NOAEC of 3.2/1.2 % and LOAEL/NOAEL of 80/30 mg/kg bw day (lesions of larynx and pharynx, oesophagus and stomach inflammation) and for "RP 3:2" with a LOAEC/NOAEC of 1.2/0.4 % and LOAEL/NOAEL of 60/20 mg/kg bw day (chronic ulcerative gastritis). Also breathing sounds and mortality were observed in the 90 day study with "RP 1:1" at ≥ 80 mg/kg bw day (3.2%) and granulocytes increase and lymphocytes decrease were observed in the 90 day study with "RP 3:2" at ≥ 60 mg/kg bw day (1.2%). However RAC classified "RP 3:2" and "RP 1:1" for STOT RE 2 due to the local effects observed at doses and concentrations within the guidance values and below respective acute toxicity values.

A teratogenicity study in the rabbit is available for "RP 3:2", which does not indicate concern for developmental toxicity: Developmental toxicity (like increased number of early and late resorptions, decreased number of foetuses, increase in post-implantation loss, mortality of foetuses) was only observed at the high dose of 135 mg/kg bw day/6.75% (i.e. LOAEL/LOAEC) which caused also severe maternal toxicity (like a decrease in body weight, increased mortality, abortions in addition to local lesions in the stomach, increased dilatation of

the renal pelvis). Also these systemic maternal effects are considered to be a consequence of local effects. A NOAEL/NOAEC of 90 mg/kg bw day/4.5% was proposed, though there is some evidence that at least an increased incidence of lesions in the stomach occurred also at 45 mg/kg bw/2.25%. Furthermore also a one generation study (OECD TG 415) is available for "RP 3:2", which does not indicate concern for reproductive toxicity: Histopathological changes in the forestomach of males were observed with a LOAEC/NOAEC of 0.3/0.1% and LOAEL/NOAEL of 15/5 mg/kg bw day. At higher doses in addition to local stomach effects also reduced male food consumption and bw gain were observed as well as an increased sum of post-implantation and post-natal loss. Consequently a systemic LOAEL/NOAEL of 45/15 mg/kg bw for parents as well as F1 was derived from this study. The absence of a dose-response relationship for post-implantation loss and post-natal loss data after correction for cannibalism, the lack of concomitant findings in the fertility study and the developmental study and strong local effects in parts of the affected high dose dams was considered to conclude that there is no sufficient concern for classification. This conclusion is also supported by the available subchronic data for "RP 3:2" that included negative histo/pathological results for reproductive organs. Also the toxicological data from the hydrolysis product formaldehyde support the negative conclusion. The data are also considered relevant for the evaluation and concordant conclusion of "RP 1:1", for which also a subchronic study including a negative histo/pathological evaluation of reproductive organs is available. The conclusion for no classification of "RP 1:1" and "RP 3:2" was confirmed by RAC (December 2015). Functional observation test batteries were included in the 90 day studies and did not indicate a concern for neurotoxicity for "RP 1:1" or "RP 3:2".

The available guinea pig maximisation tests for "RP 1:1" and "RP 3:2" indicate a high skin sensitization potential of both substances (Cat 1A), i.e. with intradermal induction concentrations ≤ 1% positive reactions to non-irritant challenge were observed in ≥ 60% of the animals. Human data support the principal skin sensitizing property of "RP 3:2". Also mechanistic consideration of formaldehyde release upon contact with biological tissues supports this conclusion. "RP 1:1" and "RP 3:2" result positive within bacterial gene mutation tests, in vitro chromosomal aberration tests and an in vitro mammalian gene mutation tests. For both substances the in vivo mouse micronucleus tests are negative and the bone marrow chromosome aberration tests are ambiguous. No carcinogenicity studies are available for "RP 1:1" or "RP 3:2". However the toxicological profile of "RP 1:1" and "RP 3:2" and the respective hydrolysis study data provide sufficient evidence to read across the local effects data from formaldehyde to "RP 1:1" and "RP 3:2": The toxicity of the active substances is dominated by local irritation and local (in vitro) but not systemic genotoxicity and the hydrolysis study and efficacy mode of action support that the equilibrium within the "RP 1:1" and "RP 3:2" quickly shifts towards formaldehyde and 2-hydroxypropylamine by dilution and by the reaction of formaldehyde with biological media.

This is essentially the basis for reading across the classification of formaldehyde for germ cell mutagenicity category 2 and carcinogenicity category 1B.

An ED assessment has been carried out according to the EFSA/ECHA (2018) guidance. For the T-modality the ED criteria are not met. EAS mediated adversity (impact on semen quality parameters and testes histopathology) was observed in recent conducted rodent studies carried out with the hydrolysis product formaldehyde, the toxicological relevant component of the

UVCB [redacted] ted by human data (male workers exposed to formaldehyde). The mode of action leading to observed testes effects remains unclear, multiple mode of actions are hypothesised. Further testing with the active substance is not considered appropriate in that specific case, because 'testing does not appear scientifically necessary' (first heading of Annex IV of the Regulation (No) 528/2012) and because 'testing is technically challenging' (referring to second heading of Annex IV), as detailed below:

- It is uncertain, if further mechanistic studies with "RP 3:2" (as well as "RP 1:1") would allow establishing a mode of action keeping in mind that endocrine mediated endpoints may be impacted secondary to general, non-endocrine toxicity and that in vivo apical endpoints can be triggered by several modes of action, including endocrine and non-endocrine modalities.

- Due to the properties of "RP 3:2" (as well as "RP 1:1") as skin corrosive, skin sensitising and local acting genotoxic carcinogen and the corresponding low effect concentration(s), it is difficult to select an appropriate test system to get meaningful results.

- The main hydrolysis product formaldehyde of "RP 3:2" (as well as "RP 1:1") is an endogenously formed substance with a high turn-over rate. Exogenous FA due to biocidal product use might be a minor contributor to total systemic exposure.

Further facts to be regarded for the consideration of additional testing:

- "RP 3:2" (as well as "RP 1:1") have already a severe hazard profile: they fulfil the exclusion criteria of Article 5(1)a) of the BPR (REGULATION (EU) No 528/2012) based on the harmonized classification as Carc. 1B.

- Therefore, strict risk management measures are already in place for occupational exposure with an OEL for workers of 0.3 ppm for FA. For the intended biocidal uses of "RP 3:2" (as well as "RP 1:1"), there is no concern that this OEL is exceeded.

With exception of the T-modality (ED criteria are not met), no conclusion on ED properties for "RP 3:2" (as well as for "RP 1:1") based on the present data set, including also data/information of hydrolysis products formaldehyde and HPA, can be drawn. As a consequence, a risk estimation for potential ED effects of "RP 3:2" cannot be carried out for biocidal products.

2.2.2.2. Effects assessment

Furthermore in the absence of inhalation studies with "RP 1:1" and "RP 3:2" the local respiratory AEC of formaldehyde (0.12 µg/L air) derived from human and animal data is read across to "RP 1:1" = 0.43 µg/L air ([redacted]
and to "RP 3:2" = 0.25 µg/L air ([redacted]).
No local dermal AEC can be derived due to the sensitizing properties of "RP 1:1" and "RP 3:2", but the general classification limit for Cat 1A substances, i.e. 0.1% can be engaged for a qualitative risk characterisation. Oral AECs are not relevant for the intended applications.

Repeated gavage toxicity data for "RP 1:1" indicated dominant local effects in the GIT. The 90 day LOAEL/NOAEL of 80/30 mg/kg bw covers the local lesion of larynx and pharynx as well as the consequent breathing sounds and mortality. Applying a standard assessment factor of 100 for inter-species and intra-species differences to the LOAEL/NOAEL indicates a relevant AEL $_{\text{medium term}}$ range of 0.8 to 0.3 mg/kg bw day for the "RP 1:1". Reading across the lowest LOAEL/NOAEL for "RP 3:2" (discussion see below, 45/15 mg/kg bw day, apply factor 1.6, see table 3.1) and applying the standard assessment factor of 100 would result in a relevant AEL $_{\text{medium term}}$ range of 0.7 to 0.24 mg/kg bw day. Reading across the systemic AEL $_{\text{short, medium and long term}}$ for formaldehyde (0.15 mg/kg bw day, factor 3.6, see table 3.1.) would result in an AEL $_{\text{short, medium and long term}}$ of 0.54 mg/kg bw day. This value is within the AEL range derived from the NOAEL and the LOAEL of the critical study with "RP 1:1" (0.3 and 0.8 mg/kg bw day). Considering

- that the LOAELs and NOAELs for "RP 1:1" are based on dominant local effects (lesions of larynx and pharynx, oesophagus and stomach inflammation), breathing sounds and mortality.
- that the AEL for formaldehyde is below (i.e. protective for) the LOAEL for RP1:1 divided by standard assessment factor of 100
- that all potential AEL estimates are in the same order of magnitude (range from 0.8 to 0.3 mg/kg bw day) and there is always uncertainty from reproducibility of study results and interpretation of complex data,
- that "RP 1:1" hydrolyses with dilution and contact with biological media, the ultimate hydrolysis product after systemic uptake is formaldehyde
- that there is an extensive database available for formaldehyde, including human data
- and including long term exposure data
- and a harmonized systemic AEL for formaldehyde was derived in the formaldehyde CAR and it was decided that this AEL is protective for short, medium and long term exposure
- that the data available for the second hydrolysis product 2-hydroxypropylamine support that the latter is of low concern compared to formaldehyde (see overview table 3.11)

an AEL based on read across to formaldehyde is proposed:

AEL short, medium and long term = 0.54 mg/kg bw day for the "RP 1:1"

Repeated gavage toxicity data for "RP 3:2" indicated predominantly local effects. The 90 day LOAEL/NOAEL of 60 / 20 mg/kg bw covers the chronic ulcerative gastritis and peritonitis as well as the consequent increased granulocytes and decreased lymphocytes effect. Applying a standard assessment factor of 100 for inter-species and intra-species differences to the LOAEL/NOAEL indicates a relevant AEL $_{\text{medium term}}$ range of 0.6 to 0.2 mg/kg bw day for the "RP 3:2". Within the 1-generation study a systemic overall LOAEL/ NOAEL of 45/ 15 mg/kg bw day was defined on the basis of reduced male food consumption and body weight gain as well as an increased sum of post-implantation and post-natal loss. Though the food consumption and body weight effects may be secondary to local GI effects and the post-implantation and post-natal loss effect is confounded with cannibalism and is toxicologically not consistent with the other study results (low biological significance), the LOAEL/NOAEL range may be

precautionary considered: application of a standard assessment factor of 100 for interspecies and intra-species uncertainty would result in a relevant range for the AEL $_{\text{medium term}}$ between 0.45 and 0.15 mg/kg bw day. Reading across the lowest LOAEL/NOAEL for "RP 1:1" (discussion see above, 0.8 to 0.3 mg/kg bw day) would result (factor 0.62, see table 3.1) in a relevant AEL $_{\text{medium term}}$ range of 0.5 to 0.19 mg/kg bw day. Reading across the systemic AEL $_{\text{short, medium and long term}}$ for formaldehyde (0.15 mg/kg bw) to the "RP 3:2" (factor 2.2, see table 3.1.) would result in an AEL $_{\text{short, medium and long term}}$ of 0.33 mg/kg bw day. This value is within the AEL range derived from the NOAEL and the LOAEL of the critical study with "RP 3:2" (0.15 and 0.45 mg/kg bw day). Considering

- that the LOAELs and NOAELs for "RP 3:2" are based on dominant local effects (chronic ulcerative gastritis, increase granulocytes, decreased lymphocytes in 90 day study; and moderate to massive ulcerations and other less severe histopathology in forestomach accompanied with slightly reduced male food consumption and male bw reduction in one generation study)
- that the AEL for formaldehyde is below (i.e. protective for) the LOAEL for "RP 3:2" divided by standard assessment factor of 100
- that all potential AEL estimates are in the same order of magnitude (range from 0.15 to 0.45 mg/kg bw day) and there is always uncertainty from reproducibility of study results and interpretation of complex data,
- that "RP 3:2" hydrolyses with dilution and contact with biological media, the ultimate hydrolysis product after systemic uptake is formaldehyde
- that there is an extensive database available for formaldehyde, including human data
- and including long term exposure data
- and a harmonized systemic AEL for formaldehyde was derived in the formaldehyde CAR and it was decided that this AEL is protective for short, medium and long term exposure
- that the data available for the second hydrolysis product 2-hydroxypropylamine support that the latter is of low concern compared to formaldehyde (see overview table 3.11)

an AEL based on read across to formaldehyde is proposed:

AEL $_{\text{short, medium and long term}}$ = 0.33 mg/kg bw day for the "RP 3:2"

In summary, the following AELs and AECs were used for risk assessment:

"RP 1:1" systemic AEL, $_{\text{short, medium and long term}}$	0.54 mg/kg bw day
"RP 1:1" local AEC, $_{\text{short, medium and long term}}$	0.43 µg/L air
"RP 3:2" systemic AEL, $_{\text{short, medium and long term}}$	0.33 mg/kg bw day
"RP 3:2" local AEC, $_{\text{short, medium and long term}}$	0.25 µg/L air
Formaldehyde systemic AEL $_{\text{short, medium and long term}}$	0.15 mg/kg bw day
Formaldehyde local AEC $_{\text{short, medium and long term}}$	0.12 µg/L air

No ADI and ARfD are derived for "RP 1:1" and "RP 3:2" for the following reasons:

- As indicated in the intended use sections and the human risk assessment no dietary exposure is expected.
- "RP 1:1" and "RP 3:2" is expected to ultimately hydrolyse to formaldehyde due to application of "RP 1:1" and "RP 3:2" in aqueous dilution, contact with organic material, contact with biological tissue and eventual systemic uptake into aqueous body fluids.
- Systemic AELs for "RP 1:1" and "RP 3:2" were derived considering the systemic AEL for formaldehyde.
- Within the CAR for formaldehyde the following was concluded: "ADI and ARfD are not considered necessary based on the 2014 evaluation of the EFSA FEEDAP Panel (SCIENTIFIC REPORT OF EFSA, Endogenous formaldehyde turnover in humans compared with exogenous contribution from food sources. EFSA Journal 2014;12(2):3550). It concluded that the relative contribution of exogenous formaldehyde from consumption of animal products (milk, meat) from target animals exposed to formaldehyde-treated feed was negligible compared with formaldehyde turnover and the background levels of formaldehyde from food sources."
- In case of future needs due to new recognitions in science all data are available in this CAR to easily derive an ADI and ARfD.

2.2.2.3. Exposure assessment

General remark: Referring to the risk characterization, the term negligible exposure is used qualitatively for describing that exposure via a particular use is expected to be negligible (in relation to the total human exposure). The contribution of this particular use to total exposure is expected be sufficiently covered by the other quantitative exposure estimates predicted. The term negligible exposure is not intended to characterize any risk potential.

PT2 - Private area and public health area disinfectant

The main routes of human exposure towards the "RP 3:2" and hydrolysis products originating in the application of the biocidal products for PT 2 are listed in the table below.

Table 2.2.2.3-1: Main paths of human exposure to "RP 3:2", formaldehyde and 2-hydroxypropylamine via use for PT 2

Exposure path	Primary (direct) exposure, during use of b.p.		Secondary (indirect) exposure Incidental contact after application	Via the environment
	Professional use	General public	General Public	General Public
Inhalation	Yes	Not relevant	Not relevant	Not relevant[1]

Dermal	Yes	Not relevant	Not relevant	Not relevant[1]
Oral	Not relevant	Not relevant	Not relevant	Not relevant[1]

[1] From TNsG on Human Exposure, 2007: "Exposure via the environment is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food. These scenarios are not considered relevant in this case.

Referring to a statement of the applicant, most sites apply "RP 3:2" in closed systems using automatic dosage during the formulation of system cleaners. Nevertheless, potential exposure scenarios like handling of biocidal product or formulated system cleaners outside of the vessels are identified as possible as well. The formulated system cleaners are used by professionals and not intended for the general public. Therefore, inhalation and dermal exposures of professionals are expected and considered for this assessment.

Formulation and application of system cleaners are not performed by non-professionals, therefore, potential human exposure of the general public is considered to be not relevant. Secondary exposure and human exposure via the environment are expected to be not relevant for the same reasons, as exposure is considered to be limited to work places at industrial sites.

The exposure values relevant for risk characterisation are presented in chapter 2.2.2.4 of this document.

PT6 - In-can preservative

The main routes of human exposure towards "RP 3:2" originating in the application of b.p. as PT6 are listed in the table below.

Table 2.2.2.3-2: Main paths of human exposure to "RP 3:2" via use for PT6

Exposure path	Primary (direct) exposure, during use of b.p.		Secondary (indirect) exposure Incidental contact after application	Via the environment
	Professional use	General public	Professional use/General Public	General Public
Inhalation	Yes	Not relevant	Yes	Yes1
Dermal	Yes	Not relevant	Yes	Not relevant1
Oral	Not relevant	Not relevant	Not relevant	Not relevant1

1 From TNsG on Human Exposure, 2007: "Exposure via the environment is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food.

Most fuel formulators apply the b.p. in closed systems using automatic dosage during the formulation of fuels. Nevertheless, potential exposure scenarios like handling of biocidal product or fuel outside of the vessels are identified as well. Therefore, inhalation and dermal

exposures of professionals are expected to be possible in principle and considered for this assessment. Formulation of fuels is not performed by non-professionals, therefore, human exposure of the general public via this application is considered to be not relevant.

Anyhow contact with the active substance might take place during refuelling of engines. Exposure to the active substance via the use of fuels is considered to be primary exposure for refuelling and secondary for bystanders. Inhalation and dermal exposure is considered to be possible for professionals like filling station attendants and the general public during refuelling engines. The inhalational route is considered to be the only relevant route for bystanders (e.g. a child as a bystander during refuelling).

PT11 - Preservatives for liquid cooling and processing systems

The main routes of human exposure towards "RP 3:2" and hydrolysis products originating in the application of the biocidal product as PT 11 is listed in the table below.

Table 2.2.2.3-3: Main paths of human exposure "RP 3:2", formaldehyde and 2-hydroxypropylamine via use for PT11

Exposure path	Primary (direct) exposure, during use of b.p.		Secondary (indirect) exposure Incidental contact after application	Via the environment
	Professional use	General public	General Public	General Public
Inhalation	Yes	Not relevant	Not relevant	Not relevant[1]
Dermal	Yes	Not relevant	Not relevant	Not relevant[1]
Oral	Not relevant	Not relevant	Not relevant	Not relevant[1]

[1] From TNsG on Human Exposure, 2007: "Exposure via the environment is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food. These scenarios are not considered relevant in this case.

The biocidal product is applied by professionals as preservative for closed liquid cooling systems in industry. Several identified tasks like loading of the product or sampling might result in inhalative and dermal exposure of professionals. Oral exposure of professionals is considered to be not relevant due to awareness and expected/stipulated hygiene at the workplace.

Exposure of non-professionals using the biocidal product is considered to be not relevant as this use applies only for industrial sites. Secondary exposure is unlikely, due to the use of the biocidal product in closed systems. Indirect exposure via the environment is expected to be not relevant due to the properties of the active substance and the hydrolysis products (e.g. not bioaccumulative, biodegradable).

The exposure values relevant for risk characterisation are presented in chapter 2.2.2.4 of this document.

PT12 - Slimicide

The main routes of human exposure towards "RP 3:2" and hydrolysis products originating in the application of the biocidal products for PT12 are listed in the table below.

Table 2.2.2.3-4: Main paths of human exposure to "RP 3:2", formaldehyde and 2-hydroxypropylamine via use for PT12

Exposure path	Primary (direct) exposure, during use of b.p.		Secondary (indirect) exposure Incidental contact after application	Via the environment
	Professional use	General public	General Public	General Public
Inhalation	Yes	Not relevant	Not relevant	Not relevant[1]
Dermal	Yes	Not relevant	Not relevant	Not relevant[1]
Oral	Not relevant	Not relevant	Not relevant	Not relevant[1]

[1] From TNsG on Human Exposure, 2007: "Exposure via the environment is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food. These scenarios are not considered relevant in this case.

The biocidal active substance as manufactured is directly used as biocidal product for the preservation of drilling mud in offshore processes (PT12).

Potential human exposure to "RP 3:2" via use of the biocidal product in PT12 is given during the use of slimicides in offshore processes. Therefore, inhalation and dermal exposures of professionals are expected and considered for this assessment.

As this use represents a downstream application of the biocide, limited information on this process is available to the applicant and for this assessment.

Drilling activities are not performed by non-professionals, therefore, potential human exposure of the general public is considered to be not relevant. Secondary exposure and human exposure via the environment are expected to be not relevant for the same reasons, as exposure is considered to be limited to professionals and to the drilling rigs only.

.

PT 13 - Metal working fluids

The main routes of human exposure towards "RP 3:2" and hydrolysis products originating in the application of b.p. as PT13 are listed in the table below.

Table 2.2.2.3-5: Main paths of human exposure to "RP 3:2", formaldehyde and 2-hydroxypropylamine via use for PT13

Exposure path	Primary (direct) exposure, during use of b.p.		Secondary (indirect) exposure Incidental contact after application	Via the environment
	Professional use	General public	General Public	General Public
Inhalation	Yes	Not relevant	Not relevant	Not relevant[1]
Dermal	Yes	Not relevant	Not relevant	Not relevant[1]

Oral	Not relevant	Not relevant	Not relevant	Not relevant[1]

[1] From TNsG on Human Exposure, 2007: "Exposure via the environment is an element of secondary exposure. It includes bystanders and consumers, including children, who are inadvertently exposed to biocides by inhalation of plumes drifting off-site and ingesting contaminated food. These scenarios are not considered relevant in this case.

The area primary exposure of professionals covers workers, who prepare lubricant concentrates and workers, who prepare/apply metal working fluids. As some of the identified tasks require manual handling, inhalation and dermal exposures of workers are considered to occur. Oral exposure is not expected to be relevant, as workers are assumed to be aware of the risk and due to good hygiene practices.

As the pure biocidal product and the lubricant concentrate are not intended for non-professionals, exposure of the general public via primary respectively secondary exposure is not considered for this assessment.

The exposure values relevant for risk characterisation are presented in chapter 2.2.2.4 of this document.

2.2.2.4. Risk characterisation

The risk from the application of "RP 3:2" as **PT2 within system cleaners** within industrial processes is characterised in this CAR. Application concentrations are typically 10%. Risk is estimated for the formulation and use of system cleaners. Due to the high concentration of "RP 3:2" in the systems cleaner incomplete hydrolysis to formaldehyde and 2-hydroxypropylamin is expected. Therefore dermal risk estimates are provided for 2 situations: non-hydrolysed "RP 3:2" and full hydrolysis to formaldehyde and 2-hydroxypropylamin. The second hydrolysis product 2-hydroxypropylamine is not further considered since the respective AEL is much higher and the exposure potential is not higher compared to formaldehyde. However for respiratory exposure just the situation of complete hydrolysis is considered: The vapour pressures of the products and the composition of the gaseous phases are expected to be already determined inter alia by hydrolysis products. Therefore it is considered to be appropriate to estimate the respiratory exposure for the situation of complete hydrolysis of "RP 3:2" to formaldehyde. The second hydrolysis product 2-hydroxypropylamine is not further considered since the respective AEL is much higher and volatility, i.e. exposure potential, is lower compared to formaldehyde.

Risk for mixing and loading of "RP 3:2" to system cleaner formulation vessels, sampling for formulation control, filling, bottling and cleaning of vessels in formulation plants is considered. Due to the corrosive and sensitizing hazard of 100% "RP 3:2" as well as the 10% dilution in system cleaners, closed systems (including sampling task) and high industrial organisational and technical RMM have to be used in order to allow concluding that the risk for local respiratory and local dermal effects is acceptable. In this case also risk for systemic effects is acceptable

Table 2.2.2.4_1 Risk for local respiratory effects: Application of "RP 3:2" to system cleaner (PT2)

Exposure Scenario: Mixing and loading of “RP 3:2” to system cleaner formulation vessels, sampling for formulation control, filling, bottling and cleaning of vessels in formulation plants		Local (external) respiratory exposure estimate [mg/m^3]	Local respiratory AEC [mg/m^3]	Local respiratory exposure / AEC
formaldehyde	Consexpo, Tier 1	0.7	0.12	5.8
formaldehyde	Consexpo, Tier 2a*	0.14	0.12	1.2
formaldehyde	Tier 2b[#]	negligible	0.12	acceptable

* Assuming sample open for some minutes and 80% efficacy of LEV

[#] Due to inacceptable risk resulting from tier 2a assessment, for sampling a practically closed system is required as risk mitigation measure. Use of closed bottles and appropriate LEV is considered to be easily technically achievable.

Table 2.2.2.4_2 Risk assessment for **local** dermal effects: Application of "RP 3:2" to system cleaners in formulation vessels (PT2)

Hazard			Exposure						Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed?	Tasks, uses processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1B, H314: severe skin burns and eye damage Cat 1A, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0,1% (sensitization) respiratory AEC = 0.25 mg/m³ air	2	industrial	most formulation sites have closed systems using automatic dosage systems: **addition of "RP 3:2" to system cleaners**; **sampling**	Skin Eye RT	1 hour per day or less	n.r.	Technical and organisational RMM adequate for the high hazard category are achievable transfer in closed systems and industrial RMM excluding risk for skin, eye and RT exposure use of appropriate gloves and mask	Acceptable: No exposure expected since +Technical and organisational RMM adequate for the high hazard category are achievable
medium	Cat 1, H317: may cause allergic skin reaction	System cleaner is diluted with water by 1:100 to 1:1000 when vessels are cleaned. This results in concentrations below the concentration limit for irritation but still above concentration limit for skin sensitization. respiratory AEC = 0.25 µg/L air	2	industrial	most formulation sites have closed systems using automatic dosage systems: **cleaning of vessels**	Skin Eye RT	once per week	n.r.	Technical and organisational RMM of standard industrial work place ensuring well controlled exposure may be expected. Minimization of manual phases, local exhaust ventilation, trained workers, use of appropriate gloves, intensive supervision of workers for proper use of RMM	Acceptable: used with low frequency and low likelihood of exposure

n.r. = not relevant

Table 2.2.2.4_3 Risk for systemic effects from use of system cleaners (PT2)

Exposure Scenario: cleaning of vessels in formulation plants		Systemic (internal) exposure [mg/kg bw day]				Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		oral	inhalation	dermal	total		
"RP 3:2"	Respiratory exposure Consexpo and Dermal exposure to system cleaner from sampling, tier 2, including 10% penetration through gloves (see Doc II-B.4.1.4)	n.r.	n.r.	0.014	0.014	0.33	0.04
formaldehdyde	Respiratory exposure Consexpo and Dermal exposure to system cleaner from sampling, tier 2, including 10% penetration through gloves (see Doc II-B.4.1.4)	n.r.	n.r.	0.007	0.007	0.15	0.05

n.r. not relevant

Risk for the application of "RP 3:2" as **PT6 for the preventive as well as curative treatment of fuels** is characterised in terms of application to fuel and use of treated fuel. 100% "RP 3:2" as manufactured is added to fuels with a final concentration of usually in the range of 0.005% to 0.04% and up to 0.1% for "shock doses". Exposure to "RP 3:2" has to be completely excluded due to the corrosive and sensitizing hazard. Exposure to treated fuel may happen due to sampling the mixing vessels and use of the fuel (tanking). Due to the low water content in fuel "RP 3:2" is considered to be present largely in the non-hydrolysed state. Consequently the risk estimates are provided just for the situation of no hydrolysis. However it is recognised that toxicological reference values for the active substance are assured to be protective also for a release of formaldehyde at the site of contact since they are read across from formaldehyde AEC and AEL. The toxicological reference values for the active substance are also assured to be protective for the hydrolysis product 2-hydroxypropylamine, since its AEL and AEC are higher compared to those of "RP 3:2". Risk for loading of "RP 3:2" to fuel mixing systems, sampling of treated fuels, cleaning of containers and maintenance of the system is considered. For the loading of the corrosive and sensitizing "RP 3:2" to fuel mixing systems closed systems have to be used in order to allow concluding that the risk for local respiratory and local dermal effects is acceptable. Exposure to the fuel containing maximally 0.1% of "RP 3:2" (below or borderline to classification limits for the mixture) shall be minimised with closed systems for the sampling procedure and at filling stations appropriate ventilation according to respective actual technical standards (Directive 2009/126/EC). In this case also risk for systemic effects is acceptable.

Table 2.2.2.4_4 Risk for local respiratory effects: Application of Grotamar®71 or ContramTM MBO to fuel (PT6)

Exposure Scenario: sampling for formulation control		Local (external) respiratory exposure estimate [mg/m^3]	Local respiratory AEC [mg/m^3]	Local respiratory exposure / AEC
“RP 3:2”	Tier 1, consexpo-model estimate	0.023	0.25	0.09

Table 2.2.2.4_5 Risk assessment for **local** dermal effects: Application of Grotamar®71 or ContramTM MBO to fuel in formulation vessels and (second line only) use of fuel at filling stations(PT6)

Hazard			Exposure							Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1, H314: severe skin burns and eye damage Cat 1A, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0.1% (sensitization) respiratory AEC = 0.25 µg/L air	6	industrial	most formulation sites have closed systems using automatic dosage systems: **addition of bp to the dosage system or directly to fuels**;	Skin Eye RT	few minutes per day or less	n.r.	Technical and organisational RMM adequate for the high hazard category are achievable transfer in closed systems and industrial RMM excluding risk for skin, eye and RT exposure use of appropriate gloves and mask	Acceptable: No exposure expected since +Technical and organisational RMM adequate for the high hazard category are achievable
no	-	Concentration of 0.1% in fuel is ≤ class limits for corrosion (5%), irritation (1%) and skin sensitization (0.1%); respiratory AEC = 0.25 µg/L air	6	industrial	most formulation sites have closed systems using automatic dosage systems: **closed system sampling of fuel for control**	Skin Eye RT	few minutes per day or less	n.r.	Technical and organisational RMM of standard industrial work place may be expected. use of gloves recommended	Acceptable: No hazard classification

n.r. = not relevant

Table 2.2.2.4_6. Risk for **systemic** effects from the application of Grotamar®71 or ContramTM MBO to fuel in formulation vessels (PT6)

Exposure Scenario: sampling for formulation control		Systemic (internal) exposure [mg/kg bw day]				Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		oral	inhalation	dermal	total		
"RP 3:2"	Respiratory exposure estimate (tier1) and Dermal exposure to treated fuel from sampling, tier 2, including 10% penetration through gloves (see Doc II-B.4.2.4)	n.r.	0.00036	0.0164	0.0168	0.33	0.05

n.r. not relevant

Table 2.2.2.4_7 Risk for **local** respiratory effects: Use of fuel treated with Grotamar®71 or Contram™ MBO - refuelling of engines (PT6)

Exposure Scenario: Refuelling of engines		Local (external) exposure [µg/L]	Local respiratory AEC [µg/L]	Local respiratory exposure / AEC
Tier 2	Respiratory exposure Consexpo model estimate refined by assuming 85% of vapours captured	0.002	0.25	0.01

Table 2.2.2.4_8 Risk for **systemic** effects from the professional use of fuel treated with Grotamar®71 or Contram™ MBO – refuelling engines by professionals (PT6)

Exposure Scenario: Refuelling engines by professionals		Systemic (internal) exposure [mg/kg bw day]				Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		oral	inhalation	dermal	total		
Tier 1	Respiratory exposure Consexpo model estimate and Dermal exposure to a.s. tier 2, no gloves (see Doc II-B.4.1.3)	n.a.	0.00035	0.073	0.073	0.33	0.22

n.a. not applicable

Also the risk from the application of "RP 3:2" as **PT11 within liquid cooling systems** within industrial processes is characterised in this CAR. 100% "RP 3:2" as manufactured is loaded to cooling liquids with a final concentration of typically 0.025%. Exposure to "RP 3:2" has to be completely excluded due to the corrosive and sensitizing hazard. Exposure to treated cooling liquids may happen. Due to the high dilution of "RP 3:2" in cooling liquids full hydrolysis to formaldehyde and 2-hydroxypropylamin is expected. Therefore risk estimates are provided just for the situation of full hydrolysis. However risk estimates are provided only for formaldehyde, not for 2-hydroxypropylamin, since for the latter the AEL is much higher and the vapour pressure, i.e. exposure potential, is much lower compared to formaldehyde. Risk for loading of "RP 3:2" to liquid cooling systems, sampling of cooling liquid, cleaning of containers and maintenance of the system is considered. For the loading of the corrosive and sensitizing "RP 3:2" to liquid cooling systems closed systems have to be used in order to allow concluding that the risk for local respiratory and local dermal effects is acceptable. Exposure to the cooling liquid containing just 0.025% of "RP 3:2" (~0.01% formaldehyde, below classification limits for formaldehyde) results in an acceptable risk with standard industrial organisational and technical RMM. In this case also risk for systemic effects is acceptable.

Table 2.2.2.4_9 Risk for local respiratory effects: Application of "RP 3:2" in liquid cooling systems (PT11)

Exposure Scenario: Sampling the cooling liquid and cleaning of containers		Local (external) respiratory exposure estimate [µg/L]	Local respiratory AEC [µg/L]	Local respiratory exposure / AEC
Formaldehyde	Consexpo, Tier 1	0.0051	0.12	0.04

Table 2.2.2.4_10 Risk assessment for **local** dermal effects: Application of "RP 3:2" in liquid cooling systems (PT11)

Hazard			Exposure							Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed ?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1B, H314: severe skin burns and eye damage Cat 1A, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0,1% (sensitization) respiratory AEC for "RP 3:2" = 0.25 mg/m³ air	11	industrial	closed systems: **loading** by connecting tubes and **dosing**	Skin Eye RT	once per month	n.r.	Technical and organisational RMM adequate for the high hazard category are achievable transfer in closed systems and industrial RMM excluding risk for skin, eye and RT exposure use of appropriate gloves and mask	Acceptable: No exposure expected since +Technical and organisational RMM adequate for the high hazard category are achievable
no	-	"RP 3:2" is diluted to 0.025% in liquid cooling system, corresponding to 0.012 % formaldehyde, which is below the classification limits for skin irritation (5% for formaldehyde) and sensitization (0.2% for formaldehyde)	11	industrial	**sampling** the cooling liquid via discharge tips and **cleaning** of containers	Skin Eye RT	once per day	surface area of finger tips	Technical and organisational RMM of standard industrial work place may be expected. use of gloves recommended	Acceptable: No hazard classification

		For cleaning the containers the cooling liquid is further diluted by water respiratory AEC for formaldehyde = 0.12 mg/m^3 air								

n.r. = not relevant

Table 2.2.2.4_11 Risk for systemic effects from the application of "RP 3:2" within liquid cooling systems (PT11)

Exposure Scenario: Sampling the cooling liquid and cleaning of containers		Systemic (internal) exposure [mg/kg bw day]				Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		oral	inhalation	dermal	total		
Formaldehyde	Respiratory exposure Consexpo, tier 1 and Dermal exposure to treated cooling liquid, tier 2, w/o gloves	n.r.	0.0000089	0.002	0.002	0.15	0.01

"RP 3:2" is also intended to be used as **PT12 slimicide for offshore drilling processes**, in a typical concentration of 0.1 to 0.15% within the drilling mud. This is done by direct application of the biocidal product (a.s. as manufactured) to the mud. "RP 3:2" is added via closed automatic dosage systems as 100% concentrate (task = connecting tubes). Due to the expected and required closed systems technology exposure might occur just from exposure to the drilling mud containing "RP 3:2" and the hydrolysis products. Due to the high dilution of "RP 3:2" in the mud it is assumed that RP3:2 is fully hydrolysed to formaldehyde and 2-hydroxypropylamine. Furthermore due to the high vapour pressure of formaldehyde and due to the similar AEL of formaldehyde and "RP 3:2" (AEL was read across on a molar basis) the risk assessment for PT 12 is based just on the consideration of formaldehyde. The second hydrolysis product 2-hydroxypropylamine is not further considered since the respective AEL is much higher and volatility, i.e. exposure potential, is lower compared to formaldehyde. Drilling muds contain a wide range of other substances including base fluids, weighting agents (e.g. barite), viscosifers (e.g. bentonite), surfactants (e.g. imidazolines) and biocides (e.g. glutaraldehyde). They may also contain contaminants from formations (e.g. oil, condensate and H_2S). Health effects included dermatitis, respiratory irritation, narcosis and cancer. For example, H_2S is a very toxic gas that can irritate the eyes and throat but also unconsciousness and death.

Human exposure to the biocide in the shaker house is calculated for formaldehyde that have been released in the used mud. The risk for local and systemic effects appears acceptable since personal protective equipment, including respiratory protective equipment and gloves are standard in this specific working environment.

Table 1.2.2.2.4_12 Risk for local respiratory effects from formaldeyhyde: Application of "RP 3:2" to drilling mud (PT12)

Exposure Scenario: shaker room		Local (external) respiratory exposure estimate [mg/m^3]	Local respiratory AEC [mg/m^3]	Local respiratory exposure / AEC
formaldehyde	Consexpo, Tier 2 (use of RPE: efficiency 90%)	0.0042	0.12	0.035

Table 1.2.2.2.4_13 Risk assessment for **local** dermal effects: Application of “RP 3:2” to drilling mud (PT12)

Hazard			Exposure						Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1B, H314: severe skin burns and eye damage Cat 1A, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0,1% (sensitization) respiratory AEC for “RP 3:2” = 0.25 mg/m³ air	industrial	closed systems: **loading** by connecting tubes and **dosing**	Skin Eye RT	daily	n.r.	Technical and organisational RMM adequate for the high hazard category are achievable transfer in closed systems and industrial RMM excluding risk for skin, eye and RT exposure use of appropriate gloves and mask	Acceptable: No exposure expected since +Technical and organisational RMM adequate for the high hazard category are achievable
-	no	“RP 3:2” is diluted in drilling mud to a concentration of 0.15% b.p. corresponding to 0.07% formaldehyde, which is below which is below the classification limits for skin irritation (5% for formaldehyde) and sensitization (0.2% for formaldehyde) respiratory AEC for formaldehyde = 0.12 mg/m³ air	industrial	sampling and analysis of mud/cuttings, working at the drilling hole, clearing of blockades and replacement of screens, checking the shaker screens for wear	Skin Eye RT	1-3 times per day	n.r.	Technical and organisational RMM adequate for the risk from mechanical injury and exposure to other chemicals are in place use of appropriate gloves and mask	Acceptable: concentration of formaldehyde below concentration limits for classification technical and organisational RMM adequate for the dangerous workplace

Table 1.2.2.2.4_14 Risk for **systemic** effects of formaldehyde from the application of "RP 3:2" to drilling muds (PT12)

Representative Scenario: shaker room		Systemic (internal) exposure [mg/kg bw day]				Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		oral	inhalation	dermal	total		
Formaldehyde	Respiratory exposure: Atmosphere in shaker room: 4 h/d inhalation exposure RMM: 15 ACH per hour, use of RPE and Performance of tasks in shaker room RMM: gloves	n.r.	0.001	0.113	0.114	0.15	0.76

Also the risk from the application of "RP 3:2" as **PT13 within metal working fluids within industrial processes** is characterised in this CAR. 100% "RP 3:2" as manufactured may be used to formulate a 3% lubricant concentrate. 100% "RP 3:2" or a 3% lubricant concentrate is loaded to metal working fluids with a final concentration of typically 0.15%. However exposure to 100% "RP 3:2" has to be completely excluded due to the corrosive and sensitizing hazard and consequently this was not considered for risk assessment for systemic effects. Due to the high concentration of "RP 3:2" in the lubricant concentrate incomplete hydrolysis to formaldehyde and 2-hydroxypropylamin is expected therein. Therefore for lubricant concentrate dermal risk estimates are provided for 2 situations: non-hydrolysed "RP 3:2" and full hydrolysis to formaldehyde and 2-hydroxypropylamin. The second hydrolysis product 2-hydroxypropylamine is not further considered since the respective AEL is much higher and the exposure potential is not higher compared to formaldehyde. However for respiratory exposure just the situation of complete hydrolysis is considered: The vapour pressures of the products and the composition of the gaseous phases are expected to be already determined inter alia by hydrolysis products. Therefore it is considered to be appropriate to estimate the respiratory exposure for the situation of complete hydrolysis of "RP 3:2" to formaldehyde. The second hydrolysis product 2-hydroxypropylamine is not further considered since the respective AEL is much higher and volatility, i.e. exposure potential, is lower compared to formaldehyde.

In contrast "RP 3:2" is highly diluted in the metal working fluids and therefore full hydrolysis to formaldehyde and 2-hydroxypropylamin is expected therein. Consequently for the use of metal working fluids risk estimates are provided just for the situation of full hydrolysis. However risk estimates are provided only for formaldehyde, not for 2-hydroxypropylamin, since for the latter the AEL is much higher and the vapour pressure, i.e. exposure potential, is much lower compared to formaldehyde. Risk for the formulation of lubricant concentrates (mixing and loading, sampling, filling and bottling, cleaning of vessels) as well as risk for the use of "RP 3:2" in metal working fluids (mixing and loading of lubricant concentrates, machine work, control and cleaning of work pieces, fluid monitoring, swarf removal and discharging of

system and sump maintenance) is estimated. Exposure to 100% "RP 3:2" has to be completely excluded due to the corrosive and sensitizing hazard. Exposure to the 3% lubricant concentrate should also be avoided by use in closed systems and/or high industrial organisational and technical RMM due the skin irritating, eye damaging and sensitizing hazard. Exposure to the metal working fluid containing just 0.15% of "RP 3:2" (~ 0.07% formaldehyde, below classification limits of formaldehyde) results in an acceptable risk for local effects with standard industrial organisational and technical RMM. In this case also risk for systemic effects is acceptable.

Table 2.2.2.4_15 Risk for **local** respiratory effects from the formulation of lubricant concentrates (PT13)

Exposure Scenario: Formulation of lubricant concentrate		Local respiratory exposure to formaldehyde [mg/m^3]	Local respiratory AEC [mg/m^3]	Local respiratory exposure / AEC
formaldehyde	sampling of lubricant concentrate, tier 2 (reducing open sample phase to 2 minutes)	0.11	0.12	0.92

Table 2.2.2.4_16: Risk for **local** dermal effects from "RP 3:2" – mixing and loading to lubricant concentrate formulation (PT13)

Hazard			Exposure						Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1B, H314: severe skin burns and eye damage Cat 1, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0.1% (sensitization) respiratory AEC = 0.25 µg/L air	Industrial worker	**manual addition of "RP 3:2"** via manholes: opening of vessel, weighting "RP 3:2", addition to metal working fluid and stirring for lubricant concentrate formulation	Skin Eye RT	3x per day	n.r.	Technical and organisational RMM adequate for the high hazard category Industrial RMM including minimization of manual phases, high ventilation and use of appropriate gloves and face shield allowing to exclude risk for skin, eye and RT exposure	Not acceptable: - Irreversible or severe effect - higher degree of operational and organisational RMM applicable - task is of high frequency
high	Cat 1B, H314: severe skin burns and eye damage Cat 1, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0.1% (sensitization) respiratory AEC = 0.25 µg/L air	Industrial worker	**closed dosage system addition of "RP 3:2"** for lubricant concentrate formulation	Skin Eye RT	3x per day	n.r.	Technical and organisational RMM adequate for the high hazard category Industrial RMM including minimization of manual phases and high ventilation allowing to exclude risk for skin, eye and RT exposure use of appropriate gloves and face shield	Acceptable: No exposure expected since + high degree of operational and organisational RMM in use and recommended + short duration of potential exposure

Table 2.2.2.4_17: Risk for **local** dermal effects from "RP 3:2" – sampling of lubricant concentrate (PT13)

high	Cat 2, H315: causes skin irritation Cat 1 H318: causes serious eye damage Cat 1, H317: may cause allergic skin reaction	"RP 3:2" is diluted to 3%, which is within the class limit for skin irritation (1-5%) and borderline to serious eye damage (class limit=3%) above the class limit for skin sensitization (0.1%) respiratory AEC = 0.25 µg/L	industrial	**sampling** the lubricant concentrate via discharge tips	Skin Eye RT	9x per day	surface area of finger tips	Technical and organisational RMM adequate for the medium hazard category Industrial RMM including minimization of manual phases, high ventilation and use of appropriate gloves and face shield allowing to minimize risk for skin, eye and RT exposure	Acceptable: + sufficiently high degree of operational and organisational RMM in use and recommended

Table 2.2.2.4_18: Risk for **local** dermal effects from "RP 3:2" – cleaning of vessels from lubricant concentrate (PT13)

no	-	3% lubricant concentrate is diluted by 1:100 to 1:1000, which is below the class limit for skin and eye irritation (1%) and below the class limit for skin sensitization (0.1%) respiratory AEC = 0.25 µg/L	industrial	**Cleaning of vessels** from lubricant concentrate	Skin Eye RT	1x per week	surface area of both hands	Technical and organisational RMM of standard industrial work place may be expected. use of gloves recommended	Acceptable: + No hazard classification + use of coveralls and gloves obligatory

Table 2.2.2.4_19 Risk for systemic effects from use of "RP 3:2" to formulate lubricate concentrates (PT13)

Exposure Scenario: sampling, filling and bottling, cleaning of vessels		Systemic (internal) exposure [mg/kg bw day]			Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		Inhalation	dermal	total		
"RP 3:2"	Tier 2, use of gloves, excluding dermal exposure to corrosive RP3:2, including dermal exposure to lubricant concentrate (see Doc II-B. table 4.3.4-1)	n.r.	0.094	0.094	0.33	0.28
Formaldehyde	Tier 2, as above	0.002	0.046	0.048	0.15	0.32

Table 2.2.2.4_20 Risk for **local** respiratory effects from formaldehyde released from "RP 3:2" during use of metal working fluids (P13)

Exposure Scenario: mixing and loading of lubricant concentrate; machine work; control and cleaning of work pieces; fluid monitoring; gathering shavings/ chippings/ turnings; cleaning/discharging of system		Local respiratory exposure to formaldehyde [mg/m^3]	Local respiratory AEC [mg/m^3]	Local respiratory exposure / AEC
formaldeyhde	Tier 2, based on refinement of measured data	0.022	0.12	0.18

Table 2.2.2.4_21 Risk for **local** dermal effects from "RP 3:2" – mixing and loading to metal working fluid (PT13)

Hazard			Exposure							Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1B, H314: severe skin burns and eye damage Cat 1, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0.1% (sensitization) respiratory AEC = 0.25 mg/m³ air	13	Industrial worker	**manual addition of "RP 3:2"** via manholes: opening of vessel, weighting "RP 3:2", addition to metal working fluid and stirring to metal working fluid or	Skin Eye RT	1x per month: 5-30 min	n.r.	Technical and organisational RMM adequate for the high hazard category Industrial RMM including minimization of manual phases, high ventilation and use of appropriate gloves and face shield allowing to exclude risk for skin, eye and RT exposure	Not acceptable: - Irreversible or severe effect - higher degree of operational and organisational RMM applicable - task is of high frequency

Hazard			Exposure							Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
high	Cat 1B, H314: severe skin burns and eye damage Cat 1, H317: may cause allergic skin reaction	classification limits: 5% (corrosion) 0.1% (sensitization) respiratory AEC = 0.25 µg/L air	13	Industrial worker	**closed dosage system addition of “RP 3:2”** to metal working fluid or	Skin Eye RT	1x per month: 5-30 min	n.r.	Technical and organisational RMM adequate for the high hazard category Industrial RMM including minimization of manual phases and high ventilation allowing to exclude risk for skin, eye and RT exposure use of appropriate gloves and face shield	Acceptable: No exposure expected since + high degree of operational and organisational RMM in use and recommended + short duration and low frequency of potential exposure
high	Cat 1, H317: may cause allergic skin reaction Cat 2, H315: skin irritation	Lubricate concentrate = 3% “RP 3:2” within class limits for skin irritation (1%-5% for “RP 3:2”) and borderline to	13	Industrial worker	**manual addition of** **lubricant concentrate** to metal working fluid via manholes: opening of vessel, weighting lubricant concentrate, addition to metal working fluid and stirring	Skin Eye RT	1x per month: 5-30 min	surface area of finger tips	Technical and organisational RMM adequate for the medium hazard category Industrial RMM including minimization of manual phases, high ventilation and use	Acceptable: + sufficiently high degree of operational and organisational RMM in use and recommended + short duration and low frequency

Hazard			Exposure							Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
	Cat 1 H318: causes serious eye damage	serious eye damage (class limit=3%) above class limit for skin sensitization (0.1% for "RP 3:2") respiratory AEC = 0.25 mg/m³ air for "RP 3:2"							of appropriate gloves and face shield allowing to minimize risk for skin, eye and RT exposure	of potential exposure
no	no	Concentration of 0.15% ~ 0.07% FA ≤ class limits for skin irritation (1% for FA) and skin sensitization (0.2% for FA) respiratory AEC = 0.12 mg/m³ air	13	Industrial worker	machine work (drilling grinding etc; tool setting and dismantling, operator near to machine)	Skin Eye RT	4x 1h operator near machine, 10 min tool setting and dismantling / day	surface area of finger tips	machine work in closed systems with exhaust ventilation	Acceptable: No hazard classification use of coveralls and gloves obligatory
					- control and cleaning of work pieces		4x 1h/ day		control and cleaning of work pieces in closed chamber with air stream, automated brushing with water	

Hazard			Exposure							Risk
Hazard Category	effects in terms of C&L	additional relevant hazard information	PT	Who is exposed?	Tasks, uses, processes	Potential exposure route	frequency and duration of potential exposure	Rough degree of exposure	Relevant RMM & PPE	Conclusion on risk
					- fluid monitoring: control of pH, formaldehyde concentrations etc.		5 min/week		fluid monitoring via separate discharge taps	
					- gathering shavings/chippings/turnings (swarf removal) for recycling before mwf is going to the ultrafiltration system main source of exposure: drying of shippings, handling wet workpieces and leakages of metalworking fluids in the production hall		8 h / day		gathering via automated systems	
					discharging of system (and sump maintenance)		30 min / year		discharging via automated systems, connection of tubes	

Table 2.2.2.4_21 Risk for systemic effects from use of "RP 3:2" in metalworking processes (PT13)

Exposure Scenario: mixing and loading of lubricant concentrate; machine work; control and cleaning of work pieces; fluid monitoring; gathering shavings/ chippings/ turnings; cleaning/discharging of system		Systemic (internal) exposure [mg/kg bw day]			Systemic AEL [mg/kg bw day]	Systemic exposure / AEL
		Inhalation	dermal	total		
Formaldehyde	tier 2, systemic exp. via inhalation assuming 8 hour metal work processes and efficient LEV and tier 2 systemic exp. via dermal route, use of gloves and coverall; workshift 2 (see Doc II-B, table 4.4.4.-1)	0.004	0.117	0.12	0.15	0.8

No exposure of general public, no exposure of pets and no dietary exposure is expected due to the intended PT2, PT11, PT12 and PT13 use. For PT6 dermal and respiratory exposure to general public may occur via treated fuels, however due to the longer exposure intervals the professional exposure is considered worst case and resulted in acceptable risk ratios. No pets and dietary exposure are expected for PT6. Dermal contact against dried concentrates in dirty clothes in home laundry of working clothes is assumed to be not relevant as "RP 3:2" residues will quickly hydrolyse and generate gaseous formaldehyde, which is transferred to the gaseous phase and will not remain on the clothes.

2.2.3. Environmental Risk Assessment

Data from two sources i.e. Contram™ MBO and GrotaMAR 71® are presented. Based on the studies on acute toxicity to fish, daphnia, algae, aquatic microbes and biodegradation the ecotoxicological profile of the two sources is comparable.

2.2.3.1. Fate and distribution in the environment

Degradation

Two closed bottle tests on ready biodegradability (OECD guideline 301D) of "RP 3:2" (Contram™ MBO and GrotaMar 71®) confirmed that the test item was not readily biodegradable though biodegradation reached between 30% and 77% depending on the consideration of nitrification. A recently performed GLP compliant and reliable CO_2 evolution test according to OECD guideline 301B with a higher Klimisch rating indicated 89.8% degradation within the study duration. The 10 d-window was met. GrotaMar 71® reached a

positive result in a biodegradation test with seawater in a non GLP OECD guideline study 306, closed bottle procedure. Therefore "RP 3:2" has the potential for ultimate biodegradation in the marine environment.

The interpretation of the biodegradation tests performed with the UVCB substance "RP 3:2" is complicated by the fact that actually a mixture of substances is tested. According to the OECD Guidelines, tests for ready biodegradability are not generally applicable for complex mixtures containing different types of chemicals.

In conclusion there are negative and positive test results for the endpoint ready biodegradability available with both formaldehyde releasing substances, "RP 3:2" and "RP 1:1". Formaldehyde and 2-hydroxypropylamine are both readily biodegradable. The ready biodegradability of formaldehyde was investigated in 4 tests. Due to the results of a test according to OECD guideline 301A formaldehyde is expected to be readily biodegradable. The risk characterisation was performed with the two hydrolyses products.

The most influencing factors on the study outcomes with the reaction products seemed to be the type and source of the inoculum, the test protocol (e.g. CO_2 versus O_2 measurements) and the test substance concentrations. Also no information is available to prove if the negative ready biodegradation results are attributed to more stable intermediates (which would contradict the fast hydrolysis), repression and time delay of the different microorganisms that are responsible for the degradation of formaldehyde and 2-hydroxypropylamine or the limitations of the OECD ready biodegradability test protocol for complex mixtures or both.

Based on the ready biodegradability results in two GLP compliant and reliable studies for "RP 3:2" (OECD 301B, Klimisch 1, higher inoculum concentrations, measurement of ultimate degradation i.e. CO2) and "RP 1:1" (OECD 301D, Klimisch 2) and the arguments and evidence presented above, "RP 3:2" can be considered as readily biodegradable.

The equilibrium of hydrolysis is strongly dependent on the concentration in water. At concentration levels being expected in the environment, CONTRAM™ MBO is assumed to be completely hydrolysed to formaldehyde and 2-hydroxypropylamine. As the equilibrium was reached within a few hours in the performed test investigating a 1% w/w solution, the hydrolysis DT_{50} is expected to be less than 1 hour at all pH values under environmentally relevant conditions (temperature, concentration, and pH).

Hydrolysis of formaldehyde and 2-hydroxypropylamine can be excluded because of the absence of a hydrolysable group in the molecules.

There is no study on photolysis of "RP 3:2" in aqueous solution available. The UV spectrum indicates no absorption of light at wave-lengths >290 nm.

There are no tests on photolysis in water of formaldehyde in aqueous solutions available either. The UV spectrum of formaldehyde indicates a weak absorption of light at wavelengths between 240 and 360 nm assuming possible direct photolysis of formaldehyde in water and air. However, in aqueous solutions formaldehyde hydrate is formed having no chromophore that is capable of absorbing sunlight and thus should not decompose by direct photolysis in water. Because of the ready biodegradability, photolysis in surface waters is expected to be of minor importance.

No study on aqueous photolysis for 2-hydroxypropylamine has been submitted. Because of the absence of a chromophore 2-hydroxypropylamine is not expected to be susceptible to direct photolysis by sunlight in the atmosphere or in aqueous solutions.

The reaction rate of 3,3'-methylene-bis [5-methyl-oxazolidine], the main constituent of CONTRAM™ MBO, with OH-radicals in the atmosphere was calculated with 1.23 hours. Degradation by nitrate and ozone is considered to be comparatively negligible.

In the gas phase, formaldehyde is degraded in air via reaction with OH radicals; the half-life was estimated to be 1.97 days. Degradation by nitrate and ozone is negligible.

Estimated half-lives for the reaction of 2-hydroxypropylamine with OH-radicals and hydrogen abstraction in the atmosphere are 9.6 hours.

The substance "RP 3:2" and its hydrolysis products are expected to be removed in biological treatment plants as well as in surface water, soil, and air.

Distribution

The estimated K_{OC} value determined of 10 L/kg can be adopted for N,N'-methylene-bis(5-methyloxazolidine or 3,3'-methylene-bis(5-methyl-oxazolidine). The estimated Koc value determined for 5-methyl-oxazolidine was 6.5 L/kg.

The K_{OC} for formaldehyde was estimated to be 15.9 L/kg. For 2-hydroxypropylamine the QSAR (for ionizable compounds) predicted K_{OC} value was determined to be 70.4 L/kg at a pH of 7.

The low adsorption coefficient indicates that the hydrolysis products are highly mobile in soils and will not adsorb onto sewage sludge and sediment solids to any significant extent.

Accumulation

In view of the rapid hydrolysis, a test on aquatic or terrestrial bioconcentration of "RP 3:2" seems scientifically not justified. The likelihood of bioaccumulation is greatly reduced and the determination of a BCF value is not necessary in this specific case. So it is more appropriate to consider the identified hydrolysis products.

A bioaccumulation potential for the hydrolysis products formaldehyde and 2-hydroxypropylamine could not be identified based on very low log Kow values <1, predicted low BCF values of <4 L/kg_{ww} and experimental evidence indicating no bioaccumulation.

In conclusion a bioaccumulation potential for "RP 3:2" could not be identified based on a log Kow value <0 and a DT50 hydrolysis of <1 hour. Also formaldehyde and 2-hydroxypropylamine show no bioaccumulation potential.

2.2.3.2. Effects assessment

In media used for aquatic toxicity tests, the constituents of "RP 3:2" are expected to be hydrolysed to formaldehyde, 2-hydroxypropylamine and other intermediate compounds. Therefore, the observed toxicity is assumed to be caused by a mixture of the hydrolysis products.

The acute toxicity of the reaction products "RP 3:2" was tested on 3 trophic levels, while chronic tests results are available for invertebrates and algae.

The overview presented in Table 2.2.3.2-1 reveals similar characteristics of the ecotoxic effects of "RP 3:2", "RP 1:1" and formaldehyde, the acute effect values from tests on *Desmodesmus subspicatus* are comparable; the chronic NOECs for cladocerans are nearly identical.

Based on the releasable formaldehyde content of [redacted] (cf. Chapter 1.1) the ecotoxicity of the reaction products (mixture) cannot be attributed to formaldehyde alone.

The acute toxicity of 2-hydroxypropylamine is less. ECOSAR predictions for chronic toxicity also indicate lower toxicity compared to "RP 3:2" and formaldehyde. Possible pH effects in the environment of the hydrolysis metabolite were not considered, because the STP and receiving compartments are expected to have sufficient buffering.

Table 2.2.3.2-1 Summary of aquatic toxicity data

Endpoint		**"RP 1:1"**	**"RP 3:2"**	**Formaldehyde**	**2-Hydroxypropylamine**
Acute	Fish	96h-LC_{50} = 130 mg/L (*Danio rerio*) Klimisch 1	96h-LC_{50} = 57.7[a]/ 71[b] mg/L (*Danio rerio*) Klimisch 1 96h-LC_{50} = 135[a]mg/L (*Scopthalmus maximus*) Klimisch 2	96h-LC_{50} = 24.1 mg/L (*Pimephales promelas*), Klimisch 1 96h-LC_{50} = 5.7 mg/L (*Morone saxatilis*) Klimisch 2	96h-LC_{50} >1000 mg/L (nominal) for buffered test medium Klimisch 2 (*Leuciscus idus* L) 96h-LC50 >215-<464 mg/L (nominal, unbuffered) Klimisch 2 (*Leuciscus idus* L)
	Invertebrates	48h-EC_{50} = 29 mg/L (*Daphnia magna*) Klimisch 2	48h-EC_{50} = 28[b] / 37.9[a] mg/L (*Daphnia magna*) Klimisch 2 48h-EC_{50} = 4.1 mg/l (*Acartia tonsa),* Klimisch 3	24h-EC_{50} = 15 mg/L (*Daphnia magna*) Klimisch 2 48h-EC_{50} = 5.8 mg/L (*Daphnia pulex*) Klimisch 2	48h-EC50 = 148.8 mg/L (nominal, buffered). Klimisch 3 (*Daphnia magna*) 48h-EC_{50} = 91.5 mg/L and 108.8 mg/L (nominal, unbuffered) (*Daphnia magna*) Klimisch 3

Endpoint		**"RP 1:1"**	**"RP 3:2"**	**Formaldehyde**	**2-Hydroxypropylamine**
	Algae	72h-E_rC_{50} = 6.9 mg/L (*Desmodesmus subspicatus*) 72h-E_rC_{50} = 2.95 mg/L (*Pseudokirchneriella subcapitata*) Klimisch 2	72h-E_rC_{50} = 2.4[b] / 5.7[a] mg/L (geometr. mean 3.7 mg/L) (*Desmodesmus subspicatus*) Klimisch 3 72h-E_rC_{50} = 3.77[a] mg/L (*Skeletonema costatum)* Klimisch 3	72h-ErC_{50} = 5.7 mg/L (geometr. mean) (*Desmodesmus subspicatus*) Klimisch 2	96h-E_bC_{50} = 118.4 mg/L (nominal, buffered) (*Pseudokirchneriella subcapitata*) Klimisch 2 72h- E_rC_{50} = 32.7 mg/L (nominal, unbuffered) (*Desmodesmus subspicatus*) Klimisch 2
Chronic	Fish	Not available	Not available	6d-LC_{50} = 6.9 mg/L (*Danio rerio*, sac-fry stages), Klimisch 2	ChV = 211.1 mg/L (ECOSAR v1.11) QSAR estimate
	Invertebrates	21 d-NOEC = 1.3 mg/L (*Daphnia magna*, test substance "RP 3:2") Klimisch 1		21 d-NOEC = 1.04 mg/L, Klimisch 1 (*Daphnia magn*a)	ChV = 6.3 mg/L (ECOSAR v1.11) QSAR estimate
	Algae	72h-NOE_rC = 0.9 mg/L (*Desmodesmus subspicatus*) 72h-E_rC_{10} = 0.148 mg/L (*Pseudokirchneriella subcapitata*) Klimisch 2	72h-NOE_rC = 0.5[b] / 2.2[a] mg/L (geometr. mean 1.1 mg/L) (*Desmodesmus subspicatus*) Klimisch 3	Not available	ChV = 45.3 mg/L (ECOSAR v1.11) E_rC_{20} =19.7 mg/L (nominal, unbuffered) (*Desmodesmus subspicatus*) Klimisch 2
microbial activity	Aquatic microbial activity	3 h-EC_{50} = 110 mg/L (Respiration inhibition of sludge, domestic, Klimisch 2) 3 h-EC_{50}= 29 mg/L (industrial, Klimisch 1)	3 h NOEC = 16 mg/L 3 h-EC_{50} = 44 mg/L (domestic) (Respiration inhibition of sludge, Klimisch 1) 3 h-EC_{50}= 10.4 mg/L (industrial, Klimisch 1)	3 h-EC_{50} = 20.4 mg/L (Respiration inhibition of sludge, Klimisch 2)	3 h-EC_{50} >261 mg/L (Respiration inhibition of sludge, domestic, Klimisch 3) 30 min-EC_0 = 250 mg/L (*Pseudomonas putida,* Klimisch 4)

[a]results for GrotaMar 71®, [b]results for Contram™ MBO

The following PNECs were derived for risk characterisation:

Table 2.2.3.2-2 Predicted No Effect Concentrations (PNECs) for formaldehyde and 2-hydroxypropylamine

Compartment	PNEC $_{formaldehyde}$	PNEC $_{2\text{-}hydroxypropylamine}$
Microorganisms (STP)	0.2 mg/L	1.296 mg/L
Freshwater	0.010 mg/L	0.1184 mg/L
Seawater	0.00104 mg/L	0.01184 mg/L
Terrestrial	0.00416 mg/kg soil ww	0.161 mg/kg soil ww

ED properties for non-target organisms:

An ED assessment has been carried out according to the EFSA/ECHA (2018) guidance. EAS mediated adversity (impact on semen quality parameters and testis histopathology) was observed in recent conducted rodent studies carried out with the hydrolysis product formaldehyde. The adverse effects in mammals are supported by data on birds with formaldehyde showing effects on testes and testosterone also at dose levels, which comprise no or limited general toxicity. The mode of action leading to observed testes effects remains unclear, multiple mode of actions are hypothesised. Further testing with the active substance is not considered appropriate in that specific case, because 'testing does not appear scientifically necessary' (first heading of Annex IV of the Regulation (No) 528/2012) and because 'testing is technically challenging' (referring to second heading of Annex IV), as detailed below:

- It is uncertain, if further mechanistic studies, particularly with mammals with "RP 3:2" (as well as "RP 1:1") would allow establishing a mode of action, keeping in mind that endocrine mediated endpoints may be impacted secondary to general, non-endocrine toxicity and that in vivo apical endpoints can be triggered by several modes of action, including endocrine and non-endocrine modalities. Also for aquatic species it would be challenging to get meaningful results in further tests as correct dose setting and detangling the ED mode of action from non-ED modes of action are hampering the performance and interpretation of such tests. For birds no agreed and adequate study protocols are available to determine endocrine modes of action.

- Due to the properties of "RP 3:2" (as well as "RP 1:1") as skin corrosive, skin sensitising and local acting genotoxic carcinogen and the corresponding low effect concentration(s), it is difficult to select an appropriate test system to get meaningful results, at least for mammals.

- The targeted hydrolysis product formaldehyde of "RP 3:2 (as well as "RP 1:1") is an endogenously formed substance with a high turn-over rate in mammals and potentially also other non-target organisms. Exogenous FA due to biocidal product use might be a minor contributor to total systemic exposure.

Further facts to be regarded for the consideration of additional testing:

- "RP 3:2" (as well as "RP 1:1") have already a severe hazard profile: they fulfil the exclusion criteria of Article 5(1)a) of the BPR (REGULATION (EU) No 528/2012) based on the harmonized classification of Carc. 1B of formaldehyde. The use of a biocidal product containing active substances approved in accordance with the derogations of BPR Art. 5(2) are already subject to appropriate risk-mitigation measures to ensure that exposure of humans, animals and the environment to those active substances is minimised.

- Conducting further tests to clarify whether the ED criteria for environmental non-target organisms are fulfilled, would have very limited additional benefit for the environment, since the consequence of ED identification would "only" result in the fulfilment of BPR Art. 10 (candidates for substitution) and BPR Art. 19(4) (no authorization for use by general public). In case of approval of "RP 3:2" (as well as for "RP 1:1"), both BPR articles will already be fulfilled, based on the classification of "RP 3:2" (as well as RP "1:1") as Carc 1B. For these reasons, further tests with fish or amphibians may considered not necessary for RP "3:2" as well as for "RP 1:1" and their hydrolysis products formaldehyde and HPA.

- In ECHA-EFSA-ED-Guidance it is stated that "In some cases, the ED assessment may not change the applicable regulatory consequences if the substance already fulfils any of the other exclusion criteria set out in Article 5(2) of the BP Regulation (…). However, the assessment of the ED properties is still to be considered in case the active substance may be approved under restricted conditions or may be subject to mitigation measures as set out in Article 5(2) of the BP Regulation (…)."
This point was considered, but taking into account the principle of proportionality and considering the 3R principle, the performance of further tests are expected to have only very limited value (as a NTO-ED status triggers "only" BPR Art 10, whereas BPR Art 5(1) is already fulfilled by being classified as Carc. 1B).

No conclusion on ED properties for "RP 3:2" (as well as for "RP 1:1") based on the present data set, including also data/information of hydrolysis products formaldehyde and HPA, can be drawn. As a consequence, a risk estimation for potential ED effects of "RP 3:2" cannot be carried out for biocidal products.

2.2.3.3. PBT assessment

Persistence

"RP 3:2" can be considered as readily biodegradable based on experimental evidence (OECD guideline 301B), results from the hydrolysis products as well as from "RP 1:1". The hydrolysis DT50 is expected to be less than 1 hour under environmentally relevant conditions (temperature, concentration, and pH).

"RP 3:2" is therefore considered not to persist in the environment. Formaldehyde and 2-hydroxypropylamine are expected to be readily biodegradable.

It can be concluded based on the hydrolysis results that the persistence criterion of Annex XIII Commission Regulation (EU) No 253/2011 is not met.

Bioaccumulation

A bioaccumulation potential for "RP 3:2" could not be identified based on a log Kow value <0 and a DT50 hydrolysis of <1 hour. Also formaldehyde (log K_{OW} 0.35; estimated BCF_{fish} 0.396 L/kg_{ww}) and 2-hydroxypropylamine (log Kow -0.96; predicted and experimental BCFs in the range of 2.7-3.6 L/kg) show no bioaccumulation potential.

It can be concluded that the bioaccumulation criterion of Annex XIII Commission Regulation (EU) No 253/2011 (bioconcentration factor in aquatic species higher than 2 000) is not met.

Toxicity

Adequate chronic ecotoxicity data for "RP 3:2" are available for cladocerans and algae. The lowest effect value was determined in algae with a NOE_rC of 0.5 mg/L (Klimisch 3). However, based on a weight of evidence approach enough experimental information is presented to evaluate the toxicity to freshwater algae. For formaldehyde the lowest chronic value was the 21 d-NOEC of 1.04 mg/L for *Daphnia magn*a. The lowest acute toxicity descriptor for 2-hydroxypropylamine was the 96 h-E_bC_{50} for *Pseudokirchneriella subcapitata* in buffered solution of 118.4 mg/L.

It can be concluded that the toxicity criterion 1.1.3(a) of Annex XIII Commission Regulation (EU) No 253/2011 (NOEC or EC10 for marine or freshwater organisms <0.01 mg/l) is not met.

However "RP 3:2" is carcinogenic (CLP category 1B) and locally genotoxic (CLP category 2) on the basis of read across to formaldehyde (harmonised decision via RAC, December 2015).

T-criterion: Due to classification for carcinogenicity category 1B the T criterion is fulfilled.

Also the criteria set out in paragraph 1 of Annex D to the Stockholm Convention are not meet for "RP 3:2" and its hydrolysis products 2-hydroxypropylamine and formaldehyde. "RP 3:2" and its hydrolysis products do not exhibit characteristics of persistent organic pollutants.

2.2.3.4. Exposure assessment

General aspects

In aqueous solutions a dynamic equilibrium occurs whose composition depends on the concentration, temperature and pH-value. A complete hydrolysis of "RP 3:2" to formaldehyde and 2-hydroxypropylamine is expected under environmental conditions. The equilibrium is rapidly reached, the DT_{50} is determined to be <1 hour. Therefore, the environmental risk assessment will be based on hydrolysis products only as it is expected that all "RP 3:2" has been hydrolysed.

The environmental exposure assessment concerning the hydrolysis products formaldehyde and 2-hydroxypropylamine covers the use as system cleaner of metal working systems, this application can be actually assigned to product type 2 (PT2), as a preservative exclusively for fuels (PT6), as a preservative in closed liquid cooling systems (PT11), as slimicide in offshore processes (PT12) and as preservative for metal working fluids (MWF), only when directly dosed into the metal working system (PT13).

Expected releases into the environment during use of system cleaners (PT2) are identical with releases caused by metal working fluids, i.e local releases during use of system cleaners are covered by the emission scenarios for metalworking fluids (PT13). This approach was agreed at BPC WG-II-2017 and it has to be emphasised that only this specific use as system cleaners of metal working systems is covered by the ESD of PT13.

PT2 - Private and public health area disinfectants and other biocidal products
PT13 – Preservative for metal working fluids

"RP 3:2" is applied in system cleaners in the metal working industry (PT2). System cleaners are used to treat microbiological contamination of metal working machines i.e. disinfection of inner surfaces of vessels and tubes. The concentrations of reaction product in the concentrate is typically 10% w/w, the final dilution in the ready to use solution is 0.25% w/w up to 2% w/w depending on the duration of the disinfectant cleaning process.

Biocidal products containing "RP 3:2" are used as preservative of water-based metalworking fluids (MWF) only when directly dosed in the metal working system (PT13). In general, these metal working fluids can be divided in two application fields, emulsifiable and water soluble metal working fluids. In the "Refinement of the Emission Scenario Document for Product Type 13" they are usually discussed together, as the amount of water soluble metalworking fluids is small compared to emulsions and the resulting waste is mostly treated together with the emulsifiable types. Therefore, the risk assessment is performed for emulsifiable metalworking fluids only as a worst case. According to the Intended Use the in-use concentration is 0.15% w/w "RP 3:2"/kg metal working fluid.

The estimation of environmental exposure is made by calculating the emissions and then the concentrations for each environmental compartment on the basis of all direct and indirect emissions. Both environmental exposure assessments (PT2 and PT13) are based on the EU-Emission Scenario Document (ESD) "Refinement of the Emission Scenario Document for Product Type 13" (ECHA, 2015a[4]).

It is assumed that no (relevant) emissions occur during industrial use and it is designed to calculate the environmental release resulting from the waste treatment phase of metalworking

4 ECHA (2015a): Refinement of the Emission Scenario Document for Product Type 13, May 2015, European Chemicals Agency, Reference: ECHA-15-B-11-EN, ISBN: 978-92-9247-412-6

fluids. Emissions during the use phase of metalworking fluids are possible, but eventual emissions from industrial use are considered not relevant as compared with emissions from waste treatment plant.

PT6 - In-can preservative (PT 6.5 Fuels)

The active substance "RP 3:2" is exclusively used as in-can preservative of fuels

Preservatives in fuels are used to prevent microbial growth in presence of water, the formation of slime and sludge and finally the deterioration of the fuels during storage in the tanks. The applicant indicated that "RP 3:2" is only used for diesel fuel and the storage of diesel; crude oil is not treated.

The concentration in fuel ranges from 0.005 to 0.04% and 0.1% if fuel is contaminated. The applied biocide concentration is depending on the ratio of biodiesel in the fuel. Biodiesel can be blended and used in many different concentrations. At higher biodiesel concentrations (e.g. B-20) the concentration of biocide has to be adjusted for sufficient efficacy.

The formulation of fuels in refineries is a highly automated process in which nearly no emission into the environment is expected. In the ESD for PT6 (2004[5]) it is stated that "Emissions to the environment predominantly occur when the water phase of a storage tank is discharged into the sewer (Van der Poel and Bakker, 2002)".
In the Technical Agreements for Biocides (TAB, June 20166) it is stated that application and service life are not relevant for this sub-category because for fuel ending up in an engine, it is assumed that 100% of the preservative will be burnt completely thus, emissions of the in-preservative into the environment do not occur and therefore should not be considered. The draft ESD for PT6 (July 2015) considers the calculation of the life cycle step "formulation" for the sub-category 6.5 (fuels). However, this revised ESD is not endorsed yet.

Storage tank

Large storage tanks at the refinery's site may contain amounts of water which are discharged separately. Considering that the compound is miscible in all proportions with water and hydrolyses rather fast the active substance will not accumulate in the oil phase, but will be discharged together with the waste water. Discharge to the STP is likely, but due to the presence of hydrocarbons in the aqueous phase (the so-called water-accommodated fraction) waste water must be treated according to environmental legislations. However, the aqueous phase is eventually discharged to the sewer after waste water treatment or directly released to surface water. A scenario for emission of fuel preservatives from large oil storage tanks along with the

[5] European Commission DG ENV / RIVM (2004): Environmental Emission Scenarios Biocides: PT 6 – In-can Preservatives. Reference 4L1784.A0/R018/FBA/TL/Nijm.

[6] ECHA (2016): Technical Agreements for Biocides (TAB) version 1.1

http://echa.europa.eu/documents/10162/20733977/technical_agreements_for_biocides_en.pdf

aqueous phase does not exist currently. Considering that PT13 was assessed for the hydrolysis products formaldehyde and 2-hydroxypropylamine as well, for which the volumes discharged to the sewer are expected similar to that of large storage tanks, the later may in principle cover the risk assessment for fuel preservatives as well.

Motor boating

According to EC (2002) release to surface water may happen from motor boating as well. Petrol can be spilled directly into the surface water while switching or loading of petrol tanks and carburettor overflow while tilting the motor. This release is estimated to be less than 0.1% of total fuel consumption (EC, 2002).

PT11 – Preservatives for liquid-cooling and processing systems

The biocidal active substance as manufactured is directly used as a preservative in closed liquid cooling systems in a typical concentration of 0.025% w/w biocidal product as preservative in industrial closed liquid cooling systems to avoid microbial infestation, which would influence the cooling potential negatively.

The exposure assessment follows the recommendations of the Emission Scenario Documents for Biocides for PT11 (Royal Haskoning, 2003)[7]. In closed recirculating cooling water systems cooling water recirculates in a closed loop. The cooling water is not discharged after cooling. These systems have minimal loss of water, since there is no direct contact with the atmosphere. Process heat is transferred to the cooling water in one heat exchanger, and in a second heat exchanger the cooling water is cooled off by air or water. The cooled water is then returned to the heat exchanger that cools the process. Residence times in closed cooling water systems can be up to 6 months (Royal Haskoning, 2003). A closed recirculating cooling system has no evaporation and wind- of spray losses.

For Tier 1a calculations the worst case scenario of a complete drainage of the cooling system was calculated. The discharge was directed without any pre-treatment to municipal STP.

For Tier 1b calculations the cumulative release from design and dosing losses were taken into account. A simultaneous release on a single day from a dosing event and design loss was estimated as worst case scenario for design and dosing losses, covering the releases from both emission sources. The discharge is estimated to be directed to municipal STP.

Tier 2

7 „Harmonisation of Environmental Emission Scenarios for biocides used as preservatives for liquid cooling systems (product type 11)", European Commission DG ENV / RIVM, September 2003

For Tier 2 the release of the complete drainage with preceding treatment in either an on-site STP or an STP of a specialized waste treatment company before the discharge enters into the municipal STP was calculated, which represent a realistic scenario.

In accordance with metal working fluids, waste treatment of preservatives in industrial closed liquid cooling systems is usually done by an external treatment plant due to the high number of industrial users and medium sized companies. The waste water is purified microbially prior to final discharge to a municipal STP. So, in fact there are two STPs in a row: the pre-treatment and subsequent a municipal STP. To do justice to this fact, the emissions calculated in Tier 1a were reduced by the fraction degraded in the STP (according to Simple Treat).

PT12 – Slimicides in Offshore Processes

Generally, biocidal products containing "RP 3:2" can be used directly for the prevention or control of slime growth on materials, equipment and structures in industrial processes. The biocidal products (a.s. as manufactured) are mainly applied as slimicide in the oil industry (offshore) for the preservation of drilling muds.

The presence of microorganisms in drilling mud causes slime formation, which may lead to clogged filters. Drilling mud is pumped down in the drilling tube and comes to the surface again between the tube and the drilling hole. Drilling mud functions are lubricant for the drill head and transport of the cuttings to the surface. Drilling mud also provides the hydro-static pressure that prevents collapse of the drilling hole.

The biocidal product is directly added to the mud without previous formulation steps.

In oil production processes the mud, composing of water, clay and additives is pumped down into the drilling hole to lubricate the drill head and to transport the cuttings out of the drilling hole to the surface. Due to the presence of microorganism in the mud slime formation occurs, which can lead to clogged filters. Here slimicides are used as water soluble concentrates in a typical concentration of 0.15% in the drilling mud.

Aggregated exposure assessment

A qualitative assessment is provided based on the decision tree on aggregated exposure assessment in the CAR template looking e.g. at relevant PTs and pathways.

It has to be noted that several formaldehyde releasers are still in the Review Programme and not yet evaluated and approved. In addition because the risk characterization is based on formaldehyde exposure from the intended uses of formaldehyde itself should be considered in such an assessment.

The question of a need regarding an aggregated risk assessment basically comprises the following product types: the hydrolysis products formaldehyde and 2-hydroxypropylamine via use as system cleaner of metalworking systems (PT2), as in-can preservative exclusively in fuels (PT6), as a preservative in closed liquid cooling systems (PT11), as slimicide in offshore processes (PT12) and as preservative for metalworking fluids (MWF), only when directly dosed into the metal working system (PT13).

The application and service life of "R 3:2" in the PT 6 (PT6.5 – fuels) generate no emission to the environment, because if the fuel ends up in an engine, the preservative will be burnt

completely and thus no emissions of the in-preservative into the environment occur. Therefore, this product type is not relevant for an aggregated risk assessment (agreement included in the Technical Agreements for Biocides: TAB, June 2016 [8])

Regarding PT12 the release pathway of the hydrolysis products formaldehyde and 2-hydroxypropylamine is not via a municipal STP since in general the biocidal product used in water-based drilling mud is discharged to sea for continuous release, however for batch wise release the fluids are managed on land and the user has to ensure that spend drilling muds are not discharged overboard to the marine compartment. In the use phase, when discharging cuttings to sea, the adherent drilling mud will be discharged to the sea as well. Therefore, this product type is not considered for an aggregated risk assessment.

The remaining product types PT2, PT11 and PT13 have in common that their release pathways end up in a municipal STP. The annual tonnage of the biocide use is not known and subsequently it is not known if the biocide use is <10% of the total use. Since "R 3:2" is used in more than one product type, the pathway "Part 2" of the decision tree on need for aggregated exposure assessment was followed. The releases of the biocide within the various product types show an overlap in time and space, as the possibility exists that the different releases end up in the same municipal STP. Possible releases into the environment during use of system cleaners (PT2) are identical with releases caused by metalworking fluids (PT13). Moreover, both biocidal products are used in the same industrial machine and are discharged together. However, it might be reasonably assumed that a degradation and dissipation during the use occur. Therefore, an adding up of the concentrations used in PT2 and PT13 would probably overestimate the risk.

Assuming an analytical monitoring after treatment (Tier 2) to ensure that the measured concentration of the hydrolysis product formaldehyde in the water phase before release to sewer is below 40 ppm (independently of the treatment method), it can be supposed that in the light of the considerations set out above, the releases of both, PT2 and PT13, are included in this mixture of waste water. Summing up these risk characterisation ratios with those of PT 11, no unacceptable risks are indicated.

Finally, it should be pointed out that in the report "Aggregated Environmental Exposure Assessment and Risk Characterisation of Biocidal Products" issued by the Umweltbundesamt Germany (UBA 2016 9), it is stated that if the PEC/PNEC ratio is < 1 for only one single use of an active substance the authorisation has to be granted, despite the fact that PEC/PNEC ratio might be > 1 for all uses of that active substance. Because according to Art. 4 (1) BPR it is sufficient to grant an authorisation if at least one biocidal product complies with the requirements. In this case a competent authority cannot refuse an approval of an active substance based on the argument that a risk resulting from an aggregated exposure exists.

8 ECHA (2016): Technical Agreements for Biocides (TAB) version 1.1, chapter 2.4.6.6 PT 6.5 Fuels, page 22. http://echa.europa.eu/documents/10162/20733977/technical_agreements_for_biocides_en.pdf

9 https://www.umweltbundesamt.de/publikationen/aggregated-environmental-exposure-assessment-risk

2.2.3.5. Risk characterisation

PT2 and PT13

The risk characterisation will be based on the hydrolysis products as it is expected that during the disinfection and use of the metal working system "RP 3:2" has almost completely hydrolysed. The parent compound itself is therefore not expected to reach any environmental compartment.

For PT2 the model product is a 10% aqueous dilution of "RP 3:2" and is intended to be used as disinfectant system cleaner for metal working: disinfection of inner surfaces of vessels and tubes with in-use concentrations of 0.25% up to 2% depending on the duration of the disinfectant cleaning process. Though the use is assigned to PT2 the exposure calculations followed the recommendations for PT13 in this specific case because the use as system cleaners of metal working systems is best described by the PT13 scenarios.

For PT13 the representative biocidal products are CONTRAM™ MBO or Grotan OX® or GrotaMar 71® with a typical in-use concentration in metal working fluids (MWF) of 0.15% w/w, only when the product is directly applied into the MWF, directly dosed in the metal working system. Only emissions during waste treatment after refreshment are considered.

Atmosphere

Direct exposure to air from the described uses of "RP 3:2" as well as of its metabolites is considered to be negligible.

Interference of formaldehyde with atmospheric processes (e.g., global warming, stratospheric ozone depletion and the acidification or formation of hydroxymethane¬sulfonate, etc.) is regarded to be negligible. Accumulation of formaldehyde in the air is not expected ($T_{1/2}$ 47.9 h (estimation)). 2-Hydroxypropylamine has a short calculated chemical half-life in the troposphere ($T_{1/2}$ 9.6 h; estimation) and a low Henry's law constant.

According to these findings, accumulation and long-distance transport of these compounds in the air are not to be expected. Also the main constituent N,N'-methylene-bis(5-methyloxazolidine), formaldehyde and 2-hydroxypropylamine are not listed in Annex I and II of Regulation (EC) No 1005/2009 of the European Parliament and of the Council of 16 September 2009 on substances that deplete the ozone layer. Therefore the environmental risk to air is considered to be acceptable.

Aquatic compartment

STP:

The following RCRs (PEC/PNEC) have been calculated (cf. Table 2.2.3.5-1 and Table 2.2.3.5-2):

Table 2.2.3.5-1: PEC/PNEC ratios for **2-hydroxypropylamine** in STP for PT 2 and PT 13

Exposure scenario (ECHA 2015)		PEC_{STP} (mg/L)	PEC/PNEC
Tier 1		**$PNEC_{STP}$: 1.296 mg/L**	
End-user, on-site treatment			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0	**0**
	Split,Kow	1.69	**1.30**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	0	**0**
	Split,Kow	13.50	**10.44**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0	**0**
	Split,Kow	1.02	**0.79**
Waste management company			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0	**0**
	Split,Kow	0.63	**0.49**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	0	**0**
	Split,Kow	5.07	**3.92**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0	**0**
	Split,Kow	0.38	**0.29**

Table 2.2.3.5-2: Tier 1 and 2 PEC/PNEC ratios for formaldehyde in STP

Exposure scenario (ECHA 2015a)		PEC_{STP} (mg/L)	PEC/PNEC
Tier 1		**$PNEC_{STP}$: 0.2 mg/L**	
End-user, on-site treatment			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0.95	**4.73**
	Split,Kow	0.84	**4.22**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	7.56	**37.80**
	Split,Kow	6.76	**33.82**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0.57	**2.84**
	Split,Kow	0.51	**2.54**
Waste management company			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0.35	**1.77**
	Split,Kow	0.32	**1.59**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	2.84	**14.18**
	Split,Kow	2.54	**12.68**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0.21	**1.07**
	Split,Kow	0.19	**0.95**

Exposure scenario (ECHA 2015a)	PEC_{STP} (mg/L)		PEC/PNEC
Tier 1	**$PNEC_{STP}$: 0.2 mg/L**		
Tier 2			
Emulsifiable fluids PT2/PT13 including monitoring	40 mg/L	0.0506	**0.25**

Conclusion

As unacceptable risks for 2-hydroxypropylamine and formaldehyde have been identified due to the use of formaldehyde for the preservation of metal working systems (PT2 and PT13) in Tier 1, "Tier 2" including monitoring based on a pilot degradation study was introduced for illustration to show a safe use.

In general, degradation of biocide between the last dosing and the start of waste treatment will further reduce the biocide concentration as it is often practiced to stop dosing of the biocide some time before the MWF is removed from the installation in order to save biocide and, as a consequence, money. In addition, the used emulsion will be stored (and transported) before oil-water splitting will be performed. However, for an accurate estimation of the exposure reduction information about the degradation in used MWF has to be available (ECHA 2015a). Therefore a study (MBO – Doc. IV Study 7.10.2, cf. Doc. II-B, Chapter 5.1.2) was submitted to underpin "Tier 2" (monitoring, the analytical detected concentration of the hydrolysis products in the water phase before release to sewer is below 40 ppm, independently of the treatment method). Therefore "Tier 2" exposure calculations ("emulsifiable fluids PT2/PT13 including monitoring") performed for the concerned environmental compartments illustrate a possibly safe use.

For the PNEC for 2-hydroxyproylamine data on "RP 3:2" were used in absence of full documented experimental data for this compound. However there is evidence that the toxicity towards aquatic microorganisms is lower compared to the "RP 3:2". %. Supportive information presented in Doc. II-A, Chapter 4.2.1, Table 4.2.1-7 indicate that the 3 h-EC_{50} value for inhibition of aquatic microbial activity for 2-HPA is considerable higher compared to the value from "RP 3:2". Nevertheless, an acceptable risk could be demonstrated for waste management companies and in-use concentrations of 0.25% and 0.15%. PT2 end-user, on site treatment (0.25%) was only marginally exceeded with a risk ratio of 1.3.

Surface water:

Aquatic organisms

The following RCRs (PEC/PNEC) have been calculated (cf. Table 2.2.3.5-3 and Table 2.2.3.5-4):

Table 2.2.3.5-3: Tier 1 PEC/PNEC ratios for **2-hydroxypropylamine** for the aquatic compartment

Exposure scenario	$PEC_{surface\ water}$ (mg/L)	PEC/PNEC
Tier 1	**$PNEC_{aquatic}$: 0.1184 mg/L**	

Exposure scenario		$PEC_{surface\ water}$ (mg/L)	PEC/PNEC
End-user, on-site treatment			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0	**0**
	Split,Kow	0.17	**1.43**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	0	**0**
	Split,Kow	1.35	**11.4**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0	**0**
	Split,Kow	0.102	**0.86**
Waste management company			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0	**0**
	Split,Kow	0.06	**0.05**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	0	**0**
	Split,Kow	0.51	**4.28**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0	**0**
	Split,Kow	0.04	**0.31**

Table 2.2.3.5-4: Tier 1 and Tier 2 PEC/PNEC ratios for **formaldehyde** for the aquatic compartment

Exposure scenario		$PEC_{surface\ water}$ (mg/L)	PEC/PNEC
Tier 1		**$PNEC_{aquatic}$: 0.0104 mg/L**	
End-user, on-site treatment			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0.09	**9.12**
	Split,Kow	0.08	**8.14**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	0.76	**72.69**
	Split,Kow	0.68	**65.00**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0.06	**5.47**
	Split,Kow	0.05	**4.87**
Waste management company			
Emulsifiable fluids **PT 2**, in-use concentrations **0.25%**	Split,evap	0.04	**3.40**
	Split,Kow	0.03	**3.04**
Emulsifiable fluids **PT 2**, in-use concentrations **2%**	Split,evap	0.28	**27.31**
	Split,Kow	0.25	**24.42**
Emulsifiable fluids **PT 13**, in-use concentrations **0.15%**	Split,evap	0.02	**2.07**
	Split,Kow	0.02	**1.83**
Tier 2			

Emulsifiable fluids PT2/PT13 including monitoring	40 mg/L	5.06E-03	**0.49**

Conclusion

As unacceptable risks for 2-hydroxypropylamine (PT2) and formaldehyde (PT2, PT13) have been identified due to the use of formaldehyde for the preservation/cleaning of metal working systems, further refinements and/or risk mitigation measures (RMM) need to be applied in order to allow a safe use in these scenarios. Acceptable risks for 2-hydroxypropylamine were demonstrated for PT13. Also RCRs <1 for PT2 waste treatment companies, in-use concentrations of 0.25% as well as for end-user, on-site treatment, scenario emulsion splitting by evaporation were calculated. End-user on-site treatment scenario emulsion splitting by Kow covered the most commonly applied emulsion splitting techniques (e.g. chemical splitting, ultrafiltration) and therefore it is assumed that the majority of cases will result in RCR >1.

"Tier 2" exposure calculations ("emulsifiable fluids PT2/PT13 including monitoring") using 40 mg/L as a waste water concentration before STP treatment were performed. This scenario leads to an acceptable risk concerning surface water.

Surface water used for drinking water

The concentrations for 2-hydroxypropylamine and formaldehyde in surface water exceed the parametric value of 0.1 µg/L according to Directive 98/83/EC in some calculated scenarios (see Table 2.1.1.2-1 and Table 2.1.1.2-2).

Regulation EU (No) 528/2012, Annex VI, Article 69 states that surface water in or from the area of envisaged use intended for the abstraction of drinking water should not exceed the value for organic pesticides of 0.1 µg/L fixed by Directive 98/83/EC.

On the other hand the PEC surface water does not necessarily correspond with the PEC for the concentration at the water abstraction point. The calculations do not take into account the rapid degradation of formaldehyde in water, dilution in surface water and the "background concentration" of the compounds. At present there are no tools available to calculate such a PEC, taking into account these processes that may occur during the water flow from the STP to the water abstraction point.

Therefore the release of biocides used as disinfectant for metalworking fluids line and metalworking fluids may be considered by the relevant national authorities when issuing permits for recovery plants.

Sediment assessment and persistence:

According to ECHA (2015b) substances with a K_{oc} <500 L/kg are not likely to sorb to sediment in general. The K_{oc} values of 2-hydroxypropylamine and formaldehyde are 70.4 L/kg and 15.9 L/kg, respectively. Therefore, no risk assessment for the sediment compartment was performed.

For persistence please see section 2.2.3.3

Terrestrial compartment

Terrestrial organisms:

The PEC/PNEC ratios for soil were calculated by dividing the local $PECs_{soil}$ by the $PNECs_{soil}$ (see Table 2.2.3.5-5 and 2.2.3.5-6 for PT 2 and Table 2.2.3.5-7 and 2.2.3.5-8 for PT13).

Table 2.2.3.5-5: PEC/PNEC ratios for **2-hydroxyproylamine** for the terrestrial compartment for PT2

Exposure scenario	Emulsion splitting by evaporation Split,evap		General emulsion splitting Split,Kow	
Tier 1	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**
	$PNEC_{soil}$: 0.161 mg/kg soil$_{ww}$			
End-user, on-site treatment				
Arable soil (30 days), in-use **0.25%**	0	**0**	0.26	**1.61**
Arable soil (180 days), in-use **0.25%**	0	**0**	0.08	**0.52**
Grassland (180 days), in-use **0.25%**	0	**0**	0.03	**0.20**

Exposure scenario	Emulsion splitting by evaporation Split,evap		General emulsion splitting Split,Kow	
Tier 1	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**
	PNEC$_{soil}$: 0.161 mg/kg soil$_{ww}$			
Arable soil (30 days), in-use **2%**	0	**0**	2.08	**12.9**
Arable soil (180 days), in-use **2%**	0	**0**	0.66	**4.12**
Grassland (180 days), in-use **2%**	0	**0**	0.26	**1.58**
Waste management company				
Arable soil (30 days), in-use **0.25%**	0	**0**	0.0873	**0.61**
Arable soil (180 days), in-use **0.25%**	0	**0**	0.0279	**0.19**
Grassland (180 days), in-use **0.25%**	0	**0**	0.0107	**0.007**
Arable soil (30 days), in-use **2%**	0	**0**	0.703	**4.86**
Arable soil (180 days), in-use **2%**	0	**0**	0.225	**1.55**
Grassland (180 days), in-use **2%**	0	**0**	0.0863	**0.60**

Table 2.2.3.5-6: PEC/PNEC ratios for **formaldehyde** for the terrestrial compartment for PT2

Exposure scenario	Emulsion splitting by evaporation Split,evap		General emulsion splitting Split,Kow	
Tier 1	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**
	PNEC$_{soil}$: 0.00416 mg/kg soil$_{ww}$			
End-user, on-site treatment				
Arable soil (30 days), in-use **0.25%**	0.031	**7.38**	0.027	**6.59**
Arable soil (180 days), in-use **0.25%**	8.58E-03	**2.06**	7.67E-03	**1.84**
Grassland (180 days), in-use **0.25%**	2.80E-03	**0.67**	2.51E-03	**0.60**
Arable soil (30 days), in-use **2%**	0.245	**58.90**	0.219	**52.60**
Arable soil (180 days), in-use **2%**	0.067	**16.50**	0.061	**14.80**
Grassland (180 days), in-use **2%**	0.022	**8.28**	0.020	**4.81**
Waste management company				
Arable soil (30 days), in-use **0.25%**	0.012	**2.76**	0.010	**2.48**
Arable soil (180 days), in-use **0.25%**	3.22E-03	**0.77**	2.88E-03	**0.69**

Exposure scenario	Emulsion splitting by evaporation Split,evap		General emulsion splitting Split,Kow	
Tier 1	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**
	PNEC$_{soil}$: 0.00416 mg/kg soil$_{ww}$			
Grassland (180 days), in-use **0.25%**	1.05E-03	**0.25**	9.42E-04	**0.23**
Arable soil (30 days), in-use **2%**	0.092	**22.20**	0.083	**19.80**
Arable soil (180 days), in-use **2%**	0.026	**6.20**	0.023	**5.55**
Grassland (180 days), in-use **2%**	8.42E-03	**2.02**	7.54E-03	**1.81**
Tier 2				
Arable soil (30 days)	1.47E-03			**0.35**
Arable soil (180 days)	4.13E-04			**0.10**
Grassland (180 days)	1.35E-04			**0.03**

Table 2.2.3.5-7: PEC/PNEC ratios for **2-hydroxypropylamine** for the terrestrial compartment for PT13

Exposure scenario	Emulsion splitting by evaporation Split,evap		General emulsion splitting Split,Kow	
Tier 1	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**
	PNEC$_{soil}$: 0.0859 **mg/kg soil$_{ww}$**			
End-user, on-site treatment				
Arable soil (30 days), in-use 0.15%	0	**0**	0.156	**0.97**
Arable soil (180 days), in-use 0.15%	0	**0**	0.050	**0.30**
Grassland (180 days), in-use 0.15%	0	**0**	0.019	**0.12**
Waste management company				
Arable soil (30 days), in-use 0.15%	0	**0**	0.059	**0.37**
Arable soil (180 days), in-use 0.15%	0	**0**	0.019	**0.12**
Grassland (180 days), in-use 0.15%	0	**0**	7.20E-03	**0.04**

Table 2.2.3.5-8: PEC/PNEC ratios for **formaldehyde** for the terrestrial compartment for PT13

Exposure scenario	Emulsion splitting by evaporation Split,evap		General emulsion splitting Split,Kow	
Tier 1	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**	**PEClocal $_{soil}$ (mg/kg$_{wwt}$)**	**PEC/PNEC**
	PNEC$_{soil}$: 0.00416 mg/kg soil$_{ww}$			
End-user, on-site treatment				
Arable soil (30 days), in-use 0.15%	0.018	**4.42**	0.017	**3.97**
Arable soil (180 days), in-use 0.15%	5.15E-03	**1.24**	4.60E-03	**1.11**
Grassland (180 days), in-use 0.15%	1.68E-03	**0.404**	1.50E-03	**0.361**
Waste management company				
Arable soil (30 days), in-use 0.15%	6.93E-03	**1.67**	6.19E-03	**1.49**
Arable soil (180 days), in-use 0.15%	1.94E-03	**0.47**	1.73E-03	**0.42**
Grassland (180 days), in-use 0.15%	6.33E-04	**0.15**	5.65E-04	**0.14**

Exposure scenario	Emulsion splitting by evaporation Split,evap	General emulsion splitting Split,Kow
Tier 2		
Arable soil (30 days)	1.47E-03	**0.35**
Arable soil (180 days)	4.13E-04	**0.10**
Grassland (180 days)	1.35E-04	**0.03**

Conclusion

As unacceptable risks for 2-hydroxypropylamine (PT2) and formaldehyde (PT2 and PT13) have been identified due to the use of formaldehyde for the treatment of metal working systems in the terrestrial compartment, further risk mitigation measures (RMM) or exposure refinements need to be applied in order to allow a safe use in these scenarios.

The PEC calculations used a default half-life for soil according to ECHA (2015b) of 30 days. Also no decline during the in-use period in the metal working fluid lines was assumed. As formaldehyde is a very reactive compound the PEC calculations are very conservative and do not account for the potential of the chemical to react quickly with organic matter in sewer pipeline, STP, sludge or soil. Concerning "Tier 2" exposure calculations that considered monitoring/measurements of formaldehyde (<40 mg/L) the risk for the terrestrial compartment was acceptable.

2-hydroxypropylamine showed an acceptable risk for PT13. Also for PT2, in-use concentration 0.25% waste treatment company as well as end-user, on-site treatment with evaporation techniques all RCR ratios were below 1. Only for end-user, on-site treatment, general emulsion splitting Kow (e.g. ultrafiltration) the ratio was slightly exceeded with 1.61 for arable soil (30 day). For end-users who treat water soluble MWFs on-site an acceptable risk was identified if both techniques are available. Concerning the use of STP sludge as a fertiliser it is recognised that this may not be applicable for all member states, as there may be the tendency to use only (or additional) on-site biological treatment before release into municipal STPs in some countries. In these cases the on-site STP sludge will probably be incinerated and the release into soil via agricultural uses will be negligible (ECHA, 2015a).

Persistence in soil:

For persistence please see section 2.2.3.3

Groundwater:

According to ECHA (2015b) the concentration in pore water of soil is taken as an indication for potential groundwater levels.

For PT 2, in-use concentrations 0.25% PECs groundwater for both hydrolysis products are >0.1µg/L (range 0.0549 to 0.007 mg/L, cf. Doc. II-B, Chapter 5.1.2.6, Table 5.1.2.6-1). For PT 2, in-use concentrations 2% predicted environmental concentrations in groundwater are even higher (see Doc. II-B, Chapter 5.1.2.6, Table 5.1.2.6-2). For PT 13 the values are between 0.0332 to 0.004 mg/L (see Doc. II-B, Chapter 5.3.2.6, Table 5.3.2.6-1).

These values are far above the parametric value of 0.1 µg/L according to according to Directive 98/83/EC and the quality standard of 0.1 µg/L for pesticide according to the Groundwater Directive 2006/118/EC.

Therefore, potential groundwater concentrations for both hydrolysis products are calculated using FOCUS Pearl v. 4.4.4 (cf. Doc II-B for details).

For end-user, regarding on-site treatment, in-use concentration PT 2 of 0.25%, both, 2-hydroxypropylamine and formaldehyde, shows in three scenarios (Porto, Sevilla, Thiva) no unacceptable risk and regarding waste management company four groundwater scenarios (Piacenza, Porto, Sevilla, Thiva) indicate an acceptable risk regarding sludge applications on arable land. All scenarios deliver an acceptable risk regarding sludge applications on grassland.

For PT13 four groundwater scenarios (Piacenza, Porto, Sevilla, Thiva) show no unacceptable risk regarding groundwater concentrations of formaldehyde considering sludge application on arable land and all nine groundwater scenarios show an acceptable risk regarding groundwater concentrations of formaldehyde considering sludge application on grassland if on-site waste treatment is assumed. 2-Hydroxypropylamine shows in five scenarios no unacceptable risk regarding sludge applications on arable land and no unacceptable risk on grassland.

All values regarding the concentration of formaldehyde in groundwater based on Tier 2 calculation values (report "Determination of the Formaldehyde content in different samples from used emulsions of CONTRAM^{TM} MBO during treatment") go well below the trigger value of 0.1µg/L of the EU Drinking Water Directive.

Non compartment specific effects relevant to the food chain (secondary poisoning):

According to ECHA (2015b) concern for a bioaccumulation potential of a chemical is given when a substance has a log Kow >3, is highly adsorptive (or belongs to a structural class of substances that is known to bioaccumulate) and no mitigations regarding its degradation properties exist.

Screening data on bioconcentration indicate that there is no concern for bioconcentration neither for the constituents of "RP 3:2", nor the hydrolysis products (cf. Doc. II-A, Chapter 4.1.2). A bioaccumulation potential for "RP 3:2" could not be identified based on a log Kow value <0 and a DT50 hydrolysis of <1 hour. A bioaccumulation potential for the hydrolysis products formaldehyde and 2-hydroxyprobylamine could not be identified based on very low log Kow values <1, predicted low BCF values of <4 L/kg$_{ww}$ and experimental evidence indicating no bioaccumulation. Therefore no risk assessment for secondary poisoning was performed.

PT6

In PT6 the biocidal product CONTRAM™ MBO and GrotaMar 71® are intended to be exclusively used as in-can preservative for fuel (mainly diesel).

Large storage tanks at the refinery's site may contain vast amounts of water which are discharged separately. Therefore hydrolysis products are expected to be discharged together with the waste water. Discharge to the STP is likely, but due to the presence of hydrocarbons in the aqueous phase (the so-called water-accommodated fraction) waste water must be treated according to environmental legislations. However, the aqueous phase is eventually discharged to the sewer after waste water treatment. Also the risk assessment on Methyl-tert-butylether (MTBE) stated that there are large numbers of terminal sites in the EU storing and handling gasoline. Some of the sites do not have actual wastewater treatment system for tank waters (EC, 2002)[10]. However the water phase from storage tanks might contain oil droplets, and thus it can be assumed that disposal treatment similar to PT13 (e.g. oil-water splitting) and according to environmental legislations occurs. Regarding the amount of water in storage tanks the applicant stated that only small amounts of water can be found due to good occupational hygiene and state-of-the-art-techniques. In addition to the above issues condensation of air humidity and tank cleaning processes which are performed only every 10 years cause water content in the tanks. It should be pointed out, that the European specification for the water content in diesel fuel is max 200 mg/kg. Therefore, diesel fuel that meets this water specification also contains just a small amount of 'free' or 'dispersed' water.

A scenario for emission of fuel preservatives from large oil storage tanks along with the aqueous phase does not exist currently. Considering that PT13 was assessed for the hydrolysis products formaldehyde and 2-hydroxypropylamine as well, for which the volumes discharged to the sewer are expected similar to that of large storage tanks, the later may cover the risk assessment for fuel preservatives as well.

Application and service life are not relevant for this sub-category 6.5, because if the fuel ends up in an engine, the preservative will be burnt completely and thus no emissions of the in-preservative into the environment occurs. However, according to EC (2002) release to surface water may happen from motor boating. Petrol can be spilled directly into the surface water while switching or loading of petrol tanks and carburettor overflow while tilting the motor. This release is estimated to be less than 0.1% of total fuel consumption (EC, 2002).

The life cycle stage formulation of the end-product for the sub-category 6.5 should be considered once the emissions scenario document (ECHA, 2015, draft ESD)[11] is endorsed.

In conclusion an unacceptable risk for PT13 for formaldehyde was identified therefore risk management measures are needed which are relevant for PT 6 as well. However the risk

[10] EC (2002): European Union Risk Assessment Report TERT-BUTYL METHYL ETHER CAS No: 1634-04-4 EINECS No: 216-653-1 RISK ASSESSMENT. http://www.efoa.eu/documents/document/20100715150023-mtbe_-_eu_risk_assessment_report_-_2002.pdf (2016-03-21)

[11] Schweitzer M., Galler M. (2015): DRAFT version v1, Revision of the Emission Scenario Document for In-can preservatives PT6 „Abschätzung der Umweltbelastung durch Konservierungsmittel: Fortentwicklung der Bewertungsmethodik" SCC Scientific Consulting Company, Bad Kreuznach, July 2015.

characterisation for PT6 has a higher uncertainty due to a lack of available agreed and endorsed exposure guidance.

PT11

For closed liquid cooling systems, releases to the environment are likely during dosing, leakages (design losses) and during the periodical refreshment (complete drainage). In the case of refreshment the discharges are predominantly handled by a specialised company, i.e. in sewage treatment plants. Waste treatment is usually done by an external treatment plant due to the number of industrial users and medium sized companies. Usually it is likely that these waste treatment companies will treat several aqueous wastes together (such as waste from e.g. MWF, waste from tank cleaning, waste from liquid cooling).

So predominantly all discharges will be either treated on-site or by a specialized waste treatment company before entering the municipal waste water system. In both cases the on-site STP sludge will probably be incinerated and the release into soil via agricultural uses will be negligible, however this will depend on national legislation for sewage sludge.

There may be the tendency to use only (or additional) on-site biological treatment before release into municipal STPs in some countries. Direct release to surface water is therefore not taken into account for the environmental exposure assessment. For the environmental exposure assessment following scenarios were included:

1. Releases during complete drainage without any pre-treatment into the municipal STP, which represents a rather unrealistic worst case situation, but resembles the standard EUSES calculation without any refinement (Tier 1a). Tier 1a scenario considers complete drainage of the cooling system for maintenance or in case of uncontrolled microbial growth, resulting from lack of a routine monitoring programme.

2. Releases during complete drainage with preceding treatment in either an on-site STP or a STP of a specialized waste treatment company before the discharge enters into the municipal STP, which represent a realistic scenario (Tier 2: two STPs in a row trigger that the emissions calculated in Tier 1a were reduced by the fraction degraded in the STP). Tier 2 is based on the assumption that the waste water is e.g. purified microbially prior to final discharge to a municipal STP.

3. Releases from design and dosing losses without any pre-treatment into the municipal STP (Tier 1b).

It has been shown that in the EU emulsions are categorised as hazardous waste, therefore they are not allowed to be led directly into rivers or other water compartments without prior treatment collection of cooling liquid and disposing it off as hazardous waste is an acceptable assumption for closed cooling system in PT11.

For PT 11 the representative biocidal products are CONTRAM™ MBO or Grotan OX® or GrotaMar 71®. According to the intended use (cf. Doc II-B, Chapter 3) the in-use concentration of "RP 3:2" as preservative in industrial closed liquid cooling systems is 0.025% w/w. The innate efficacy has been shown at 0.025% against bacteria but not fungi.

No marine risk assessment was performed because no direct exposure to the marine compartment was anticipated given the intended uses (closed recirculated cooling water systems). The use of marine/brackish water in the cooling system is excluded in the current assessment.

Atmosphere

Direct exposure to air from the described uses in industrial closed liquid cooling systems of "RP 3:2" as well as of its metabolites is considered to be negligible.

Interference of formaldehyde with atmospheric processes (e.g., global warming, stratospheric ozone depletion and the acidification or formation of hydroxymethane¬sulfonate, etc.) is regarded to be negligible. Accumulation of formaldehyde in the air is not expected ($T_{1/2}$ 47.9 h (estimation)). 2-Hydroxypropylamine has a short calculated chemical half-life in the troposphere ($T_{1/2}$ 9.6 h (estimation)) and a low Henry's law constant.

According to these findings, accumulation and long-distance transport of these compounds in the air are not to be expected. Also the main constituent N,N'-methylene-bis(5-methyloxazolidine), formaldehyde and 2-hydroxypropylamine are not listed in Annex I and II of Regulation (EC) No 1005/2009 of the European Parliament and of the Council of 16 September 2009 on substances that deplete the ozone layer. Therefore the environmental risk to air is considered to be acceptable.

Aquatic compartment

STP:

The following RCRs (PEC/PNEC) have been calculated (cf. Table 2.2.3.5-9 and Table 2.2.3.5-10).

Table 2.2.3.5-9: PEC/PNEC ratios for **2-hydroxypropylamine** in STP

Exposure scenario	**PEC_{STP} (mg/L)**	**PEC/PNEC**
	$PNEC_{STP}$: 1.296 mg/L	
Tier 1a (drainage)		
Waste treatment	0.383	**0.30**
Tier 1b (design + dosing)		
Waste treatment	2.04E-03	**1.57E-03**
Tier 2 (drainage)		
Waste treatment	5.06E-02	**3.90E-02**

Table 2.2.3.5-10 PEC/PNEC ratios for **formaldehyde** in STP

Exposure scenario	**PEC_{STP} (mg/L)**	**PEC/PNEC**
	$PNEC_{STP}$: 0.2 mg/L	
Tier 1a (drainage)		
Waste treatment	0.214	**1.07**
Tier 1b (design + dosing)		
Waste treatment	1.14E-03	**5.70E-03**

Exposure scenario	PEC_{STP} (mg/L)	PEC/PNEC
Tier 2 (drainage)		
Waste treatment	2.74E-02	**0.14**

Conclusion:

Tier 1a PEC/PNEC value for formaldehyde is with 1.07 slightly exceeded, indicating a risk to microorganisms. It has to be kept in mind, that a worst case scenario was calculated. For all Tier calculations no primary degradation of formaldehyde is assumed in the liquid cooling systems. Formaldehyde is a very reactive compound so it can be assumed that during and after application of the product the concentration of formaldehyde will decrease by a chain of chemical reactions. However because no data were provided for the degradation of formaldehyde during use, this elimination route was not considered in the exposure estimates. Also adaption of microbes can occur as shown by Eiroa et al. (2004, 2005) cited in the Formaldehyde Core Dossier. Batch experiments with adapted inoculum from a resin producing factory using 30 - 3890 mg/L formaldehyde showed fast degradation of formaldehyde (<24h). The sludge used in this study tolerated much higher formaldehyde concentrations than reported in the literature. The much higher concentrations removed in the assays could have resulted from the long-term adaptation of the sludge to formaldehyde in the industrial wastewater treatment plant from which the present inoculum was obtained according to Eiroa et al. (2004). Eiroa et al. (2005) showed that the elimination of formaldehyde in industrial biological STPs based on results on lab-scale activated sludge units under aerobic conditions is high. The synthetic influent contained nutrients and stepwise increasing concentrations of formaldehyde (26 – 3168 mg/L) over the incubation period of 160 days. Based on formaldehyde measurements, a degree of elimination of approximately 99.5% was maintained at all influent concentrations; the reactor originated from an industrial STP of a resin producing industry (Eiora et al. 2005, cf. Doc III-A7.1.2.1.1/01 Formaldehyde Core Dossier). These data show that adaption and tolerance of microorganisms to very high formaldehyde concentration is possible in industrial settings.

For Tier 1a for 2-hydroxypropylamine as well as for Tier 1b and Tier 2 exposure calculation for both compounds an acceptable risk was found. Based on the slight exceedance of PEC/PNEC of 1.07 in Tier 1a for formaldehyde further risk management measure are needed. Tier 2 calculations are displayed in the CAR only for information to cover potential national situation at product authorisation stage.

Aquatic organisms

The following RCRs have been calculated (cf. Table 2.2.3.5-11 and Table 2.2.3.5-12):

Table 2.2.3.5-11: PEC/PNEC ratios **for 2-hydroxypropylamine** for the aquatic compartment

Exposure scenario	**$PEC_{surface\ water}$ (mg/L)**	**PEC/PNEC**
	$PNEC_{aquatic}$: 0.1184 mg/L	
Tier 1a (drainage)		
Waste treatment	3.83E-02	**3.23E-01**
Tier 1b (design + dosing)		
Waste treatment	2.04E-04	**1.7E-03**
Tier 2 (drainage)		
Waste treatment	5.06E-03	**4.27E-02**

Table 2.2.3.5-12: PEC/PNEC ratios for **formaldehyde** for the aquatic compartment

Exposure scenario	**$PEC_{surface\ water}$ (mg/L)**	**PEC/PNEC**
	$PNEC_{aquatic}$: 0.0104 mg/L	
Tier 1a (drainage)		
Waste treatment	2.14E-02	**2.06**
Tier 1b (design + dosing)		
Waste treatment	1.14E-04	**1.10E-02**
Tier 2 (drainage)		
Waste treatment	2.74E-03	**0.26**

Conclusion:

The Tier 1a PEC/PNEC value formaldehyde is 2.06 indicating a risk to aquatic organisms. Tier 1a for 2-hydroxypropylamine as well as Tier 1b and Tier 2 calculations for 2-hydroxypropylamine and formaldehyde indicate an acceptable risk to aquatic organisms. Therefore for formaldehyde further risk management measures are needed. Tier 2 calculations are displayed only for information to cover potential national situation at product authorisation stage.

Surface water used for drinking water

The concentrations for 2-hydroxypropylamine and formaldehyde in surface water exceed the parametric value of 0.1 µg/L according to Directive 98/83/EC in all scenarios (see Table 2.2.3.5-11 and Table 2.2.3.5-12).

Regulation EU (No) 528/2012, Annex VI, article 69 states that surface water in or from the area of envisaged use intended for the abstraction of drinking water should not exceed the value for organic pesticides of 0.1 µg/L fixed by Directive 98/83/EC.

On the other hand the $PEC_{surface\ water}$ doesn't necessarily correspond with the PEC for the concentration at the water abstraction point. The calculations do not take into account the rapid degradation of formaldehyde in water, dilution in surface water and the "background concentration" of the compounds. At present there are no tools available to calculate such a

PEC, taking into account these processes that may occur during the water flow from the STP to the water abstraction point.

Sediment assessment and persistence:

According to ECHA (2015b) substances with a K_{oc} <500 L/kg are not likely to sorb to sediment in general. The K_{oc} values of 2-hydroxypropylamine and formaldehyde are 70.4 L/kg and 15.9 L/kg, respectively. Therefore, no risk assessment for the sediment compartment was performed.

For persistence please see section 2.2.3.3.

Terrestrial compartment

Terrestrial organisms:

Depending on the national legislation sludge from an industrial STP (Tier 2) is prevented to be spread on agricultural land. In such situations sludge from industrial treatment operations is not spread to soil in agriculture, horticulture and grassland. This is also in line with the Urban Waste Water Treatment Directive 91/271/EEC[12] where it is indicated that "Industrial waste water entering collecting systems and urban waste water treatment plants shall be subject to such pre-treatment as is required in order to ensure that sludge can be disposed of safety in an environmentally acceptable manner". This exposure pathway has not been assessed.

The PEC/PNEC ratios for soil were calculated by dividing the local $PECs_{soil}$ by the $PNECs_{soil}$ (see Table 2.2.3.5-13 and 2.2.3.5-14).

Table 2.2.3.5-13: PEC/PNEC ratios for **2-hydroxyproylamie** for the terrestrial compartment for PT 11

Exposure scenario	PEC local (mg/kgww)	PEC/PNEC
	$PNEC_{soil}$: 0.161 mg/kg $soil_{ww}$	
Tier 1a (drainage)		
Arable soil (30 days)	5.31E-02	**3.30E-01**
Grassland (180 days)	1.70E-02	**1.06E-01**
Arable soil (180 days)	6.52E-03	**4.05E-02**
Tier 1b (design + dosing)		
Arable soil (30 days)	2.84E-04	**1.76E-03**
Grassland (180 days)	9.05E-05	**5.62E-03**
Arable soil (180 days)	3.48E-05	**2.16E-04**
Tier 2 (drainage)		
Arable soil (30 days), waste treatment	7.02E-03	**4.36E-02**
Grassland (180 days), waste treatment	2.24E-03	**1.39E-02**
Arable soil (180 days), waste treatment	8.61E-04	**5.35E-03**

[12] http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:31991L0271&from=EN

Table 2.2.3.5-14: PEC/PNEC ratios for **formaldehyde** for the terrestrial compartment for PT 11

Exposure scenario	**PEC local (mg/kgww)**	**PEC/PNEC**
	$PNEC_{soil}$: 0.00416 mg/kg $soil_{ww}$	
Tier 1a (drainage)		
Arable soil (30 days)	6.24E-03	**1.50**
Grassland (180 days)	1.75E-03	**0.42**
Arable soil (180 days)	5.70E-04	**0.14**
Tier 1b (design + dosing)		
Arable soil (30 days)	3.31E-05	**7.96E-03**
Grassland (180 days)	9.27E-06	**2.23E-03**
Arable soil (180 days)	3.03E-06	**7.28E-04**
Tier 2 (drainage)		
Arable soil (30 days)	7.99E-04	**0.19**
Grassland (180 days)	2.23E-04	**0.05**
Arable soil (180 days)	7.29E-05	**0.02**

Conclusion

Risk characterization ratios for the soil compartment indicate no unacceptable risk to soil organisms for 2-hydroxypropylamine in all Tiers and formaldehyde concerning Tier 1b and Tier 2 calculations. The risk for formaldehyde Tier 1a is with 1.5 slightly exceeded. Risk mitigation measures are needed to reduce the identified risk. Tier 2 calculations are displayed only for information to cover potential national situations at product authorisation stage.

Persistence in soil:

For persistence please see section 2.2.3.3

Groundwater:

2-Hydroxypropylamine and formaldehyde are not likely to have unacceptable effects on groundwater according to Directives 98/83/EC and 2006/118/EC for PT11.

Non compartment specific effects relevant to the food chain (secondary poisoning):

Please see PT2 and PT13, respectively.

PT12

Exposure estimates have been conducted according to EUBEES (2003). There are different types of drilling muds and fluid selection will influence the choice of waste management technique. For this risk characterisation slimicides in the oil extraction processes are used for control of slime forming microorganisms in water-based drilling mud/fluid (WBMF). For the use phase in offshore oil wells, only marine water is considered as receiving compartment and PEC values for direct release in sea water have been estimated. The biocidal products used are GrotaMAR 71®, CONTRAM™ MBO and Grotan® OX at the dose rates of 0.15% according to the intended use (cf. Doc II-B, Chapter 3).

The PEC values and the corresponding PEC/PNEC ratios in the marine environment for formaldehyde and 2-hydroxypropylamine resulting from the use of the above mentioned biocidal products as slimicides are listed below. Retrieved mud, without drilling cuttings, is either recirculated back into the drilling line together with new drilling mud or discharged if the drilling operation requires a new type of drilling mud (EUBEES, 2003).

The exposure calculation and risk characterisation followed therefore two scenarios, namely:

- Drilling chemicals - Continuous discharge
- Drilling chemicals - Batchwise discharge

Continue discharge refers to the fraction that could not be extracted and discharged overboard bound to the cuttings. This is therefore only a fraction of the total volume of drilling fluids initially added.

Batchwise discharge occurs during drilling operations when the mud needs to be diluted. Some of the mud system may have to be discharged and the remainder of the system diluted. Batchwise discharges also occur at the end of a section where a new or different mud will be required in the next section. Finally, these discharges will also occur at the end of the well drilling when all operations are finished and the rig is to be moved to a new location. These discharges are larger both in volume and rate of discharge (EUBEES, 2002). For both scenarios an acceptable risk is needed for substance approval.

Marine compartment (incl. sediment)

Marine organisms

The following RCRs (PEC/PNEC) have been calculated (cf. Table 2.2.3.5-15, Table 2.2.3.5-16):

Table 2.2.3.5-15: PEC/PNEC ratios for **2-hydroxypropylamine** for the marine compartment for PT12

Exposure scenario	**$PEC_{seawater}$ (mg/L)**	**PEC/PNEC**
	$PNEC_{seawater}$: 0.0118 mg/L	
Drilling chemicals, continuous discharges	1.33E-03	**1.21E-01**
Drilling chemicals, batchwise discharges	1.94E+00	**1.64E+02**

Table 2.2.3.5-16: PEC/PNEC ratios for **formaldehyde** for the marine compartment for PT12

Exposure scenario	**$PEC_{seawater}$ (mg/L)**	**PEC/PNEC**
	$PNEC_{seawater}$: 0.00104 mg/L	
Drilling chemicals, continuous discharges	6.84E-04	**6.58E-01**
Drilling chemicals, batchwise discharges	1.00E+00	**9.62E+02**

Conclusion:

No risk was identified for the application in drilling muds with continuous discharges, however for batch wise discharges a risk for both hydrolysis products were identified in the marine compartment.

Formaldehyde is highly reactive, and thus spent water based mud contains significantly less amounts of biocide than originally applied. Moreover, batch wise discharge of the spent mud is applied after drilling period, so that biocide in spent mud could be degraded during storage. Overall, the elimination of the biocide within usage will be high, and only a fraction of the unused concentration could be considered for discharge. Usually, the discharge quantity still generally needs to be approved in advance as part of the discharge permit (e.g. OCR 2002[13], PON 15 in the UK). In addition, offshore Netherlands are quite strict in the regulation of biocide discharge offshore. During the permission process, a risk assessment has to be performed, probably based on analytical measurements of the residues of biocides in the spent mud. Overall, a maximum residue level for default discharge was proposed by the applicant (15 ppm = 0.0015% b.p. in spent mud). Using this maximum residue level a safe use can be demonstrated according to the applicant. However no example or analytical measurement of the proposed residue levels has been provided by the applicant. Therefore the proposed concentration limit could not be considered in the current assessment. Because batch wise release results in unacceptable risks, preservation of drilling muds may be possible with risk mitigation measures in place to reduce the identified risk and to ensure that spend drilling muds are not discharged overboard to the marine compartment.

[13] https://www.gov.uk/guidance/oil-and-gas-offshore-environmental-legislation#the-offshore-chemicals-regulations-2002-as-amended

2.2.4. Exclusion Criteria and Candidate for substitution

2.2.4.1. Exclusion criteria according Art. 5(1) BPR (EU 528/2012)

Article 5(1) of the BPR states that an active substance cannot be approved if it: (a, b, c) is classified or meets the criteria for classification as CMR 1A or 1B in accordance with the CLP Regulations; (d) is considered to have endocrine disrupting properties; (e) or meets the criteria for PBT or vPvB according to Annex XIII to the REACH Regulation.

Available evidence indicates that item (a) is met with regard to carcinogenic properties of "RP 3:2" (please see Chapter 2.1.3. Classification and Labelling of the active substance) whereas on (d) cannot be concluded (please see Chapter 2.2.2.1) and (e) is not met (please see Chapter 2.2.3.3 PBT assessment).

As a consequence an evaluation according Art 5(2) has been carried out. The results of this evaluation are summarised below.

2.2.4.2. Assessment of possible chemical alternatives to "RP 3:2"

"RP 3:2" 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.

Since the eCA came to the conclusion that "RP 1:1" does meet the conditions laid down in Article 10(1)(a) of Regulation (EU) No 528/2012, and should therefore be considered as a candidate for substitution by meeting the exclusion criteria a public consultation in accordance with Article 10(3) of BPR has been launched by ECHA. No information on possible chemical or non-chemical alternatives to "RP 1:1" was received from interested third parties during the public consultation in accordance with Article 10(3) of BPR.

During the public consultation the applicants provided a comprehensive discussion on possible chemical alternatives. Since no third party opinion has been received the eCA decided to contact the AUVA (Allgemeine Unfallversicherungsanstalt - the Austrian Workers' Compensation Board) for support. The AUVA is the social insurance for occupational risks for more than 3.3 million employees and 1.4 million pupils and students in Austria. It is financed mainly by contributions paid by employers. Its legal duties are prevention of occupational accidents and diseases, occupational medical care, first aid for occupational accidents, post traumatic treatment, rehabilitation, financial compensation and research.

In the following we will go through the applicant's arguments providing the assessment by the AUVA expert.

PT2: The applicants claim that for PT2 "RP 3:2" can be compared to glutaraldehyde, concluding that due to the required stability at high pH values, "RP 3:2" cannot be replaced by other bactericidal actives supported under PT 2.
The AUVA expert concluded that the arguments are conclusive and suggests to limit the maximum concentrations of MBO and "RP 3:2" in system cleaners to the labelling limits for Cat 1B.

PT6: The applicants argue that for PT6 "RP 3:2" can be compared with CMI/MI, concluding that there is "no significantly beneficial alternative for MBO/"RP 3:2" 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". In addition it is argued that for this application the human exposure to formaldehyde is very low.
The AUVA expert concluded that the arguments brought forward are conclusive, but points out that he has no practical experience and knowledge concerning preservation of fuels.

PT11/12: The applicants claim that for PT11 "RP 3:2" can be compared with glutaraldehyde, THPS and acrolein, concluding that "there is no significantly beneficial alternative for "RP 3:2" available. 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.". However the applicants do not provide a conclusion on the comparison of "RP 3:2" with acrolein.
The AUVA expert did not provide a comment on the conclusiveness of the arguments, but pointed out, that for formaldehyde releasers which are used in closed recirculating cooling water systems, exposure to airborne formaldehyde may only occur in case of refilling or cleaning. In addition he suggests limiting the maximum concentrations of MBO and "RP 3:2" in cooling fluids to the labelling limits for Cat 1B.

PT13: For PT13 the applicants compare "RP 3:2" with CMIT/MIT, MIT, BIT, diamine, phenoxyethanol, MBIT and DBNPA, presenting the advantages and disadvantages of using these substances. They conclude that isothiazolinones would be the only practical alternatives to "RP 3:2" as bactericide. Furthermore they claim that: CMIT/MIT is a very strong skin sensitizer and would potentially have adverse effects on workers' health; MIT has also limitations (lower stability, higher skin sensitizer) compared to "RP 3:2"; BIT has a gap of efficiency against pseudomonas species and would need to be used in combination with "RP 3:2" or MIT; and MBIT will not be approved for PT13.
As for the other substances, it is claimed that: diamine is an alternative to "RP 3:2" in PT13 niche applications only; phenoxyethanol has a limited use in metalworking fluids due to its low partition coefficient; and DBNPA has technical limitations (fast decomposition at pH>7 and in presence of nucleophilic compounds) that prevent it from replacing "RP 3:2" in PT13 applications.
The AUVA expert states that for commonly used biocides in metal working fluids with a view to efficacy a table is published in „VKIS - VSI - IGM Stoffliste für Kühlschmierstoffe nach DIN 51385 für die Metallbearbeitung". This table includes 6 different isothiazolinones, 8 different formaldehyde releasers and 10 other biocides. The 6 alternative preservatives described in the applicant's statement are listed in the table as well as the 6 preservatives mentioned therein. Most common alternative preservatives in this PT are e.g. Kathon (mixture of 5-chloro-2-methyl-2,3-dihydroisothiazol-3-on (=CIT) and 2-methyl-2,3-dihydroisothiazol-3-on (=MIT)), MIT without CIT, 3-iodo-2-propinylbutylcarbamate (IPBC) and o-phenylphenol (OPP).
The AUVA expert points out that he has performed numerous measurements on workplaces with metal working or cutting fluids, where airborne formaldehyde was never detected as problematic compared with the Austrian MAK-value. He claims that his findings are also in accordance with results of a study carried out by IFA Institut für

Arbeitsschutz in Germany. In addition he mentions his knowledge of allergic reactions on workers working with MIT. He concludes that CIT and MIT are strong skin sensitizers and therefore no suitable alternatives for formaldehyde releasers.

The eCA concluded that based on the arguments and information available no chemical alternatives which would provide a significant lower risk profile compared to "RP 3:2" in the field of intended uses which was assessed in the CAR could have been identified.

2.2.4.3. Candidate for substitution according Art. 10 BPR (EU 528/2012)

Article 10 BPR states that an active substance should be considered a candidate for substitution if:

(a) it meets one of the exclusion criteria but there is negligible risk and/or socioeconomic need (BPR Article 5.2.)

(b) it is classified or meets the criteria for classification as a respiratory sensitiser (Resp Sens 1) under the CLP Regulation;

(c) its AEL and/or AEC values are significantly lower than those of the majority of approved active substances for the same product type and use scenario;

(d) it meets two of the criteria for PBT according to Annex XIII to the REACH Regulation;

(e) there are reasons for concern linked to the nature of the critical effects that in combination with the use patterns and amount used could still cause concern, such as high potential of risk to groundwater;

(f) it contains a significant proportion of non-active isomers or impurities.

Available evidence at this time indicates that item (a) is met whereas (b) and (d) are not met (please see Chapter 2.2.3.3 PBT assessment). No conclusion can be drawn if (e) is potentially met in regard to ED properties for non-target organisms as the data allow no firm conclusion on the ED status (please see Chapter 2.2.3.2). No comparative evaluation is available to allow a conclusion on (c), but the risk from the intended use of the active substance appears acceptable on the basis of the actual AEL and exposure estimates. Representing a UVCB substance (f) may be considered as fulfilled, however the toxicity appears dominated by the hydrolysis product formaldehyde, which would support that (f) is not of toxicological concern, i.e. it is not met.

Before decision on active substance approval can be taken information on already approved active substances has to be reviewed in order to identify available substitutes according BPR article 10(3).

2.2.5. List of endpoints

In order to facilitate the work of granting or reviewing authorisations, the most important endpoints, as identified during the evaluation process, are listed in Appendix I.

APPENDIX I: LIST OF ENDPOINTS

Chapter 1: Identity, Physical and Chemical Properties, Classification and Labelling

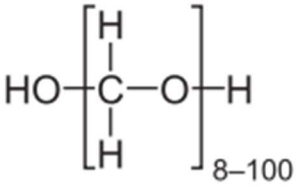
Active substance	Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2) (short: "RP 3:2")
Product-type	2, 11, 13

Identity of the active substance

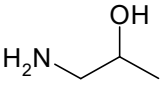
Chemical name (IUPAC)	Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)
Chemical name (CA)	Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2)
CAS No	n.a.
EC No	n.a.
Other substance No.	n.a.
Minimum purity of the active substance as manufactured (g/kg or g/l)	100% by definition because the active substance is a UVCB substance [redacted]
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	n.a. (UVCB substance)
Molecular formula	n.a. (UVCB substance)
Molecular mass	n.a. (UVCB substance)
Structural formula	n.a. (UVCB substance)

Identity of the starting material paraformaldehyde

Chemical name (IUPAC)	Polyoxymethylene
Chemical name (CA)	paraformaldehyde
CAS No	30525-89-4
EC No	
Other substance No.	
Minimum purity (g/kg or g/l)	> 940 g/kg
Identity of relevant impurities and additives (substances of concern) (g/kg)	see confidential annex on specification

Molecular formula	OH(CH2O)nH (n = 8 - 100)
Molecular mass	30.03 (monomer)
Structural formula	

Identity of the starting material 2-hydroxypropylamine

Chemical name (IUPAC)	1-Aminopropan-2-ol
Chemical name (CA)	DL-1-Amino-2-propanol Isopropanolamine 2-Hydroxypropylamine HPA
CAS No	78-96-6
EC No	201-162-7
Other substance No.	
Minimum purity of the active substance as manufactured (g/kg or g/l)	>= 990 g/kg
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	See confidential annex on specification
Molecular formula	C_3H_9NO
Molecular mass	75.11
Structural formula	

Physical and chemical properties

Melting point (state purity)	"RP 3:2":-60.5°C; HPA: 1.7°C Formaldehyde: -118°C to -92°C (formaldehyde gas) -15°C (formalin (37%))
Boiling point (state purity)	"RP 3:2": endothermic effect up to 195°C (boiling); exothermal effect at 186 °C (decomposition).

	HPA: 160°C Formaldehyde: -19.5 °C (1013 hPa) (formaldehyde gas) 96 °C (formalin (37w/w% aqueous solution, containing 10-15% methanol))
Temperature of decomposition	--
Appearance (state purity)	“RP 3:2” colourless to yellowish liquid and an amine like odour HPA: colourless liquid and a slight ammonia odour Formaldehyde: colourless gas, pungent suffocating odour (formaldehyde gas) colourless liquid, irritating, pungent odour (formaldehyde solution (30-55% w/w))
Relative density (state purity)	Relative density “RP 3:2”: 1.05 at 20°C; Density HPA: 0.9611 g/cm3 at 20°C Formaldehyde: 0.815 at - 20°C (formaldehyde gas) 1.1346 g/cm3 at 25°C (aqueous solution: 50% formaldehyde, 7% methanol)
Surface tension	“RP 3:2”: 68.1 mN/m at 20°C HPA: no data Formaldehyde: not surface active
Vapour pressure (in Pa, state temperature)	“RP 3:2”: Not relevant. The exposure assessment is based on formaldehyde. Therefore, the vapour pressure of formaldehyde was used for further calculations and not the value of the substance or one of its constituents HPA: 0.63hPa at 25°C Formaldehyde: 5490 hPa, 300 K (formaldehyde gas) 187 Pa, 25°C (formalin (37%))
Henry’s law constant (Pa m^3 mol^{-1})	“RP 3:2”: Not relevant. The exposure assessment is based on formaldehyde. Therefore, the Henry’s law constant of formaldehyde was used for further calculations and not the value of the substance or one of its constituents HPA:$4.94 \cdot 10^{-5}$ Pa m^3 mol^{-1} at 25°C Formaldehyde: 0.034 Pa*m^3/mol at 25°C (methanol-free formaldehyde, prepared from 37% formalin)

Solubility in water (g/l or mg/l, state temperature)	"RP 3:2": completely miscible in water at room temperature. "RP 3:2": 2800g/L at30°C and pH 9.77 HPA:37g/L at 11°C Formaldehyde: pH 5 at ___ °C: not determined pH 9 at ___ °C: not determined up to 55% (formaldehyde gas)

Solubility in organic solvents (in g/l or mg/l, state temperature)	"RP 3:2": completely miscible in DMSO, ethanol, n-Octanol, acetone; solubility in n-heptane is 500 – 1000 mg/L at 20.5°C. "RP 3:2" is highly soluble in standard fat (HB 307) at 37°C. HPA: soluble in all proportions in ethanol, diethyl ether, acetone, benzene and carbon tetrachloride Formaldehyde: no data
Stability in organic solvents used in biocidal products including relevant breakdown products	"RP 3:2": The substance and the biocidal products are solely handled and marketed as aqueous solution which contains no organic solvents. HPA: Not relevant for hydrolysis product Formaldehyde: no data
Partition coefficient (log P_{OW}) (state temperature)	"RP 3:2": log Pow:; result: -0.043 (mean) HPA:-0.96 Formaldehyde: 0,35 at 25 °C (formaldehyde gas)
Dissociation constant	"RP 3:2": hydrolysable, pKa is not possible. HPA:9.94 at 10°C Formaldehyde: pKa = 13.27 (of hydrate), 25 °C (aqueous solution of formaldehyde; measurement is usually performed with aqueous formaldehyde dilution (for gas or solution))
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	"RP 3:2": There are no absorption maxima above 290 nm. HPA: no data

Flammability	“RP 3:2”: non-flammable and non-hazardous. Melting point is below 100°C. Therefore, determination of flashpoint is sufficient for the test substance. HPA: no data Formaldehyde: 330 (4), 318, (5), 308(5), 298 (4) nm (formaldehyde gas) Lambda maximum (λmax) at 988 nm (aqueous solution: 50% formaldehyde, 7% methanol)
Explosive properties	“RP 3:2”: No data HPA: explosions limits in air: 1.9 – 12% (v/v) Formaldehyde: not explosive

Classification and proposed labelling

with regard to physical/chemical data	--
with regard to toxicological data	Acute Tox. 4, H302 – Harmful if swallowed Acute Tox. 3, H311 – Toxic in contact with skin Acute Tox. 4, H332 – Harmful if inhaled Skin Corr. 1B, H314: Causes severe skin burns and eye damage (just classification, not labelling: Eye Dam 1, H318 Causes serious eye damage) Skin Sens. 1A, H317: May cause an allergic skin reaction STOT RE 2, H373 May cause damage to organs (GIT tract and respiratory tract) Muta 2 H341, Suspected of causing genetic defects, Note 9 Carc. 1B H350, May cause cancer, Note 8 EUH071: Corrosive to the respiratory tract
with regard to fate and behaviour data and with regard to ecotoxicological data	Aquatic Chronic 2, H411

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method)	^{1}H- and ^{13}C-NMR method
Impurities in technical active substance (principle of method)	^{1}H- and ^{13}C-NMR method and titration method

Analytical methods for residues

Soil (principle of method and LOQ)	Not applicable
Air (principle of method and LOQ)	Not applicable
Water (principle of method and LOQ)	Not applicable
Body fluids and tissues (principle of method and LOQ)	Not applicable
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not applicable
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not applicable

Analytical methods for hydrolysis product 2-hydroxypropylamine

Soil (principle of method and LOQ)	HPA:	Not applicable
Air (principle of method and LOQ)	HPA:	Adsorption of HPA on XAD-2. Determination of HPA after extraction by LC-UV LOQ = 107 µg/m³
Water (principle of method and LOQ)	HPA:	Not avilable
Body fluids and tissues (principle of method and LOQ)	HPA:	Not applicable
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	HPA:	Not applicable
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	HPA:	Not applicable

Analytical methods for hydrolysis product formaldehyde

Soil (principle of method and LOQ)	Not required because of indoor use
Air (principle of method and LOQ)	Residue definition: formaldehyde RP-HPLC-UV; RP18 column LOQ: 0.04 µg/m³
Water (principle of method and LOQ)	Residue definition: formaldehyde GC-ECD, DB-5 and AT-1701 column, LOQ: 0.08 µg/L (drinking water, US EPA method 556.1); LOQ: 5 µg/L (surface water, US EPA method 556.1)
Body fluids and tissues (principle of method and LOQ)	Monitoring is not meaningful, since formaldehyde is permanently present in humans
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	Not required, no relevant residues expected
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required, no relevant residues expected

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals

Rate and extent of oral absorption:	Technically not feasible to determine for the active substance; assumption for risk assessment: 100%
Rate and extent of dermal absorption:	Technically not feasible to determine for the active substance; assumption for risk assessment: 100%
Rate and extent of inhalative absorption:	Technically not feasible to determine for the active substance; assumption for risk assessment: 100%
Distribution:	Technically not feasible to determine for the active substance
Potential for accumulation:	Not expected due to hydrolysis to formaldehyde with dilution and with contact with biological media
Rate and extent of excretion:	Technically not feasible to determine for the active substance
Toxicologically significant metabolite(s)	Hydrolysis product formaldehyde

Acute toxicity

Rat LD_{50} oral	630 - 920 mg/kg bw day
Rat LD_{50} dermal	760 – 6000 mg/kg bw day
Rat LC_{50} inhalation	No data
Skin irritation	Rabbit studies: Causes severe skin burns and eye damage
Eye irritation	Rabbit studies: Causes severe skin burns and eye damage
Skin sensitization (test method used and result)	GPMT, with intradermal induction dose of 0.5% a response of 60% response was observed due to classification for Skin Sens. Cat 1A, regulatory classification threshold of 0.1%

Repeated dose toxicity

Species/ target / critical effect	Rat (90 day gavage) / local effects: chronic ulcerative gastritis & peritonitis
Lowest relevant oral NOAEL / LOAEL	60 / 20 mg/kg bw day
Lowest relevant dermal NOAEL / LOAEL	No data available, local effects expected
Lowest relevant inhalation NOAEL / LOAEL	No data available, local effects expected

Genotoxicity	Positive in vitro (AMES, chromosome aberration test, mammalian gene mutation test) Negative in vivo systemic (negative micronucleus test at MTD, ambiguous bone marrow chromosome aberration test)

	No data on in vivo local genotoxic effects, but expected from hydrolysis product formaldehyde, that results by dilution and reaction with biological media

Carcinogenicity

Species/type of tumour	No data available but implementation of a long-term study scientifically unjustified; carcinogenic effects of the hydrolysis product formaldehyde sufficiently documented.
lowest dose with tumours	-

Reproductive toxicity

Species/ Reproduction target / critical effect	Rat (one generation study) / no adverse effects on reproduction in addition read across to hydrolysis product formaldehyde supports the assumption of no effects on reproduction.
Lowest relevant reproductive NOAEL / LOAEL	parental and F1 systemic effects: 15 / 45 mg/kg bw day, probably secondary to local effects
Species/Developmental target / critical effect	Rabbit (developmental toxicity study) / no primary developmental effects
Lowest relevant developmental NOAEL / LOAEL	90/ 135 mg/kg bw day, probably secondary to local effects

Neurotoxicity / Delayed neurotoxicity

Species/ target/critical effect	Rat / functional observation battery in 90 day study / no adverse effect
Lowest relevant developmental NOAEL / LOAEL.	No adverse effect

Other toxicological studies

-

Medical data

.	Medical surveillance on manufacturing plant personnel is reported by applicant and no adverse effects on human health were observed with the active substance. For effects related to formaldehyde exposure please see the formaldehyde core dossier.

Summary	Value	Study	Safety factor

“RP 3:2” systemic AEL, short, medium and long term	0.33 mg/kg bw day	[redacted] AEL formaldehyde is 0.15 mg/kg bw day, based overall rat studies (28d, 90d, 2 year) with assessment factor 100	100
“RP 3:2” local AEC, short, medium and long term	0.25 µg/L air	Read across from [redacted] AEC formaldehyde is 0.12 µg/L air, based on human, rat and monkey data	3 to human eye irritation data, 1 to human population based ocular / respiratory irritation NOAEC 10 to rat and monkey data
ARfD	Not relevant	For explanation see chapter 2.2.2.2.	
ADI	Not relevant	For explanation see chapter 2.2.2.2.	

Acceptable exposure scenarios (including method of calculation)

Production of active substance (user:)	Not assessed.
Formulation of biocidal product (user:)	Not assessed.

Application of biocidal product (user:)	PT 2: disinfectants and algaecides not intended for direct application to humans or animals Formulation and use of system cleaners: professionals - inhalation and dermal exposure PT 6: preservation of fuel Formulation of fuel by professionals as well as use of fuel by professionals and general public – inhalation and dermal exposure. PT 11: Preservatives for liquid cooling and processing systems Use of preservatives for liquid cooling and processing systems: professionals - inhalation and dermal exposure PT 12: Use as slimicide for preparation of drilling muds in offshore processes Use as preservative for drilling muds in offshore processes: professionals- inhalation and dermal exposure PT 13: Working or cutting fluids preservatives Formulation of lubricant concentrates: professionals – inhalation and dermal exposure Use in metalworking processes – inhalation and dermal exposure
Indirect exposure as a result of use	PT 2, 11, 12, 13: Not relevant
Exposure of pets	PT 2, 11, 12, 13: Not expected to be relevant
Dietary Exposure	PT 2, 11, 12, 13: Not expected to be relevant

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH 4: <1h	At concentrations which are applied in the media of exotoxicity tests or are expected in the environment, the active substance is completely hydrolysed. Hydrolysis products are formaldehyde and 2-hydroxypropylamine.
	pH 7: <1h	
	pH 9: <1h	
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	Not relevant for active substance. The active substance does not absorb UV/VIS light at wave-lengths above 290 nm and is rapidly hydrolysed assuming environmentally relevant concentrations in water (transformation to formaldehyde and hydroxypropylamine).	
Readily biodegradable (yes/no)	"RP 3:2": Yes 2-hydroxypropylamine: Yes	
Biodegradation in seawater	"RP 3:2": Yes (>60% at day 22, OECD 306 –closed bottle procedure)	
Non-extractable residues	-	
Distribution in water / sediment systems (active substance)	-	
Distribution in water / sediment systems (metabolites)	-	

Route and rate of degradation in soil

Mineralization (aerobic)	-
Laboratory studies (range or median, with number of measurements, with regression coefficient)	DT_{50lab} (20°C, aerobic):-
	DT_{90lab} (20°C, aerobic):-
	DT_{50lab} (10°C, aerobic):-
	DT_{50lab} (20°C, anaerobic):-
	degradation in the saturated zone:-
Field studies (state location, range or median with number of measurements)	DT_{50f}:-
	DT_{90f}:-
Anaerobic degradation	-
Soil photolysis	-
Non-extractable residues	-
Relevant metabolites - name and/or code, % of applied active ingredient (range and maximum)	-
Soil accumulation and plateau concentration	-

Adsorption/desorption

Ka , Kd Ka_{oc} , Kd_{oc} pH dependence (yes / no) (if yes type of dependence)	
	"RP 3:2": 10 L/kg 5 L/kg (estimated, KocWIN v2.0, Episuite); 5-methyl-oxazolidine: 6.5 L/kg (estimated, KocWIN v2.0, Episuite), experimental: <1 L/kg (Draft OECD TG 121) 2-hydroxypropylamine: Estimated K_{oc} <70.4 L/kg (ionized form; pH=7; estimated)
	2-hydroxypropylamine: yes (charged molecule at environmental relevant pH values)

Fate and behaviour in air

Direct photolysis in air	Guideline not yet available
Photo-oxidative degradation in air	The rate constant for indirect photolysis with OH radicals was estimated using the program AOPWIN v1.91: $T_{1/2}$= 1.229 h (assuming an OH-radical concentration (kOH) of 5.0 · 105 molecules·cm-3)
Volatilization	The volatility of the active substance (main constituent) is considered to be low referring to the low vapour pressure and low Henrys Law constant. Nevertheless, the substance is not hydrolytically stable and hydrolyses rapidly in the presence of water. The degradation products reveal significantly higher volatilities than the active substance.

Monitoring data, if available

Soil (indicate location and type of study)	-
Surface water (indicate location and type of study)	-
Ground water (indicate location and type of study)	-
Air (indicate location and type of study)	-

Chapter 5: Effects on Non-target Species

Toxicity data for aquatic species (most sensitive species of each group)

Species	Time-scale	Endpoint	Toxicity
Fish – Test substance "RP 3:2"			
Danio rerio – GrotarMar 71®	96h, semi-static	Mortality, LC_{50}	57.7 mg/L (nominal)
Danio rerio – Contram™ MBO (presumable)	96h, semi-static	Mortality, LC_{50}	71 mg/L (nominal)
Scopthalmus maximus – GrotarMar 71®	96h, semi-static	Mortality, LC_{50}	135 mg/L (nominal)
Invertebrates - Test substance "RP 3:2"			
Daphnia magna - Contram™ MBO (presumable)	48h, static	Mobility, EC_{50}	28 mg/L (nominal)
Daphnia magna- GrotarMar 71®	48h, semi-static	Mobility, EC_{50}	37.9 mg/L (nominal)
Daphnia magna- Grotan Ox	21d, semi-static	Reproduction, NOEC LOEC	1.3 mg/L (nominal) 3.2 mg/L (nominal)
Microorganisms - Test substance "RP 3:2"			
Activated sludge, municipal - Contram™ MBO (presumable)	3h, static	Inhibition of respiration, NOEC EC_{50}	16 mg/L (nominal) 44 mg/L (nominal)
Activated sludge, municipal - GrotarMar 71®	3h, static	Inhibition of respiration, EC_{50}	44 mg/L (nominal)
Activated sludge, industrial - GrotarMar 71®	3h, static	Inhibition of respiration, EC_{50}	10.4 mg/L (nominal)

Species	Time-scale	Endpoint	Toxicity
Fish – Test substance "RP 1:1"			
Danio rerio – Contram™ 121	96h, semi-static	Mortality, LC_{50}	130 mg/L (nominal)
Oncorhynchus mykiss – Grotan®WS	96h, semi-static	Mortality, LC_{50}	>100 mg/L (nominal)
Invertebrates - Test substance "RP 1:1"			
Daphnia magna - Contram™ 121	48h, static	Mobility, EC_{50}	29 mg/L (nominal)
Algae - Test substance "RP 1:1"			
Desmodemus subspicatus- Contram™ 121	72h, static	Growth rate, E_rC_{50} NOE_rC	3.3 mg/L (measured) 0.9 mg/L (measured))

Pseudokirchneriella subcapitata- Grotan ®WS	72h, static	Growth rate, E_rC_{50} E_rC_{10}	0.32 mg/L (corrected for 76% recovery) 0.148 mg/L (corrected for 76% recovery)

Effects on earthworms or other soil non-target organisms

Acute toxicity to …	No data available
Reproductive toxicity to …	No data available

Effects on soil micro-organisms

Nitrogen mineralization	No data available
Carbon mineralization	No data available

Effects on terrestrial vertebrates

Acute toxicity to mammals	Oral: 630 - 920 mg/kg bw day Dermal: 760 – 6000 mg/kg bw day
Acute toxicity to birds	No data available
Dietary toxicity to birds	No data available for RP 3:2 (or RP 1:1)
Reproductive toxicity to birds	No data available for RP 3:2 (or RP 1:1)

Effects on honeybees

Acute oral toxicity	No data available
Acute contact toxicity	No data available

Effects on other beneficial arthropods

Acute oral toxicity	No data available
Acute contact toxicity	No data available
Acute toxicity to ……..	No data available

Bioconcentration

Bioconcentration factor (BCF)	"RP 3:2": The QSAR model for the estimation of a aquatic or terrestrial bioconcentration factor is applicable to a logKow range of 2 to 6 (aquatic) and 1 – 8 (terrestrial). The BCF - logKow relationship applies generally to neutral organic substances which are not easily biotransformed (EC, 2003, part III, p. 41). Therefore no valid QSAR calculation for aquatic and terrestrial bioconcentration can be made "RP 3:2". 2-hydroxypropylamine: not expected to be bioaccumulative based on a low log Kow value of -0.96 and a predicted BCF of 3.16 L/kg_{ww}
Depration time (DT_{50}) (DT_{90})	-
Level of metabolites (%) in organisms accounting for > 10 % of residues	-

APPENDIX II: LIST OF INTENDED USES

PT2

Generally, the biocidal product (a.s. as manufactured) and other substances can be added by downstream users to base oils to get concentrates, which can be used to prepare a metal working fluid. The biocidal product containing the active substance "RP 3:2" is applied as preservative for water based metal working fluids. In addition, the biocidal product can be used within formulations as system cleaner of metal working systems. This application can be actually assigned to product type 2 as it is considered to be the disinfection of the inner surface of vessels and tubes.

System cleaner formulations may contain emulsifiers, surfactants and biocidal active substances. The intention of the application of the product is to clean the system at areas that are difficult to access, such as vessels, pipes, filters, etc. which cannot be reached by standard cleaning operations, before new metal working fluids will be inserted in the single or the central system. The system cleaner will be added to the used metalworking fluid 6h -24h before the exchange of the complete liquid. In order to achieve sufficient cleaning and sanitizing efficiency a contact time of at least 6-24 hours is typically recommended for such systems cleaners. After the residence time, the used metal working fluid containing system cleaner will be dumped and the system will be rinsed with additional water.

By this treatment it is guaranteed that even the dead spaces of the tank and tubing system of the machines are cleaned and sanitized and the risk of an immediate microbial recontamination by remaining biofilms after refilling with fresh metalworking fluid is eliminated.

Table 3-1: Acceptable intended uses of the disinfectant system cleaner

PT		PT2 Private area and public health area disinfectant and other biocidal products
Formu-lation	**Type**	Liquid
	Conc. of a.s. in b.p.	10 %w/w a.s.
Field of use envisaged		Disinfectant system cleaner for metal working: disinfection of inner surfaces of vessels and tubes
User		Professional and industrial users
Target Organisms		gram negative bacteria such as *P. putida, E. coli* gram positive bacteria such as *Staphylococcus aureus* and *Mycobacterium immunogenum,* yeasts such as *Candida albicans* fungi such as *Fusarium oxysporum.*
Likely amount at which the a.s. will be used (all fields of use	**Method of application**	The biocidal product is applied to system cleaners
	Applied amount of product	Product containing 0.25% (=2500 ppm) up to 2% (20000 ppm) of the active substance depending on the duration of the disinfectant cleaning process
	Application rate of a.s.	n.a.
	Number of treatments per year	n.a.
	Typical size of application area	n.a.
Limitations		-

PT6

The product is intended to be incorporated by industrial users into fuels to act as a preservative. The biocidal product is incorporated into fuels during the formulation process.

The evaluated use of the preserved fuel is used by professional and non-professionals/general public during the refuel of engines. No other matrices than fuels are covered by this evaluation.

Table 3-2: Acceptable intended uses of the in-can preservative

PT		PT6 In-can preservative
Formulation	**Type**	Liquid: a.s. as manufactured
	Conc. of a.s. in b.p.	100%w/w a.s.
Field of use envisaged		The preservative is added automatically during the formulation of Diesels fuels.
User		Professional
Target Organisms		gram-negative bacteria such as *Pseudomonas aeruginosa, Enterobacter aerogenes* and *Acinetobacter spec.*
Likely amount at which the a.s. will be used (all fields of	**Method of application**	The preservative is added during the formulation of fuels.
	Applied amount of product	0.005 – 0.04% (0.1% if fuel is contaminated)
	Application rate of a.s.	0.005 – 0.04% (0.1% if fuel is contaminated) b.p. is added directly to fuels
	Number of treatments per year	n.a.
	Typical size of application area	n.a.
Limitations		Formulation of Diesel fuels: Formulation is performed in closed systems and high degree of automation (low potential of contact e.g. manual sampling and negligible emission to the environment) Presence of LEV (Local exhaust ventilation) and use of PPE like gloves, if exposure is likely.

PT11

Generally, the biocidal product (a.s. as manufactured) can be used directly for preservation of liquid cooling systems. For this application the biocidal product is applied as manufactured, i.e. it is mixed into the process solutions by the applicants.

Three types of cooling systems are distinguished: once-through cooling, open recirculating cooling systems, and closed recirculating cooling systems. The biocidal products containing "RP 3:2" are used only in closed systems. They are not intended to be applied in once-through cooling systems or large open recirculating cooling systems. Therefore, in the following the closed recirculating cooling system will be considered for release estimation as representative application in product type 11.

In closed recirculating cooling water systems cooling water recirculates in a closed loop. The cooling water is not discharged after cooling. These systems have minimal loss of water, since there is no direct contact with the atmosphere. Process heat is transferred to the cooling water in one heat exchanger, and in a second heat exchanger the cooling water is cooled of by air or water. The cooled water is then returned to the heat exchanger that cools the process.

Table 3-3: Acceptable intended uses preservative for closed recirculating cooling water systems

PT		PT11 Preservatives for liquid-cooling and processing systems
Formu-lation	**Type**	Liquid
	Conc. of a.s. in b.p.	100 %
Field of use envisaged		Used as preservative only for closed recirculating cooling water systems
User		Professional and industrial users
Target Organisms		Gram-negative bacteria such as *Pseudomonas putida, Proteus sp*. and *Legionella pneumophila*
Likely amount at which the a.s. will be used (all	**Method of application**	a.s. is mixed into the process solutions by the user
	Applied amount of product	250 ppm biocidal product (concentration of a.s. in cooling water)
	Application rate of a.s.	n.a.
	Number of treatments per year	n.a.
	Typical size of application area	n.a.
Limitations		only for closed recirculating cooling water systems

PT12

Generally, biocidal products containing "RP 3:2" can be used directly for the prevention or control of slime growth on materials, equipment and structures in industrial processes. The biocidal products (a.s. as manufactured) are mainly applied as slimicide in the oil industry (offshore) for the preservation of drilling muds.

The presence of microorganisms in drilling mud causes slime formation, which may lead to clogged filters. Drilling mud is pumped down in the drilling tube and comes to the surface again between the tube and the drilling hole. Drilling mud functions are lubricant for the drill head and transport of the cuttings to the surface. Drilling mud also provides the hydro-static pressure that prevents collapse of the drilling hole.

The biocidal product is directly added to the mud without previous formulation steps.

In oil production processes the mud, composing of water, clay and additives is pumped down into the drilling hole to lubricate the drill head and to transport the cuttings out of the drilling hole to the surface. Due to the presence of microorganism in the mud slime formation occurs, which can lead to clogged filters.

Table 3-4: Acceptable intended uses of the slimicide

PT		PT12 slimicide
Formulation	**Type**	Liquid: a.s. as manufactured
	Conc. of a.s. in b.p.	100%w/w a.s.
Field of use envisaged		Treatment of oil-drilling muds
User		professionals
Target Organisms		sessile general heterotrophic bacteria (GHB), acid-producing general heterotrophic bacteria (APB) and sulphate reducing bacteria (SRB)
Likely amount at which the a.s. will be used (all	**Method of application**	injection
	Applied amount of product	800 ppm up to 1500ppm
	Application rate of a.s.	800 ppm up to 1500ppm
	Number of treatments per year	n.a.
	Typical size of application area	n.a.
Limitations		-

PT13

Generally, the biocidal product (a.s. as manufactured) and other substances can be added by downstream users to base oils to get concentrates, which can be used to prepare a metal working fluid. However, the applicants are only the manufacturers of the biocidal products, not of the concentrates for metal working fluids. As this formulation step is done by downstream industry, the applicants have only limited information. Nevertheless, some general assumption can be made which might fulfil the requirements for exposure information.

Biocidal products containing the active substance "RP 3:2" are applied as preservative for water based metal working fluids, only when directly dosed into the metal working system. In general, these metal working fluids can be divided in two application fields, emulsifiable and water soluble metal working fluids. In addition, the biocidal products can be used within formulations as system cleaner of metal working systems. This application can be actually assigned to product type 2. However, the application is in the field of metal working industry, and thus, the exposure to workers and the emission to the environment during application of the system cleaner are nearly identical with the application in PT13.

In the present document for active substance evaluation, the estimation of the exposure and emissions is restricted to the exemplary use as preservative in emulsifiable metal working fluids.

Table 3-5 Acceptable intended use of preservative for working or cutting fluids

PT		PT13 Working or cutting fluid preservatives
Formu-lation	**Type**	Liquid
	Conc. of a.s. in b.p.	100%
Field of use envisaged		1. Use in lubricant concentrate 2. Ready to Use concentration in water based emulsifiable metalworking fluids
User		Professional and industrial users
Target Organisms		gram-negative bacteria such as *Pseudomonas spec.* gram-positive bacteria such as *Bacillus spec.* and *Mycobacterium sp.* yeasts such as *Candida albicans and Rhodotorula mucilaginosa (rubra)* fungi such as *Fusarium oxysporum*
Likely amount at which the a.s. will be used (all fields of use envisaged)	**Method of application**	Direct application to the metal working fluid or application to a metal working fluid concentrate
	Applied amount of product	1. Use in lubricant concentrate: typically 3% w/w a.s. 2. Use concentration in metalworking fluid: typically 0.15% w/w a.s.
	Application rate of a.s.	1. Use in lubricant concentrate: typically 3% w/w a.s. 2. Use concentration in metalworking fluid: typically 0.15% w/w a.s.
	Number of treatments per year	Regularly or occasionally re-dosed if a.s. is below effective concentration of 0.15% w/w
	Typical size of application area	n.a
Limitations		• The applied risk management measures preventing inhalation exposure of men during the covered formulation processes must be efficient enough to reduce the "RP 3:2" concentration in air to concentrations below 0.75 mg/m^3 (AEC) and formaldehyde concentrations in air to concentrations below 0.12 mg/m^3 (AEC), respectively. • The use of prepared metal working fluids is limited to closed or at least partially closed chamber systems and presence of LEV. • The lubricant concentrate shall only be applied in such a rate to the MWF in use that the final concentration shall reach 0.1% w/w to 0.15% w/w

REMARK: With the use of "RP 3:2" it is intended to prevent the growth of gram-positive and gram-negative bacteria, yeasts and moulds in water miscible metal working fluids (MWF). The concentration of "RP 3:2" should be kept at 0.15% w/w (e.g. by regularly adding the biocidal product (PT13) to the metal working fluid (MWF) in use). It is noted that only a concentration of 10% w/w lubricant concentrate (containing 1.5% w/w of the product) in water will lead directly to a "RP 3:2" concentration of 0.15% w/w in the ready to use dilution of the MWF.

Dilutions of e.g. 2% w/w lubricant concentrate (containing 1.5% w/w of the product) in water (regularly used in grinding processes) will only lead to a “RP 3:2” -concentration of 0.03% w/w, whereas dilutions of e.g. 5% lubricant concentrate (containing 1.5% w/w of the product) in water (sometimes used in drilling or sawing processes) will lead to a “RP 3:2” -concentration up to 0.075% w/w. The correct dilution range should be stated in the product information or in the material safety data sheet of the lubricant concentrate (e.g. recommended dilutions 9% w/w to 12% w/w for a lubricant concentrate containing 1.5 % w/w of the product).

The use in MWF is only substantiated when “RP 3:2” is directly dosed into the metal working system, not in the concentrated MWF.

APPENDIX III: LIST OF STUDIES

Data protection is claimed by the applicant in accordance with Article 12.1(c) (i) and (ii) of Council Directive 98/8/EC for all study reports marked "Y" in the "Data Protection Claimed" column of the table below. For studies marked Yes(i) data protection is claimed under Article 12.1(c) (i), for studies marked Yes(ii) data protection is claimed under Article 12.1(c) (ii). These claims are based on information from the applicant. It is assumed that the relevant studies are not already protected in any other Member State of the European Union under existing national rules relating to biocidal products. It was however not possible to confirm the accuracy of this information.

LIST OF STUDIES FOR THE ACTIVE SUBSTANCE – SORTED BY SECTION NUMBER

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A2.6/01	2007	Contram MBO - Method of manufacture of the active substance [redacted] 15.11.2007 GLP not applicable, unpublished	Y	[redacted]
A2.6/02	2007	Manufacture of GrotaMar 71 [redacted], unpublished	Y	[redacted]
A2.7/01	2007	Purchased material specifications sheet, Product: Contram MBO/BC6120. [redacted] unpublished	Y	[redacted]
A2.7/02	2007	Release specification of GrotaMar 71. [redacted], unpublished	Y	[redacted]
A2.7/03	2007	Determination of the Formaldehyde content of different batches CONTRAM™ MBO: Oxazolidine, 3,3`-methylenebis[5-methyloxazolidine], (CAS# 66204-44-2) [redacted], unpublished	Y	[redacted]
A2.7/04	2007	Formaldehyde content of different batches of GrotaMar 71	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted], unpublished		
A2.7/05	2004	Spektroskopische Untersuchungen zum Produktvergleich Contram MBO/ GrotaMar 71 [redacted] unpublished	Y	[redacted]
A2.7/06	2005	13C NMR-Untersuchungen zum Produktvergleich II GrotaMar 71/Contram MBO [redacted], unpublished	Y	[redacted]
A2.7/07	2008	Hydrolysis of the equilibrium mixture of hexahydro-1,3,5-tris(2.hydroxypropyl)-s-triazine and N,N-methylene-bis-(5-methyloxazolidine) [redacted], unpublished	Y	[redacted]
A2.10_01	2007a	Medical statement for formaldehyde-releasing active ingredients GPL not applicable, unpublished	Y	[redacted]
A2.10_01	2007b	Statement of compliance to all maximum permissible workplace exposures GPL not applicable, unpublished	Y	[redacted]
A2.10_01	2007	Medical statement for Formaldehyde-releasing active ingredients GPL not applicable, unpublished	Y	[redacted]
A2.10/02	2007	Estimation of the Environmental Concentrations and the Preliminary Environmental Risk Assessment of "reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" (MBO)" for life-cycle step production at [redacted], unpublished	Y	[redacted]
A2.10/02	2007	Determination of total aldehyde in the waste water stream [redacted]	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted] unpublished		
A2.10/03	2007	Estimation of the Environmental Concentrations and the Preliminary Environmental Risk Assessment of "reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" (MBO)" for life-cycle step production at [redacted], unpublished	Y	[redacted]
A3.1.1/01	2001	Determination of the Melting Temperature / Freezing Temperature of 3,3'-Methylen-bis(5-methyloxazolidine) according to EC Council Directive 92/69/EEC, A.1. and OECD Guideline No. 102. [redacted] unpublished	Y	[redacted]
A3.1.1/02	2001	Melting Point of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.1.2/01	2001	Determination of the Boiling Temperature of 3,3'-Methylen-bis(5-methyloxazolidine) according to EC Council Directive 92/69/EEC, A.2. and OECD Guideline No. 103. [redacted] unpublished	Y	[redacted]
A3.1.2/02	2000	Boiling temperature of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.1.3/01	2000	Relative Density of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.1.3/02	2007	Determination of the Density of CONTRAM™ MBO. [redacted], unpublished	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A3.2/01	2000	Vapour Pressure of GrotaMAR 71 [redacted] unpublished	Y	[redacted]
A3.2/02	2001	3,3'-Methylen-bis(5-methyloxazolidin), 24773, Vapour Pressure. [redacted] unpublished	Y	[redacted]
A3.2/03	2005	EPIWIN 3.12 estimation for 3,3'-Methylene-bis [5-methyl-oxazolidine] GLP not applicable, published	N	Not applicable
A3.2.1	2005	EPIWIN 3.12 estimation for 3,3'-Methylene-bis [5-methyl-oxazolidine] GLP not applicable, published	N	Not applicable
A3.4/01 IR	2007	Determination of the Infrared (IR) Spectrum of CONTRAM™ MBO. [redacted] unpublished	Y	[redacted]
A3.4/02 IR	2007	IR-Spectrum of Grotan OX [redacted] unpublished	Y	[redacted]
A3.4/03 MS	2007	Mass spectrum of Contram MBO [redacted] unpublished	Y	[redacted]
A3.4/01 NMR	2004	Spektroskopische Untersuchungen zum Produktvergleich Contram MBO/ GrotaMar 71 [redacted] unpublished	Y	[redacted]
A3.4/02 NMR/MS	2002	Analysenbericht SMN9701, Formaldehyd/Aminopropanol Kondensate – Aufkärung der Struktur. [redacted] unpublished	Y	[redacted]
A3.4/01 UV/VIS	2007	UV Spectrum of CONTRAM™ MBO Oxazolidine, 3,3'-Methylenebis [5-methyl]- (CAS# 66204-44-2) [redacted] unpublished	Y	[redacted]
A3.4/ 02 UV/VIS	2007	UV/VIS Scan of GrotaMar 71 [redacted]	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted] unpublished		
A3.5/01	2002	Determination of the Water Solubility of 3,3'-Methylen-bis-[5-methyl-oxazolidine] according to OECD Test Guideline 105, flask method. [redacted] unpublished	Y	[redacted]
A3.5/02	2000	Water Solubility of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.7/01	2001	Fat Solubility of GrotaMAR 71. [redacted] Oct. 15, 2001 GLP, unpublished	Y	[redacted]
A3.7/02	2007	Solubility of CONTRAM™ MBO Oxazolidine, 3,3'-Methylenebis [5-methyl]- (CAS# 66204-44-2) in Various Organic Solvents. [redacted] unpublished	Y	[redacted]
A3.7/03	2006	Determination of the Solubility Range of CONTRAM™ MBO: Oxazolidine, 3,3'-methylenebis [5-methyl-], (CAS# 66204-44-2)) in n-Heptane Using a Turbidimetric Method. [redacted], unpublished	Y	[redacted]
A3.9/01	2001	Partition Co-Efficient (n-Octanol/Water) of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.9/02	2002	Partition Coefficient (n-Octanol/Water) of GrotaMAR 71 [redacted] unpublished	Y	[redacted]
A3.9/03	2002	Determination of the Partition Coefficient n-octanol/water of 3,3'-Methylen-bis-[5-methyl-oxazolidine] according to OECD Test Guideline 117 [redacted] unpublished	Y	[redacted]
A3.10/01	2003	Thermische Stabilität von MAR 71: [redacted], unpublished	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A3.10/02	2007	Safety-related evaluation of the thermal stability of "CONTRAM(TM) MBO BC 6120 / 100495595". [redacted] unpublished	Y	[redacted]
A3.11/01	2000	Flammability of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.11/02	2001	Auto-Ignition Temperature of GrotaMAR 71. [redacted], unpublished	Y	[redacted]
A3.12	2000	Flash Point of GrotaMAR 71. [redacted] unpublished	Y	[redacted]
A3.13	2007	Grotan OX, Surface Tension A.5. (OECD 115). [redacted] unpublished	Y	[redacted]
A3.14	2007	Viscosity of Grotan OX [redacted], unpublished	Y	[redacted]
A3.16	2000	Oxidation Property of GrotaMAR 71 [redacted], unpublished	Y	[redacted]
A3.17	2007	Reactivity towards container material: CONTRAM™ MBO. [redacted], unpublished	Y	[redacted]
A4.1/02	2007	Analytical method of determination the content of releasable formaldehyde of GrotaMar 71 [redacted] unpublished	Y	[redacted]
A4.2b	2008	Statement on the Vapour pressure of "3,3' methylenebis[5-methyloxazolidine] (MBO): reaction products from paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)". [redacted], unpublished	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.1.1/01	1977	Prüfung der akuten Toxizität von FO-I VP 1262, MK-ÄI2P an Ratten bei peroraler Verabreichung. [redacted] unpublished	Y	[redacted]
A6.1.1/02	1979	Prüfung der akuten Toxizität von N,N-Methylen-bis(5-methyloxazolidin) an Sprague-Dawley Ratten bei oraler Verabreichung. [redacted], unpublished	Y	[redacted]
A6.1.1/03	2002	Acute toxicity study of 3,3'-methylenebis[5-methyl- oxazolidine] by oral administration to Sprague-Dawley rats. [redacted] unpublished	Y	[redacted]
A6.1.2/01	1977	Prüfung der akuten dermalen Toxizität von FO-I VP 1262, MK-ÄI2P – kurz „FO-I VP 1262“ genannt - an der intakten und skarifizierten Rückenhaut von Sprague-Dawley Ratten. [redacted], unpublished	Y	[redacted]
A6.1.2/02	2000	Acute dermal toxicity of GrotaMAR 71 in rats. [redacted], unpublished	Y	[redacted]
A6.1.2/03	2002	Acute toxicity study of 3,3'-methylenebis[5-methyl- oxazolidine] in Sprague-Dawley rats by dermal administration. [redacted] unpublished	Y	[redacted]
A6.1.4/01	1976	Test of the local and general tolerability of N,N-Methylene-bis(5-methyloxazolidine) in NZW rabbits (Patch test). [redacted], unpublished	Y	[redacted]
A6.1.4/02	1979	Grotan OX, irritation studies in the rabbit (Part A, Draize skin irritation test).	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted] unpublished		[redacted]
A6.1.4/03	2002	3,3'-methylenebisoxazolidin/CAS-Nr. 66204-44-2. Primary skin irritation study in the rabbit. [redacted], unpublished	Y	[redacted]
A6.1.4/04	1979	Grotan OX, irritation studies in the rabbit (Part B, Modiefied Draize eye irritation test). [redacted] unpublished	Y	[redacted]
A6.1.4/05	1978	Draize eye test on ABt. FO-IL VP 1262. [redacted], unpublished	Y	[redacted]
A6.1.5/01	2001	OS157339, Skin sensitisation to the guinea-pig (Magnusson & Kligman method). [redacted] unpublished	Y	[redacted]
A6.1.5/02	2001	Skin sensitisation study of Grotamar71 in guinea pigs (guinea pig maximisation test). [redacted] unpublished	Y	[redacted]
A6.1.5/03	1984	Guinea pig maximation tests with formaldehyde releasers. Results from two laboratories. Contact Dermatitis, 10: 257-266 Non-GLP, published	No	-
A6.3.1/01	2001	Repeated dose 90-day oral toxicity study of Grotamar71 in rats. [redacted] unpublished	Y	[redacted]
A6.3.1/02	2002	4-Week dose-range finding study for a 90-Day subchronic toxicity study of 3,3'-methylenebis[5-methyl- oxazolidine] by repeated oral administration to Sprague-Dawley rats. [redacted] unpublished	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.4.1/01	2001	Repeated dose 90-day oral toxicity study of Grotamar71 in rats. [redacted], unpublished	Y	[redacted]
A6.4.1/02	2002	90-Day subchronic toxicity study of 3,3'-methylenebis[5-methyl-oxazolidine] by repeated oral administration to Sprague-Dawley rats. [redacted] unpublished	Y	[redacted]
A6.6.1/01	1997	*Salmonella typhimurium* reverse mutation test with MAR 71, [redacted] unpublished	Y	[redacted]
A6.6.1/02	2000	*Salmonella typhimurium* reverse mutation assay of Grotamar 71. [redacted] unpublished	Y	[redacted]
A6.6.1/03	2000	OS157339: Reverse mutation assay "Ames test" using *Salmonella typhimurium* and *Escherichia coli*. [redacted], unpublished	Y	[redacted]
A6.6.2	2001	OS157339: Chromosome aberration test in CHL cells in vitro. [redacted], unpublished	Y	[redacted]
A6.6.3/01	2002	Grotamar71: L5178Y TK+/- mouse lymphoma assay. [redacted], unpublished	Y	[redacted]
A6.6.3/02	2001	OS157339: L5178 TK+/- mouse lymphoma assay. [redacted], unpublished	Y	[redacted]
A6.6.4/01	2000	Chromosomal aberration study of Grotamr71 in mice. [redacted] unpublished	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A6.6.4/02	2002	Micronucleus test of 3,3'-methylenebis[5-methyl- oxazolidine] in bone marrow of the NMRI mouse by oral administration. [redacted], unpublished	Y	[redacted]
A6.8.1	2006	Prenatal developmental toxicity study of N,N'-methylene-bis(5-methyloxazolidine) MBO in rabbits by oral administration. [redacted] unpublished	Y (Exist./First	[redacted]
A6.8.2	2007	N,N'-Methylene-bis-oxazolidine (MBO): Preliminary Reproduction Toxicity Study in the Han Wistar Rat. Study Plan. [redacted], unpublished	Y	[redacted]
A6.12/01	1997	Kontaktallergien durch formaldehydab-spaltende Biozide. Allergologie, 20: 215-224 Non-GLP, published	No	-
A6.12/02	1998	Patch testing with preservatives, antimicrobials and industrial biocides. Results from a multicentre study. Brit J Dermatol, 138: 467-476 Non-GLP, published	No	-
A6.12/03	2002	Patch test reactions to Biobans in metal workers are often weak and not reproducible. Contact Dermatitis, 47: 27-31 Non-GLP, published	No	-
A7.1.1.1.1	2008	Hydrolysis of the equilibrium mixture of hexahydro-1,3,5-tris(2.hydroxypropyl)-s-triazine and N,N-methylene-bis-(5-methyloxazolidine) [redacted], unpublished	Y	[redacted]
A7.1.1.2.1/01	2002	Study on the "Ready Biodegradability" of "3,3'-Methylenbis(5-methyloxazolidin)" according to OECD-Test Guideline 301D in the version of July 17th, 1992 (Closed-Bottle-Test). [redacted], unpublished	Y	[redacted]
A7.1.1.2.1/02	2001	Ready Biodegradability of Grota MAR 71.	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted] unpublished		[redacted]
A7.1.1.2.1/03	2017	Biodegradability in the CO_2 Evolution Test according to OECD 301B, [redacted] unpublished	Y	[redacted]
A7.1.1.2.3	1996	A Study of the Aerobic Biodegradation in Seawater of MAR 71 using the Closed Bottle Procedure. [redacted] unpublished	Y	[redacted]
A7.1.3	2002	Estimation of the Adsorption Coefficient of 3,3'-Methylen-bis-[5-methyl-oxazolidine] according to Draft OECD Test Guideline 121. [redacted], unpublished	Y	[redacted]
A7.3.1	2005	EPIWIN 3.12 estimation for 3,3'-Methylene-bis [5-methyl-oxazolidine] No GLP, published	N	Not applicable
A7.4.1.1/01	1995	Acute Toxicity Testing of MAR 71 in Zebra-fish (*Brachydanio rerio*) (Teleostei, Cyprinidae) under Semi-static Conditions. [redacted], unpublished	Y	[redacted]
A7.4.1.1/02	2000	Study on the Acute Toxicity Towards Fish of "3,3'- Methylene-bis [5-methyl-oxazolidine]" according to OECD-Test Guideline 203, Edition dated July 17th, 1992. [redacted] unpublished	Y	[redacted]
A7.4.1.1/03	1997	Assessment of the aquatic-phase toxicity of MAR 71 to the marine fish *Scopthalmus maximus*. [redacted], unpublished	Y	[redacted]
A7.4.1.2/01	2000	Study on the Acute Toxicity towards Daphnia of "3,3'- Methylene-bis [5-methyl-oxazolidine]" according to OECD-Test Guideline 202, Part I ("Daphnia sp., Acute Immobilisation Test"). [redacted]	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted], unpublished		
A7.4.1.2/02	1995	Assessment of Toxic Effects of MAR 71 on *Daphnia magna* Using the 48 h Acute Immobilisation Test. [redacted], unpublished	Y	[redacted]
A7.4.1.2/03	1995	The Acute Toxicity of MAR 71 to the Marine Invertebrate *Acartia tonsa*. [redacted], unpublished	Y	[redacted]
A7.4.1.3/01	2000	Study on the toxicity towards algae of "3,3'-Methylene-bis [5-methyl-oxazolidine]" according to OECD-Test Guideline 201 ("Alga, Growth Inhibition Test"). [redacted] unpublished	Y	[redacted]
A7.4.1.3/02	1995	Testing of Toxic Effects of MAR 71 on the Single Cell Green Alga *Scenedesmus subspicatus*. [redacted], unpublished	Y	[redacted]
A7.4.1.3/03	1995	The Acute Toxicity of MAR 71 to the Marine Alga *Skeletonema costatum*. Acer [redacted], unpublished	Y	[redacted]
A7.4.1.4/01	1999	Determination of Acute Toxicity of Products towards Bacteria. [redacted] unpublished	Y	[redacted]
A7.4.1.4/02	1992	Untersuchung zur Klärschlamm-Toxizität von MAR 71 nach OECD 209 ("Activated sludge, Respiration Inhibition Test"). [redacted] unpublished	Y	[redacted]
A7.4.1.4/03	2001	Activated Sludge, Respiration Inhibition Test of Grota MAR 71. [redacted], unpublished	Y	[redacted]
A7.4.3.4	2007	Study on the Chronic Toxicity towards Daphnia of „Reaction Productsof Para-formaldehyde with 2-Hydroxypropylamin	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		(Relation 3:2)" according OECD-Guideline No. 211 (*Daphnia magna* Reproduction Test). [redacted], unpublished		[redacted]
A7.4.1.1/01-HPT	2002	Study on the Acute Toxicity towards Fish of "Contram 121" according to OECD-Test Guideline 203, Edition dated July 17th, 1992. [redacted], unpublished	Y	[redacted]
A7.4.1.1/02-HPT	2000	Acute Toxicity Study of Grotan WS in Rainbow trout, *Salmo gairdneri gairdneri*. [redacted], unpublished	Y	[redacted]
A7.4.1.2/01-HPT	2002	Study on the Acute Toxicity towards Daphnia of "Contram 121" according to OECD-Test Guideline 202, Part I (1984). [redacted], unpublished	Y	[redacted]
A7.4.1.2/02-HPT	2001	48 h EC50 Acute Immobilisation Study of Grotan WS in Daphnia magna. [redacted], unpublished	Y	[redacted]
A7.4.1.3/01-HPT	2002	Study on the Toxicity towards Algae of "Contram 121" according to OECD-Test Guideline 201 (Alga, Growth Inhibition Test), Version dated 07-Jun-84. [redacted] unpublished	Y	[redacted]
A7.4.1.3/02-HPT	2001	Alga (*Selenastrum capricornutum*) Growth Inhibition Test with Grotan WS. [redacted], unpublished	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
A7.10.2	2016	Determination of the Formaldehyde content in different samples from used emulsions of CONTRAM™ MBO during treatment. Profliud GmbH, Sponsor: [redacted], unpublished	Y	[redacted]

LIST OF STUDIES FOR THE ACTIVE SUBSTANCE – ADDITIONAL REFERENCES INTEGRATED BY eCA

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
Doc. II-A	Schuurmann, G., R. Ebert and R. Kuhne. 2006.	2006	Prediction of the sorption of organic compounds into soil organic matter from molecular structure. Environ. Sci. Technol. 40:7005-7011	N	-
Doc. II-A	Environment & Health Canada	2008	Screening Assessment for the Challenge Thiourea http://www.ec.gc.ca/ese-ees/CE2D78C6-9635-494E-9513-17D5D0C0223D/batch2_62-56-6_en.pdf 2013-12-12	N	-
Doc. II-A	ECHA	2012	Guidance on information requirements and chemical safety assessment Chapter R.7c: Endpoint specific guidance, http://echa.europa.eu/documents/10162/13632 /information_requirements_r7c_en.pdf, 2013-10-24	N	-
Doc. II-A	ECHA	2012, 2014, 2016	Guidance on information requirements and chemical safety assessment Chapter R.7b: Endpoint specific guidance http://echa.europa.eu/documents/10162/13632/information_requirements_r7b_en.pdf, 2014-01-29	N	-
Doc-I, Doc. II-B, Doc. II-C	ECHA	2015a	Refinement of the Emission Scenario Document for Product Type 13, May 2015, European Chemicals Agency, Reference: ECHA-15-B-11-EN, ISBN: 978-92-9247-412-6	N	-
Doc. I, Doc. II	ECHA	2015b	Guidance on the Biocidal Products Regulation Volume IV Environment - Part B Risk Assessment (active substances) Version 1.0 April 2015 Reference ECHA-15-G-01-EN, ISBN: 978-92-9247-093-7	N	-
Doc. I, Doc. II	Schweitzer M., Galler M	2015	DRAFT version v1, Revision of the Emission Scenario Document for In-can preservatives PT6 „Abschätzung der Umweltbelastung durch Konservierungsmittel: Fortentwicklung der Bewertungsmethodik" SCC Scientific Consulting Company, Bad Kreuznach, July 2015		
Doc. II	EC	2000	Technical Notes for Guidance on Data Requirements for Active Substances and Biocidal Products (in support of the Directive 98/8/EC concerning the Placing of Biocidal Products on the Market), Final Draft 2000	N	-
Doc. II	EC	2003	Technical Guidance Document on Risk Assessment in support of Directive 93/67/EEC on risk assessment for new	N	-

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			notified substances, Commission Regulation (EC) No. 1488/94 on risk assessment for existing substances (Parts I, II, III and IV) and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. European Commission 2003		
Doc. II-A	ECHA	2012b	Guidance on information requirements and chemical safety assessment Chapter R.7c: Endpoint specific guidance, http://echa.europa.eu/documents/10162/13632 /information_requirements_r7c_en.pdf, 2013-03-14	N	-
Doc. I, Doc. II-A	RAC	2015	Committee for Risk Assessment (RAC) Opinion proposing harmonised classification and labelling at EU level of Reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio 3:2); [MBO] CLH-O-0000001412-86-95/F https://echa.europa.eu/documents/10162/96051139-f376-4da3-b25a-130668d6db45	N	-
Doc. II-A	OECD	2002a	OECD SERIES ON TESTING AND ASSESSMENT Number 23: GUIDANCE DOCUMENT ON AQUATIC TOXICITY TESTING OF DIFFICULT SUBSTANCES AND MIXTURES. http://www.oecd-ilibrary.org/docserver/download/9750231e.pdf?expires=1385738495&id=id&accname=guest&checksum=90E189B53DA5CB93A8280F813D892394, 2013-11-8	N	-
Doc. II-A	OECD	2002b	Detailed Review Paper on Biodegradability Testing http://www.oecd-ilibrary.org/docserver/download/9750021e.pdf?expires=1488366358&id=id&accname=guest&checksum=DB88059B1F7F2F3837BA3B3E120733CF	N	-
Doc. II-A	Abeliovich A, Azov Y.	1976	Toxicity of ammonia to algae in sewage oxidation ponds. Appl Environ Microbiol. Jun;31(6):801–806	N	-
Doc. II-A	Strotmann et al.	2004	Development and Evaluation of an Online CO_2 Evolution Test and a Multicomponent Biodegradation Test System, Appl Environ Microbiol. 2004 Aug; 70(8): 4621–4628. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC492337/	N	
Doc. II-A	Pedersen et al.	1995	Environmental Hazard Classification – data collection and interpretation guide (2nd	N	-

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			edition), Nordic Council of Ministers, Copenhagen, ISBN 929120711X		
Doc. II-A	Lopez et al.	2015	Characterization of MIPA and DIPA aqueous solutions in relation to absorption, speciation and degradation Journal of Industrial and Engineering Chemistry 21 (2015) 428–435	N	-
Doc II-C	Eiroa, M., Kennes, C. and Veiga, M. C.	2004	Formaldehyde biodegradation and its inhibitory effect on nitrification. J. Chem. Technol. Biotechnol., 79: 499–504. doi:10.1002/jctb.1011	N	-
Doc. II-C	Eiroa et al.	2005	Biodegradation and effect of formaldehyde and phenol on the denitrification process Water Research, Volume 39, Issues 2–3, January–February 2005, Pages 449–455	N	-
Doc. II-C	IOGP	2016	Drilling waste management technology review. Report 557. 2016. http://www.iogp.org/pubs/557.pdf	N	-
Doc II-A, Doc III-A	Ratte, H. T.	1998	Influence of the growth pattern on the EC50 of Cell Number, Biomass Integral and Growth Rate in the Algae Growth Inhibition Test, Umweltbundesamt http://www.umweltbundesamt.de/publikationen/influence-of-growth-pattern-on-ec50-of-cell-number 20140314	N	-
Doc II-B	ECHA	2016	Technical Agreements for Biocides (TAB) version 1.1 http://echa.europa.eu/documents/10162/20733977/technical_agreements_for_biocides_en.pdf	N	-
Doc II-B	J.P.A. Lijzen and M.G.J. Rikken (eds.)	2004	EUSES Background report http://www.pbl.nl/sites/default/files/cms/publicaties/601900005.pdf	N	-
Doc II-B	M. Klein, Schmallenberg	2011	Proposal for standard scenarios and parameter setting of the FOCUS groundwater scenarios when used in biocide exposure assessment, Fraunhofer-Institut für Molekularbiologie und Angewandte Ökologie FKZ: 360 04 035	N	-
Doc II-B	RIVM	2004	Environmental Emission Scenarios Biocides: PT 6 – In-can Preservatives Reference 4L1784.A0/R018/FBA/TL/Nijm http://echa.europa.eu/documents/10162/16908203/pt6_in_can_preservatives_en.pdf	N	-
Doc II-B	Schweitzer M., Galler M.	2015	DRAFT version v1, Revision of the Emission Scenario Document for In-can preservatives PT6 „Abschätzung der Umweltbelastung	N	-

Section No / Reference No	Author(s)	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
			durch Konservierungsmittel: Fortentwicklung der Bewertungsmethodik"		
Doc II-B	European Chemicals Bureau	2002	European Union Risk Assessment Report, TERT-BUTYL METHYL ETHER http://www.efoa.eu/documents/document/20100715150023-mtbe_-_eu_risk_assessment_report_-_2002.pdf	N	-
Doc II-B	RIVM	2003	Harmonisation of Environmental Emission Scenarios for biocides used as preservatives for liquid cooling systems (product type 11) http://echa.europa.eu/documents/10162/16908203/pt11_preservatives_for_liquid_cooling_and_processing_systems_en.pdf	N	-
Doc II-B	EUBEES	2003	Harmonisation of Environmental Emission Scenarios Biocides: PT 12 – Slimicides Reference: 4L1784.A0/R0009/FBA/TL/Nijm https://echa.europa.eu/documents/10162/16908203/pt12_slimicides_en.pdf	N	-
Doc I, Doc II-B	UBA (Umweltbundes-amt Deutschland)	2016	Aggregated Environmental Exposure Assessment and Risk Characterisation of Biocidal Products. https://www.umweltbundesamt.de/publikationen/aggregated-environmental-exposure-assessment-risk	N	-
Doc I, Doc II-B	CEN	2009	EN 590, Automotive fuels - Diesel - Requirements and test methods. European Committee for Standardization. http://www.envirochem.hu/www.envirochem.hu/documents/EN_590_2009_hhV05.pdf	N	-
Doc I., Doc II-C	IOGP	2016	Drilling waste management technology review. Report 557. 2016. http://www.iogp.org/pubs/557.pdf	N	-

LIST OF STUDIES FOR THE BIOCIDAL PRODUCT – SORTED BY SECTION NUMBER

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B3.3	2000	Oxidation Property of GrotaMAR 71. [redacted] unpublished	Y (Exist./First)	[redacted]
B3.4	2000a	Flash Point of GrotaMAR 71 [redacted] unpublished	Y (Exist./First)	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B3.4	2000b	Flammability of GrotaMAR 71. [redacted] unpublished	Y (Exist./First)	[redacted]
B3.4	2001	Auto-Ignition Temperature of GrotaMAR 71. [redacted], unpublished	Y (Exist./First)	[redacted]
B3.5	2007a	Determination of the Alkalinity of CONTRAM™ MBO. [redacted], unpublished	Y (Exist./First)	[redacted]
B3.5	2007b	Determination of the pH-Value of CONTRAM™ MBO. [redacted], unpublished	Y (Exist./First)	[redacted]
B3.5 PT6, 11, 12 and 13	2007	pH value of GrotaMar 71 [redacted], unpublished	Y (Exist./First)	[redacted]
B3.6	2007	Determination of the Density of CONTRAM™ MBO. [redacted] unpublished	Y (Exist./First)	[redacted]
B3.6	2000	Relative Density of GrotaMAR 71. [redacted] unpublished	Y (Exist./First)	[redacted]
B3.7 PT6, 11, 12 and 13	2007	Stability of GrotaMar 71 [redacted], unpublished	Y (Exist./First)	[redacted]
B3.7	2007a	Safety-related evaluation of the thermal stability of "CONTRAM(TM) MBO BC 6120 / 100495595". [redacted], unpublished	Y (Exist./First)	[redacted]
B3.7	2007b	Reactivity towards container material: CONTRAM™ MBO. [redacted] unpublished	Y (Exist./First)	[redacted]
B3.10.1	2007	Grotan OX, Surface Tension A.5. (OECD 115).	Y (Exist./First)	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		[redacted], unpublished		
B3.10.2 PT2	2008	Viscosity of 10% GrotaMar 71 in water [redacted], unpublished	Y (Exist./First)	
B3.10.2 PT6, 11, 12 and 13	2007	Viscosity of Grotan OX [redacted], unpublished	Y (Exist./First)	
B4.1 PT2	2008	Analytical method of determination the content of releasable formaldehyde of 10% GrotaMar 71 in water. [redacted], unpublished	Y	
B5.10.2/01	2009	DIN EN 1040 (1997) Quantitative suspension test for the determination of bactericidal efficacy (basic test) of chemical disinfectants and antiseptics. [redacted] unpublished	Y	
B5.10.2/02	2009	DIN EN 1275 (1997): Quantitative suspension test for the determination of fungicidal or levurocidal efficacy (basic test) of chemical disinfectants and antiseptics, [redacted], unpublished	Y	
B5.10.2/03	2009	Microbiological efficacy of Reaction products from paraformaldehyde and 2 hydroxypropylamine (ration of 3:2). Minimal Inhibition Concentration (MIC), [redacted], unpublished	Y	
B5.10.2/05	2009	Microbiological efficacy of GrotaMar 71 challenge test in metal working fluid, [redacted], unpublished	Y	

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B5.10.2/06	2005	Efficacy of biocides against Mycobacterium immunogenum. [redacted] unpublished	Y	[redacted]
B5.10.2/07	2009	Bacteriostatic activities of the preservative CONTRAM MBO. Evaluation of the Minimal Inhibition Concentration (MIC) of biocides in accordance with the standard guidelines of the "Deutsche Gesellschaft für Hygiene und Mikrobiologie" (DGHM, 2001-09-01). [redacted] unpublished	Y	[redacted]
B5.10.2/08	2009	Fungistatic activities of the preservative CONTRAM MBO. Evaluation of the Minimal Inhibition Concentration (MIC) of biocides in accordance with the standard guidelines of the "Deutsche Gesellschaft für Hygiene und Mikrobiologie" (DGHM, 2001-09-01). [redacted], unpublished	Y	[redacted]
B5.10.2/09	2009	Antimicrobial effectiveness of the biocide CONTRAM MBO in a contaminated metal working fluid (MWF). [redacted] unpublished	Y	[redacted]
B5.10.2/12	2008	*Treatment of water-based metalworking fluids to prevent hypersensitivity pneumonitis associated with* Mycobacterium *spp.* Journal of Applied Microbiology 104 (2008), pp. 454-464	N	Not applicable
B5.10.2/013	2011	Laboratory report for [redacted]; Bacteriostatic and bactericidal concentrations of selected biocides. March 2011 Part I Bacteriostatic efficacy	Y	[redacted]
B5.10.2/014	2013	Laboratory report [redacted]; Comparative study of the biocide GROTAN OX. Part II Bactericidal assay	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B5.10.2/015	2015	Laboratory report [redacted] "Evaluation of the effect of one chemical on sessile sulphate-reducing bacteria and general heterotrophic bacteria	Y	[redacted]
B5.10.2/016	2001	Laboratory report for [redacted] "Bakterizide Wirkung von "Grotan® OX" gegen Legionella pneumophila nach prEN 13623:1999" 2001	Y	Schülke & [redacted]
B5.10.2/17	2009	Bacteriostatic activities of the preservative CONTRAM 121. Evaluation of the Minimal Inhibition Concentration (MIC) of biocides in accordance with the standard guidelines of the "Deutsche Gesellschaft für Hygiene und Mikrobiologie" (DGHM, 2001-09-01). [redacted], revised 16.09.2009.	Y	[redacted]
B6.6 PT11	2007	Development of standard scenarios for risk evaluation of cooling water Additives , International Journal for Electricity and Heat Generation (87), Issue 6/2007, Page 76-84	N	Not applicable
B6.6 PT11	2003	Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for biocides used as preservatives for liquid cooling systems (product type 11). Final Report, September 2003. Erratum from 26. April 2004 GLP not applicable, published	N	Not applicable
B6.6 PT11	2005	"Formaldehyde" in Ullmann`s encyclopedia of Industrial Chemistry, Wiley-VCH Verlag GmbH & Co. KGaA. Online Version GLP not applicable, published	N	Not applicable
B6.6 PT12	2004	CHARM - Chemical Hazard Assessment and Risk Management. For the use and discharge of chemicals used offshore. User Guide Version 1.4 dated 3 February 2005. CHARM Implementation Network, CIN 2004 (http://www.ogp.org.uk/pubs/CHARMManualFeb05.pdf) GLP not applicable, published	N	n.a.

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
B6.6 PT12	2008	Report- Estimation of wind speeds on offshore rigs in the North Sea; [redacted], unpublished	Y	[redacted]
B6.6 PT12	2003	Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for Slimicides (Product type 12). September 2003 GLP not applicable, published	N	Not applicable
B6.6 PT12	2005	"Formaldehyde" in Ullmann`s encyclopedia of Industrial Chemistry, Wiley-VCH Verlag GmbH & Co. KGaA. Online Version GLP not applicable, published	N	Not applicable
B6.6/02 PT13	2006	Metal-working fluids and other complex hydrocarbon-containing mixtures in work areas [Kühlschmierstoffe und sonstige komplexe kohlenwasserstoffhaltige Gemische in Arbeitsbereichen]. Gefahrst. Reinhalt. Luft 66(10), 399-405 GLP not applicable, published	N	n.a.
B6.6/02 PT13	1999	Measurement, assessment, and protective measures for handling of complex hydrocarbon mixtures [Messen, Beurteilen und Schutzmaßnahmen beim Umgang mit komplexen kohlenwasserstoffhaltigen Gemischen]. BIA-Report 5/99, 149p. GLP not applicable, published	N	n.a.
B6.6/02 PT13	2005	Lubricants and Lubrication. Ullmann´s Encyclopedia of Industrial Chemistry, Online version (Stand: 16.07.2007), Wiley-VCH Verlag GmbH &Co. KGaA, 205p GLP not applicable, published	N	n.a.
B6.6/02 PT13	2005	Ventilation requirements during work processes involving metal-working fluids [Lufttechnische Maßnahmen bei Tätigkeiten mit Kühlschmierstoffen]. German employers' liability insurance association for precision mechanics and electrical engineering [Berufsgenossenschaft der Feinmechanik und Elektrotechnik], 27p GLP not applicable, published	N	n.a.
B6.7.2 PT13	2007	Information for users of cooling lubricants - Formaldehyde depot substances and protection level classification according to	N	n.a.

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		the Ordinance on Hazardous Substances [Handlungshilfe für KSS-Anwender - Formaldehyd-Depotstoffe und Schutzstufenzuordnung nach Gefahrstoffverordnung Fachausschuss-Informationsblatt Nr. 029] GLP not applicable, published		
B7.1 PT2	2007	Estimation of the Environmental Concentrations and the Preliminary Environmental Risk Assessment of "reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" (MBO) applied as disinfectant in system cleaner (product type 2). [redacted], unpublished	Y	[redacted]
B7.1 PT2	2007	Formaldehyd-Gehalt bei der Aufbereitung von Kühlschmierstoffemulsionen. S [redacted] unpublished	Y	[redacted]
B7.1 PT6	2007	Estimation of the Environmental Concentrations and the Preliminary Environmental Risk Assessment of "reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" (MBO) applied as in-can preservative (product type 6). [redacted], unpublished	Y	[redacted]
B7.1 PT6	2001	Supplement to the methodology for risk evaluation of biocides. Emission Scenarios Document for Product Type 2: Private and public health area disinfectants and other biocidal products (sanitary and medical sector). RIVM report 601450008, P. van der Poel, March 2001 GLP not applicable, published	N	not applicable
B7.1 PT6	2004	Supplement to the methodology for risk evaluation of biocides - Environmental Emission Scenarios for biocides used as In-can Preservatives (product type 6). Final Report, January 2004	N	not applicable

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		GLP not applicable, published		
B7.1 PT11	2008	EUSES report for "Reaction products from paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" applied as preservative in product type 11 closed liquid cooling system. [redacted], unpublished	Y	[redacted]
B7.1 PT 11	2003	Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for biocides used as preservatives for liquid cooling systems (product type 11). Final Report, September 2003. Erratum from 26. April 2004 GLP not applicable, published	N	Not applicable
B7.1 PT 12	2004	CHARM - Chemical Hazard Assessment and Risk Management. For the use and discharge of chemicals used offshore. User Guide Version 1.4 dated 3 February 2005. CHARM Implementation Network, CIN 2004 (http://www.ogp.org.uk/pubs/CHARMManualFeb05.pdf) GLP not applicable, published	N	Not applicable
B7.1 PT12	2008	EUSES report for "Reaction products from paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)" applied in product type 12 as slimicide in drilling mud (offshore). [redacted], unpublished	Y	[redacted]
B7.1 PT 12	2003	Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for Slimicides (Product type 12). September 2003 GLP not applicable, published	N	Not applicable
B7.1 PT13	2007	Estimation of the Environmental Concentrations and the Preliminary Environmental Risk Assessment of "reaction products of paraformaldehyde and 2-hydroxypropylamine (ratio of 3:2)"	Y	[redacted]

Section No / Reference No	Year	Title. Source (where different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Yes/No)	Owner
		(MBO) applied as metalworking-fluid preservative (product type 13). [redacted]		
B7.1 PT13	2003	Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for biocides used as metalworking fluid preservatives (product type 13). Final Report, May 2003 GLP not applicable, published	N	not applicable
B7.1 PT13	2006	Formaldehyd-Gehalt bei der Aufbereitung von Kühlschmierstoffemulsionen. [redacted] unpublished	Y	[redacted]

APPENDIX IV-1: STANDARD TERMS AND ABBREVIATIONS

Note: The technical terms “active ingredient” and “active substance” are equivalent

Stand. Term / Abbreviation	Explanation
Ach	acetylcholine
AchE	acetylcholinesterase
ADI	acceptable daily intake
ADME	administration distribution metabolism and excretion
ADP	adenosine diphosphate
AE	acid equivalent
AEC	acceptable exposure concentration
AEL	acceptable exposure level
AF	assessment factor
AFID	alkali flame-ionisation detector or detection
A/G	albumin/globulin ratio
ai	active ingredient
as	active substance
ALT	alanine aminotransferase (SGPT)
Ann.	Annex
AOEL	acceptable operator exposure level
AMD	automatic multiple development
ANOVA	analysis of variance
AP	alkaline phosphatase
approx	approximate
ARC	anticipated residue contribution
ARfD	acute reference dose
as	active substance
AST	aspartate aminotransferase (SGOT)
ASV	air saturation value
ATP	adenosine triphosphate
BAF	bioaccumulation factor
BCF	bioconcentration factor
bfa	body fluid assay
BOD	biological oxygen demand
bp	boiling point
BP	Biocidal Product
BPD	Biocidal Products Directive

Stand. Term / Abbreviation	Explanation
BSP	bromosulfophthalein
BUN	blood urea nitrogen
bw	body weight
c	centi- (x 10^{-2})
°C	degrees Celsius (centigrade)
CAS	Chemical Abstracts Service
CEC	cation exchange capacity
cf	confer, compare to
CFU	colony forming units
ChE	cholinesterase
ChV	chronic value
CI	confidence interval
CL	confidence limits
cm	centimetre
CNS	central nervous system
COD	chemical oxygen demand
CPK	creatinine phosphatase
cv	coefficient of variation
CSF	Confidential Statement of Formula
Cv	ceiling value
d	day(s)
DIS	draft international standard *(ISO)*
DFR	Dislodgeable Foliar Residue
DMSO	dimethylsulfoxide
DNA	deoxyribonucleic acid
DO	dissolved oxygen
DOC	dissolved organic carbon
$DT_{50(lab)}$	period required for 50 percent dissipation (under laboratory conditions) (define method of estimation)
$DT_{90(field)}$	period required for 90 percent dissipation (under field conditions) (define method of estimation)
dw	dry weight
ε	decadic molar extinction coefficient

Stand. Term / Abbreviation	Explanation
E_bC_{50}	median effective concentration, biomass
E_rC_{50}	median effective concentration, growth rate
EC_{50}	median effective concentration
ECD	electron capture detector
ECOSAR	Ecological Structure Activity Relationships
eCA	Evaluating Competent Authority
ED_{50}	median effective dose
EDI	estimated daily intake
EEC	Estimated Environmental Concentration
EINECS	European inventory of existing commercial substances
ELINCS	European list of notified chemical substances
ELISA	enzyme linked immunosorbent assay
e-mail	electronic mail
EPA	U.S. Environmental Protection Agency
EPISUITE™	Estimation Program Interface Suite ™
EUSES	European Union system for the evaluation of substances
F_0	parental generation
F_1	filial generation, first
F_2	filial generation, second
FA	Formaldehyde
FIA	fluorescence immuno-assay
FID	flame ionisation detector
FOB	functional observation battery
f_{oc}	organic carbon factor (compartment dependent)
fp	freezing point
g	gram(s)
GC	gas chromatography

Stand. Term / Abbreviation	Explanation
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GEP	good experimental practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GPC	gel-permeation chromatography
GSH	glutathione
h	hour(s)
H	Henry's Law constant (calculated as a unitless value)
ha	hectare(s)
Hb	haemoglobin
HPA	2-Hydroxypropylamine
HPT	α, α′, α″-Trimethyl-1,3,5-triazine-1,3,5(2H,4H,6H)-triethanol
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HRGC	high resolution gas chromatography
Ht	haematocrit
IC_{50}	median immobilisation concentration or median inhibitory concentration 1
ID	ionisation detector

Stand. Term / Abbreviation	Explanation
ip	intraperitoneal
IR	infrared
iv	intravenous
k	rate constant for biodegradation
Ka	acid dissociation constant
Kb	base dissociation constant
K_{ads}	adsorption constant
K_{des}	apparent desorption coefficient
kg	kilogram
K_H	Henry´s Law constant (in atmosphere per cubic metre per mole)
K_{oc}	organic carbon adsorption coefficient
K_{om}	organic matter adsorption coefficient
K_{ow}	octanol-water partition coefficient
Kp	solid-water partition coefficient
kPa	kilopascal(s)
l, L	litre
LC	liquid chromatography
LC-MS	liquid chromatography- mass spectrometry
LC_{50}	lethal concentration, median
LCA	life cycle analysis
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
ln	natural logarithm
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LoA	Letter of Access
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level

Stand. Term / Abbreviation	Explanation
log	logarithm to the base 10
LOQ	limit of quantification (determination)
LSC	liquid scintillation counting or counter
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
µm	micrometer (micron)
MAC	maximum allowable concentration
MAK	maximum allowable concentration
MATC	Maximum Acceptable Toxicant Concentration
MBO	3, 3'-Methylenebis [5-methyloxazolidine]
MDL	method detection limit
µg	microgram
mg	milligram
MHC	moisture holding capacity
MIC	minimum inhibitory concentration
min	minute(s)
mL	millilitre
MLT	minimum lethal time
mm	millimetre
mo	month(s)
MOE	margin of exposure
mol	mole(s)
MOS	margin of safety
Mp	melting point
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MW	molecular weight
MWF	metal working fluid
n.a., N/A	not applicable

Stand. Term / Abbreviation	Explanation
nd	not detected
ng	nanogram
nm	nanometre
NMR	nuclear magnetic resonance
no, n°	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOE_rC	no observed effect concentration, growth rate
NOED	no observed effect dose
NOEL	no observed effect level
NR	not reported
OC	organic carbon content
OCR	Offshore chemicals regulation
OEL	occupational exposure limit
OH	hydroxide
OM	organic matter content
OPPTS	Office of Prevention, Pesticides and Toxic Substances
Pa	pascal
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PED	plasma-emissions-detector
pH	pH-value
pKa	negative logarithm (to the base 10) of the acid dissociation constant
pKb	negative logarithm (to the base 10) of the base dissociation constant

Stand. Term / Abbreviation	Explanation
PNEC	predicted no effect concentration (compartment to be added as subscript)
POP	persistent organic pollutants
ppb	parts per billion (10^{-9})
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PrT	prothrombin time
PT	product type
Q*1	The Carcinogenic Potential of a Compound, Quantified by the EPA's Cancer Risk Model
(Q)SAR	quantitative structure-activity relationship
r	correlation coefficient
r^2	coefficient of determination
RA	risk assessment
RIVM	The Dutch National Institute for Public Health and the Environment
RMM	Risk management measure
RfD	reference dose
RCR	Risk characterisation ratio
"RP 3:2"	Reaction products of para-formaldehyde and 2-hydroxy-propylamine (ratio 3:2)
"RP 1:1"	Reaction products of para-formaldehyde and 2-hydroxy-propylamine (ratio 1:1)
s	second
S	solubility
SAP	serum alkaline phosphatase
SAR	structure/activity relationship
SBLC	shallow bed liquid chromatography
sc	subcutaneous
sce	sister chromatid exchange
SCAS	semi-continous activated sludge
SD	standard deviation
se	standard error

Stand. Term / Abbreviation	Explanation
SF	safety factor
SIMS	secondary ion mass spectroscopy
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
ssp	subspecies
STP	sewage treatment plant
t	tonne(s) (metric ton)
$t_{½}$	half-life (define method of estimation)
T_3	tri-iodothyroxine
T_4	thyroxine
T_{25}	tumorigenic dose that causes tumours in 25 % of the test animals
TC	Toxic Concentration
TCD	thermal conductivity detector
TD	Toxic Dose
TDR	time domain reflectrometry
TG	technical guideline, technical group
TGD	Technical guidance document
TER_{LT}	toxicity exposure ratio following chronic exposure
tert	tertiary (in a chemical name)
TLC	thin layer chromatography
TNsG	technical notes for guidance
TOC	total organic carbon
TSH	thyroid stimulating hormone (thyrotropin)
TTC	Toxicological-Threshold-of-Concern
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
UV	ultraviolet
UVC	unknown or variable composition, complex reaction products
UVCB	undefined or variable composition, complex reaction products in biological material
v/v	volume ratio (volume per volume)
vis	visible
WBC	white blood cell
wt	weight
w/v	weight per volume
ww	wet weight
w/w	weight per weight
Yr	year
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to

APPENDIX IV-2: ABBREVIATIONS OF ORGANISATION AND PUBLICATIONS

Abbreviation	Explanation
ASTM	American Society for Testing and Materials
CA(S)	Chemical Abstracts (System)
CAS	Chemical Abstracts Service
CE	Council of Europe
CEC	Commission of the European Communities
DG	Directorate General
DIN	German Institute for Standardisation
EC	European Commission
ECHA	European Chemicals Agency
ECE	Economic Commission for Europe
ECETOC	European Chemical Industry Ecology and Toxicology Centre
EDEXIM	European Database on Export and Import of Dangerous Chemicals
EEC	European Economic Community
EHC	Environmental Health Criteria
EINECS	European Inventory of Existing Commercial Chemical Substances
EPA	Environmental Protection Agency
EU	European Union
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
IARC	International Agency for Research on Cancer
ISO	International Organization for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
NCI	National Cancer Institute (USA)
NCTR	National Center for Toxicological Research (USA)
NGO	non-governmental organisation
NTP	National Toxicology Program (USA)
OECD	Organization for Economic Co-operation and Development
SETAC	Society of Environmental Toxicology and Chemistry
WHO	World Health Organization

ANNEX V CONFIDENTIAL INFORMATION

[redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	
[redacted]	[redacted]

[redacted]

[redacted]

- [redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	
[redacted]	

[redacted]

- [redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]