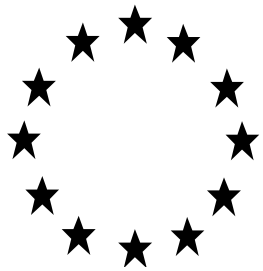
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



C(M)IT/MIT

Product-type 11
(Biocide for use as preservatives for liquid-cooling and processing systems)

May 2015

France

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1 STATEMENT OF SUBJECT MATTER AND PURPOSE

1.1 PRINCIPLE OF EVALUATION AND PROCEDURE FOLLOWED

This Competent Authority report has been established as a result of the evaluation of the active substance C(M)IT/MIT: 5-chloro-2-methylisothiazol-3(2H)-one (C(M)IT) and 2-methylisothiazol-3(2H)-one (MIT) in ratio (3:1), with CAS Nr. 26172-55-4 for C(M)IT, 2682-20-4 for MIT and 55965-84-9 for the mixture, as product-type 11 (preservatives for liquid-cooling and processing systems), carried out in the context of the work program 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[1], with the original view to the possible inclusion of this substance into Annex I or IA to that Directive, then carried out in the context of Regulation (EU) No 528/2012[2], with a view to the possible approval of this active substance

The evaluation has therefore been conducted 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 11 containing C(M)IT/MIT that will fulfil the requirements laid down in Article 5(1) b), c) and d) of that Directive.

C(M)IT/MIT was notified as an existing active substance, by Rohm and Haas Europe Trading ApS, now a subsidiary of The Dow Chemical Company (hereafter referenced as "Dow")" and Thor in product-type 11.

Data submitted were collected to compile a single dossier on the hazard assessment of the active substance. Therefore, there will be references to the data submitted by both manufacturers Dow and Thor in this report.

Commission Regulation (EC) N° 1451/2007 of the 4th of December 2007[3] 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 the Annex I or IA of the Directive.

In accordance with the provisions of Article 3 paragraph 2 of that Regulation, France was designated as Reporter Member State to carry out the assessment of C(M)IT/MIT on the basis of the dossier submitted by the applicant. The deadline for submission of a complete dossier for C(M)IT/MIT as an active substance in product-type 11 was the 31st of October 2008, in accordance with Article 9 paragraph 2 of Regulation (EC) N° 1451/2007.

On the 7th of October 2008, the French competent authority received a dossier from Dow. The Rapporter Member State accepted the dossier as complete for the purpose of the evaluation, taking into account the supported uses, and confirmed the acceptance of this dossier on the 8th of October 2009.

On the 29th of October 2008, the French competent authority received a dossier from Thor GmbH. The Rapporteur Member State accepted the dossier as complete for the purpose of

[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

[2] Regulation (EU n° 528/2012 of the European Parliament and of the council o 22 May 2012 concerning the making available on the market and use of biocidal products.

[3] Regulation EC n° 1451/2007 of december 2007 on the second phase of 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 biocidal products on the market OJ L 325, 11.12.2007, p. 3.

the evaluation, taking into account the supported uses, and confirmed the acceptance of the dossier on the 28th of April 2009.

On 22nd of April 2013, the Rapporteur Member State submitted to the Commission, the applicant and the others members states a copy of the evaluation report, hereafter referred to as the competent authority report (CAR).

In order to review the competent authority report and the comments received on it, consultations of technical experts from all Member States (peer review) were organised by the Agency. Revisions agreed upon were presented at the Biocidal Products Committee and its Working Groups meetings and the competent authority report was amended accordingly.

1.2 PURPOSE OF THE ASSESSMENT

The aim of the Competent Authority report is to support a decision on the approval of C(M)IT/MIT for product-type 11, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 11 that contain C(M)IT/MIT. 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). 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.

2 OVERALL SUMMARY AND CONCLUSIONS

2.1 PRESENTATION OF THE ACTIVE SUBSTANCE

2.1.1 Identity, Physico-Chemical properties & Methods of Analysis

2.1.1.1 Active substance

The active substance as manufactured is a mixture of 5-chloro-2-methylisothiazol-3(2H)-one (C(M)IT) and 2-methylisothiazol-3(2H)-one (MIT)[4] in ratio (3:1), with CAS Nr. 26172-55-4 for C(M)IT, 2682-20-4 for MIT and 55965-84-9 for the mixture. The active ingredient is named C(M)IT/MIT (3:1).

The active substance is manufactured as a technical concentrate (TK) with different solvents and stabilizers. The minimum purity of the technical material (TC) has been theoretically calculated based on the composition of the solutions. The different solutions have been assessed and four are acceptable and proposed as reference source with a minimum purity for the TC of: 57.9% of C(M)IT/MIT 3:1 in dry weight.
Among the different stabilisers used, two are of concern: magnesium nitrate and magnesium chloride.
Please see the confidential annex: Confidential appendix to doc IIA for details of accepted sources and calculation.

The notified active substance is manufactured by two compagnies: Thor Gmbh (hereafter reffered to as " Thor")and Dow Chemical (formally Rohm and Haas Europe Trading ApS, hereafter reffered to as "Dow")).

C(M)IT/MIT (3:1) is very reactive with some substances and should be stabilized in the product. That is the reason why the active substance is manufactured in continuous directly at the product stage. The product mostly on the market is a solution at 14% in water with stabilizers salts and most of the (eco)toxicological studies have been performed with this solution. There are three sources for this solution.
C(M)IT/MIT (3:1) at 14% in water with stabilizers is a clear liquid, colourless to pale yellow with a mild odour. It is not flammable and does not have explosive and oxidising properties. As it is classified as a corrosive substance, aluminium, grey cast iron and steel (except some approved high-grade steels) are not suitable materials. There is no reactivity with high density PE containers, glass, PP, PVC, glass fibre reinforced plastics.

C(M)IT/MIT (3:1) has a low volatility and vapour pressure at 20°C. C(M)IT and MIT are extremely soluble in water and are not bioaccumulable (log Kow are respectively 0.401 for C(M)IT and -0.486 for MIT).

Validated methods for analysis of C(M)IT, MIT, additives and impurities in the active substance as manufactured have been provided. However for one additive and for the impurities for Thor, validation data are required to validate the analytical method used in the 5-batch analysis. Moreover some validation data are missing to fully validate the

[4] Mixture of 5-chloro-2-methylisothiazol-3(2H)-one and 2-methylisothiazol-3(2H)-one : CAS Name
Reaction mass of 5-chloro-2-methylisothiazol-3(2H)-one and 2-methylisothiazol-3(2H)-one: REACH name

analytical methods used in the 5-batch analysis: complete validation data for one impurity in one source and for another impurity in another source for Dow.

Validated methods for analysis of residues of C(M)IT and MIT in soil and sediments, air, drinking and surface water and simulated food have been provided. A confirmation method for the determination of C(M)IT/MIT in soil is required at the product authorization stage for the use in PT11 which induces a continuous rejection of c(M)IT and MIT in soil. Thor has not submitted methods for analysis of C(M)IT and MIT in soil and sediments and in food. One use in PT11 induces a continuous rejection of CIT and MIT in soil, this use is now not acceptable in the dossier however if this use is claimed and acceptable at the product authorisation stage, an analytical method for the determination of CIT and MIT in soil should be provided. A validated method for analysis of C(M)IT and MIT in food is not necessary for PT11 as no contamination of food is expected.

It has been accepted that no method for determination of residues of C(M)IT and MIT in animals and human body fluids and tissues was provided, according to the toxicological profile of the substance.

The active substance hereafter named C(M)IT/MIT refers to the solution of C(M)IT/MIT (3:1) at 14% in water. In the report, it is also referred to the active ingredient C(M)IT/MIT or C(M)IT/MIT at 100%, meaning to C(M)IT/MIT (3:1) without water and additives.

2.1.1.2 Biocidal products

2.1.1.2.1 Dow Chemical's product: Kathon™ WT

Dow's product Kathon™ WT contains between 12.21 and 15.78 % w/w of C(M)IT/MIT (3:1) in water.

Kathon™ WT is a clear liquid, colourless to pale yellow with a mild odour. It is not flammable and does not have explosive and oxidising properties.

Validated methods for analysis of C(M)IT and MIT in the product are the same as analytical methods for the determination of C(M)IT and MIT in the technical active substance.

2.1.1.2.2 Thor GmbH's product: Acticide® SPX

Thor's product is Acticide® SPX which contains between 1.4 and 1.6 % w/w of C(M)IT/MIT (3:1) in water. The product Acticide SPX is an aqueous solution prepared from the active substance as manufactured.

Acticide® SPX is a clear liquid, colourless to pale yellow with a mild odour. It is not flammable and does not have explosive and oxidising properties. It is thermally stable at low (0°C) and ambient temperatures. Information about compatibility of Acticide® SPX with other products which will be used with, acidity and relative density are lacking and will have to be submitted at the product authorization stage.

Validated methods for analysis of C(M)IT and MIT in the technical active substance exist. These methods could be used to analyse C(M)IT and MIT in Acticide SPX.

2.1.2 Intended uses and efficacy

2.1.2.1 Field of use / function / Mode of action

2.1.2.1.1 Field of use / function

C(M)IT/MIT is used as a broad spectrum antimicrobial agent for preventing the growth of microorganisms (bacteria, fungi (and algae for Dow only)) that may occur within the liquid cooling and processing systems. C(M)IT/MIT biocidal products are exclusively used by professionals or industrial users in PT11.

C(M)IT/MIT exhibits rapid inhibition of growth at low level. For the preservation of liquid cooling and processing systems, typical use concentrations range claimed by Dow is from 1 to 50 mg/L of active ingredient,. Typical range use concentrations of C(M)IT/MIT claimed by Thor is from 0,2 to 1 mg/L by continuous dosing and 2 mg/L by shock dosing.

Concentrations of C(M)IT/MIT for which an efficacy is demonstrated are presented in the following tables:

- ✓ For Dow (Kathon™ WT)

MG/PT	Field of use envisaged	Likely concentration at which active ingredient of C(M)IT/MIT. will be used
MG2/PT 11	Preservative for liquid cooling and processing systems (i.e. Waste water treatment systems, Rinse baths, Photo-processing, Print fountain solutions, Textile and spinning fluids, Electrodeposition coating systems, Paint spray booths, Wood treatment solutions (not for wood protection),	1 – 50 mg a.i/L by continuous dosing:

- ✓ For Thor (Acticide® SPX)

MG/PT	Field of use envisaged	Likely concentration at which a.i. will be used
MG2/PT 11	Preservative for liquid cooling and processing systems	0.6-5 mg a.i/L by continuous dosing The application rate by shock dosing is not validated

Based on the information submitted by the applicants (Dow & Thor), the efficacy of C(M)IT/MIT against target organisms claimed is demonstrated. However in order to demonstrate the efficacy of the product in real conditions, field studies will have to be submitted for the authorization of biocidal products with C(M)IT/MIT.

2.1.2.1.2 Mode of action

C(M)IT/MIT is an isothiazolone biocide. It uses a two steps mechanism: nucleophilic attack at the activated N-S bound of isothiazolinones by amino, amido, thiol groups of large molecular systems such as proteins or nucleic acids of the micro-organisms. Consequently there is a rapid inhibition (minutes) of growth and metabolism, followed by irreversible cell damage resulting in loss of viability (hours). Cells are inhibited by disruption of the metabolic pathways and critical physiological functions are affected (respiration, ATP synthesis).

2.1.2.1.3 Object to be protected, Target organisms

C(M)IT/MIT is a biocide with a large spectrum. In the different laboratory studies presented, an efficacy has been demonstrated for the following micro-organisms:

- ✓ For Dow

Alcaligenes faecalis, Burkholderia cepacia, Desulfovibrio desulfuricans, Enterobacter cloacae, Enterobacter aerogenes, Escherichia coli, Klebsiella pneumoniae, Legionella pneumophila, Proteus vulgaris, Pseudomonas aeruginosa, Pseudomonas fluorescens, Staphylococcus aureus, Aspergillus niger, Penicillium funiculosom, Penicillium ochro-chloron, Trichoderma viride, Candida albicans, Rhodotorula rubra, Saccharomyces cerevisiae, Chlorella pyrenoidosa, Anabaena flosaquae.

- ✓ For Thor

Escherichia coli, Klebsiella pneumonia, Corynebacterium ammoniagenes, Pseudomonas aeroginosa, Proteus vulgaris, Aspergillus niger, Proteus vulgaris, Penicillium funiculosum, Saccharomyces cerevisiae.

2.1.2.2 Resistance

The organisms with most frequently reported resistance to C(M)IT/MIT are Gram negative bacteria, such as *Pseudomonas* and *Burkholderia*. Resistance to increasing levels of C(M)IT/MIT was shown for bacteria adapted in lab cultures. Under-dosing or poor stability of C(M)IT/MIT was attributed as the primary cause of developing the resistant strains in metalworking fluid systems, which displayed stronger resistance than the lab-adapted isolates. The mechanism of resistance to C(M)IT/MIT biocide has been suggested to involve the loss of specific outer membrane (porin) proteins (35-42 k Dalton mass) resulting in reduced transport of C(M)IT/MIT to the interior of the cell. The vast majority of resistance attributed to C(M)IT/MIT is the result of phenotypic changes (adaptation) and does not represent a change in resistance due to altered genetic composition or mutation (acquired resistance). Microorganisms deemed resistance to C(M)IT/MIT have also shown varying degrees of cross-resistance to other Biocides. In commercial use, C(M)IT/MIT is often used in combination or rotation with other biocides in various applications. Microbial resistance to C(M)IT/MIT could be remedied by switching or alternating biocides, using combinations with other actives.

2.1.3 Classification

2.1.3.1 Current classification

There is a harmonized classification for C(M)IT/MIT.

- Active ingredient C(M)IT/MIT (3:1) 100%

Directive 67/548/EEC	
Class of danger	T - Toxic C - Corrosive N - Dangerous for the environment
R phrases	R23/24/25: Toxic by inhalation, in contact with skin and if swallowed. R34: Causes burns. R43: May cause sensitization by skin contact. R50-53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S phrases	S2: Keep out of the reach of children. S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.
Specific concentration limit	C, R34: Causes burns C ≥ 0.6% Xi, R36/38: Irritating to eyes and skin 0.06% ≤ C < 0.6% Xi; R43: May cause sensitization by skin contact C ≥ 0.0015%
Regulation 1272/2008	
Hazard classes and categories / hazard statements	Acute Tox. 3/H331: Toxic if inhaled Acute Tox. 3/H311: Toxic in contact with skin Acute Tox. 3/H301: Toxic if swallowed Skin Corr. 1B/H314: Causes severe skin burns and eye damage Skin Sens. 1/H317: May cause an allergic skin reaction Aquatic Acute 1/H400: Very toxic to aquatic life Aquatic chronic/H410 Very toxic to aquatic life with long lasting effects.
Specific concentration limit	Skin Corr. 1B; H314: Causes severe skin burns and eye damage C ≥ 0.6% Eye Irrit. 2; H319: Causes serious eye irritation Skin Irrit. 2; H315: Causes skin irritation 0.06% ≤ C < 0.6% Skin Sens.1/H317: May cause an allergic skin reaction C ≥ 0.0015%

2.1.3.2 Proposed classification

Based on the toxicological profil described in the dossier, RMS proposes the following classification:

Directive 67/548/EEC		
	Active substance C(M)IT/MIT 14%	Active ingredient C(M)IT/MIT 100%
Class of danger	Xn: Harmful C: Corrosive Xi: Irritant N: Dangerous to the environment	T+: Very toxic C: Corrosive Xi: Irritant N: Dangerous for the environment
R phrases	R20/21/22: Harmful by inhalation, in contact with skin and if swallowed R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact R50-53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	R26: Very toxic by inhalation R24/25*: Toxic in contact with skin and if swallowed. R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact. R50-53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S phrases	S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.	
Specific concentration limit	C, R34: Causes burns C ≥ 0.6% Xi, R36/38: Irritating to eyes and skin 0.06% ≤ C < 0.6% Xi; R43: May cause sensitization by skin contact C ≥ 0.0015% This specific concentration limit is considered relevant for this dossier.	
Regulation 1272/2008		
Hazard classes and categories	Acute Tox 4 for acute oral hazard	Acute Tox. 3 for acute oral hazard

	Acute Tox 3 for acute dermal hazard Acute Tox 4 for inhalation hazard Skin Corr. 1B** Skin Sens. Cat 1A STOT SE 3 Aquatic Acute 1 Aquatic Chronic 1	Acute Tox 2 for acute dermal hazard Acute Tox 2 for acute inhalation hazard Skin Corr. 1B** Skin Sens. Cat 1A STOT SE 3 Aquatic Acute 1 Aquatic Chronic 1
Hazard statements	H332: Harmful if inhaled H312: Harmful in contact with skin H302: Harmful if swallowed H 314: Causes severe skin burns and eye damage** H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=10 H410: Very toxic to aquatic life with long lasting effects M-factor=10	H 330: Fatal if inhaled H 310: Fatal in contact with skin H 301: Toxic if swallowed H 314: Causes severe skin burns and eye damage** H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=100 H410: Very toxic to aquatic life with long lasting effects M-factor=100
Specific concentration limit	Skin Corr. 1B; H314: Causes severe skin burns and eye damage C ≥ 0.6% Eye Irrit. 2; H319: Causes serious eye irritation Skin Irrit. 2; H315: Causes skin irritation 0.06% ≤ C < 0.6% Skin Sens.1/H317: May cause an allergic skin reaction C ≥ 0.0015% This specific concentration limit is considered relevant for this dossier.	

* The C(M)IT/MIT has been supported by two different applicants. There is a disputation concerning the classification for the acute respiratory exposure, since different studies have been provided by the two applicants. This point will probably lead to an Annex XV dossier for a harmonized classification for C(M)IT/MIT. Additionally, although not readily biodegradable, C(M)IT/MIT has been shown to be fast degraded in several environmental compartiment and it should be stated by ECHA is it can be considered as rapidly biodegradable in the frame of the Regulation 1272/2008. At present, contradictory results are available and C(M)IT/MIT is considered as not rapidly biodegradable by the RMS, based on a weight of evidence approach. More explanations are provided in the document IIA and IIIA9. A final decision should be made by ECHA.

** A classification as Skin Corr. 1C H 314: Causes severe skin burns and eye damage should be required due to the study results, however a harmonised classification as Skin Corr. 1B has been set, and therefore this classification is retained in the dossier.

2.2 SUMMARY OF THE RISK ASSESSMENT

The active substance hereafter named C(M)IT/MIT refers to the solution of C(M)IT/MIT (3:1) at 14% in water. In the full CAR, it is also referred to the active ingredient C(M)IT/MIT or C(M)IT/MIT at 100%, meaning to C(M)IT/MIT (3:1) without water and additives.

2.2.1 Human health risk assessment

2.2.1.1 Hazard identification

C(M)IT/MIT induces a local irritation observed by oral, dermal and inhalation routes. No real systemic effects were observed in any available study, except on body weight gain and food consumption. These effects are considered as secondary to the local toxicity.

2.2.1.2 Effects assessment

Toxicokinetics

- Absorption

Oral absorption studies were conducted in rats, following administration of C(M)IT/MIT with either ^{14}C-CMIT or ^{14}C-MIT. Bile-duct cannulation was not systematically performed.
From this overall data set, it seems that MIT would be better absorbed than C(M)IT (55-90% versus 37-62%respectively). It is generally preferred to use data from studies where animals were cannulated, the study showed the absorption rates of 49% and 78% for C(M)IT and MIT respectively (Dow A6.2c/01).It is therefore proposed to choose the lowest absorption rate value of 49%, rounded to 50% as a worst case.

The overall oral absorption rate to be used for a systemic risk characterisation is therefore 50%.

Dermal absorption was investigated both *in vitro* (in rat and human skin) and *in vivo* (in rats).
Based on all these data, and also due to uncertainties in some studies (poor recovery, poor description of the study), it is proposed to set the dermal absorption of C(M)IT/MIT 3:1 at **50 % for aqueous solutions below corrosive concentrations**. This value is based on the maximal absorption found in an *in vitro* study 43% rounded to 50 % due to uncertainties.
Moreover, this value is in line with the EFSA guidance document for dermal absorption as a value of 50 % for oral absorption as been set.
For **corrosive concentrations** of C(M)IT/MIT (> 0.6% the specific concentration limit), no study is available, but as for the other substances of the same family it can be assumed that a **100 %** dermal absorption is appropriate.
A default inhalation absorption value of 100% has been adopted.

- Distribution

After administration of radiolabelled C(M)IT/MIT by gavage to rats, rat tissues contain less than 5% of dosed radioactivity, four days after exposure. The highest amount of radioactivity is found in blood, particularly in red blood cells, followed by muscle and liver. Therefore, CMIT and MIT are not considered to have an accumulative potential in human.

- Metabolism

Following an oral administration of radiolabelled CMIT in solution with MIT to rats, approximately twenty-nine radioactive components were observed in urine and faeces samples from the HPLC radioprofiling. No parent compound was detected in excreta, indicating an extensive metabolization of CMIT. The major component in urine was N-methyl malonamic acid, NMMA (M1A) (15.35-18.19%), and the major component in the faeces was the 3-mercapturic acid conjugate of 3-sulfinyl-N-methyl-propionamide (M15) (up to 32.54%) (it was found as a minor metabolite in urine). In bile-duct cannulated rats, M15 accounted for 8.83% of the dose in faeces, and was not detected in urine, indicating either that M15 may have been formed in the intestine and the cannulation has possibly broken up the entero-hepatic circulation, or the M15 may have been mainly produced at the hepatic level and is then excreted in the bile. All of the ten metabolites found in bile accounted for less than 5% of the dose.

- Excretion

MIT and C(M)IT are both rapidly excreted. Urine and faeces are equal major routes of excretion for C(M)IT whereas bile is a minor route of excretion (4.74%). On the contrary, MIT is largely excreted in urine and in a lesser extent in faeces, of which the major part came from the bile (29.09%). No parent compound is present in excreta.
Therefore, C(M)IT/MIT is not considered to have an accumulative potential in human.

Acute toxicity

The acute oral LD_{50} of C(M)IT/MIT in rats ranges from 457 to 472 mg/kg bw (corr. to 64 to 66 mg a.i./kg bw). Dead animals show effects on stomach and intestines which are consistent with the corrosive properties of C(M)IT/MIT. Therefore, C(M)IT/MIT meets the EU criteria for classification as 'Harmful if swallowed' and should be classified as Xn; R22 (corr. to 'toxic if swallowed', T; R25 for the active ingredient C(M)IT/MIT 100%) according to the directive 67/548/EC. A classification as Acute Tox 4 / H302: Harmful if swallowed is required according to the regulation 1272/2008/EC (corr. to Acute Tox. 3 /H 301: Toxic if swallowed for C(M)IT/MIT 100 %).

The acute dermal LD_{50} of C(M)IT/MIT in male rabbits is 660 mg/kg bw (corr. to 87 mg a.i/kg bw). In rats, the acute dermal LD_{50} is 1008 mg/kg bw (corr. to 141 mg a.i/kg bw). Observed effects are restricted to local effects or are subsequent to local effects. C(M)IT/MIT should be classified Xn; R21 'Harmful in contact with skin' according to the EU criteria for classification. (corr. to T; R24 'Toxic in contact with skin' for C(M)IT/MIT 100%) according to the directive 67/548/EC. A classification as Acute Tox 3 / H312: Harmful in contact with skin is required according to the regulation 1272/2008/EC (corr. to Acute tox 2 / H 310: Fatal in contact with skin for C(M)IT/MIT 100 %).

After acute exposure by inhalation, C(M)IT/MIT induces effects in relation with its corrosive properties.
The 4-hr nose-only acute inhalation LC_{50} of C(M)IT/MIT in rats ranges from 1.23 to 2.36 mg/L air (corr. to 0.171 to 0.33 mg a.i/L air). The effects observed are consistent with the clinical signs of respiratory irritation. It is likely that the deaths resulted from excess fluids in the respiratory tract due to the irritant/corrosive nature of C(M)IT/MIT. C(M)IT/MIT should be classified Xn; R20 'Harmful by inhalation' (corr. to T+; R26 'Very toxic by inhalation' for C(M)IT/MIT 3:1) according to the directive 67/548/EC. A classification as Acute Tox 4 / H332: Harmful if inhaled is required according to the regulation 1272/2008/EC (corr. to Acute tox 2 / H 330: Fatal if inhaled for C(M)IT/MIT 100 %).

Irritation/Sensitisation

C(M)IT/MIT is severely irritant to corrosive to the skin of rabbit in the different studies submitted. It should be classified as C; R34-'Corrosive/Causes burns' according to the EU criteria for classification with specific concentration limits: C ≥ 0.6% (C, R34) and 0.06% ≤ C < 0.6% (Xi, R36/38), according to the directive 67/548/EC. A classification as Skin Corr. 1C H 314: Causes severe skin burns and eye damage should be required due to the study results, however a harmonised classification as Skin Corr. 1B has been set, and therefore this classification is retained[5]. , Specific concentration limits: Skin Corr. 1B; H314: Causes severe skin burns and eye damage C ≥ 0.6%, according to the regulation 1272/2008/EC are proposed.

Due to the corrosivity of C(M)IT/MIT observed in the skin irritation studies, an eye irritation study was not deemed necessary since the substance has to be considered as to pose a risk of serious damage to the eyes.
The classification of the C(M)IT/MIT as corrosive includes the risk of severe damages to the eyes.

Regarding the irritation of airways, a concentration of 69 µg/l of product induced a 50% reduction in the respiratory rate in mice (RD50). C(M)IT/MIT should therefore be classified as Xi; R37-Irritating to respiratory system according to the directive 67/548/EC and STOT SE 3, H 335: May cause respiratory irritation according to the regulation 1272/2008/EC.

C(M)IT/MIT is a skin sensitizer according to a GPMT, a Bühler test, an open epicutaneous test and two LLNAs. A classification R43 − 'Sensitisation by skin contact' is appropriate according to the directive 67/548/EC and Skin Sens. Cat 1A/ H317: May cause an allergic skin reaction according to CLP regulation, with specific concentration limit of 0,0015% (equivalent to 15 ppm) set during the meeting of the commission working group on the C&L of dangerous substances of 21 January 2000. This value will be used as a threshold value in a qualitative risk assessment for local effects by dermal route.

It is not possible to evaluate the potential of respiratory sensitisation as no studies addressing respiratory sensitisation of C(M)IT/MIT are available..

Repeated dose toxicity

- Oral studies

C(M)IT/MIT was tested in several oral repeated dose toxicity studies in rabbits, rats and dogs for 4 weeks and 3 months.
The major toxic effects observed were related to a gastric irritation. Decreases in body weight and in water intake reported after exposure to C(M)IT/MIT were attributed to palatability. There was no evidence of systemic toxicity at the highest tested doses.
From the 90-day study in rats, a gastric irritation can be considered as a critical effect for setting a $NOAEC_{oral}$ at 536 ppm (corr. to 75 ppm a.i.) (w/v). In the absence of systemic effects, the NO(A)EL for systemic effects can be set at the highest tested dose (16.3 mg ai/kg bw/d).
From the 90-day study in dogs, in the absence of systemic and local effects, the NO(A)EL can be set at the highest tested dose (750 ppm ai, corr. to 22 mg ai/kg bw/d).
From the 4-week study in rabbits, a NOAEL at 27.9 mg/kg bw/d (corr. to 3.9 mg ai/kg.bw/d) based on mortality indirectly due to gastric irritation. There was no evidence of systemic toxicity at any dose level. A NOAEC of 2.9 mg/kg/day (corr. to 0.4 mg a.i./kg bw/d) based on the fundus irritation has been set.
From the 2-year study in rats, a NOAEL at 300 ppm a.i (corr. to 17.2 and 25.7 mg a.i/kg bw/d for males and females respectively) has been adopted based on no systemic effect

[5] This classification may be revised in the CLH report.

observed. A NOAEC of 210 ppm (corr. to 30 ppm a.i) based on local irritation of the forestomach has been set.

In oral toxicity studies performed with metabolites of C(M)IT/MIT, NMMA (N-methyl malonamic acid) and MA (malonic acid), no treatment-related findings were noted up to the highest tested doses (500 ppm for NMMA and 100 ppm for MA).

- Dermal studies

Two 90-day dermal repeated dose toxicity studies were performed with C(M)IT/MIT in rabbit and rat. Local skin irritation, with erythema, edema and eschar formation, was the main topic toxic response to the tested substance.
Results from the the 90-day dermal study in rabbit, submitted by Rohm & Hass (i.e. Dow) could not be fully validated, therefore, only the Thor study has been considered: in the absence of any systemic effect, a $NOAEC_{dermal}$ of 0.1 mg/kg bw/d (corr. to 0.174% a.i.), based on skin reactions like erythema, edema and eschar has been adopted.
In the 30-month study in mice, no systemic effect was observed at necropsy.

- Inhalation studies

In a 90-day inhalation study, it was demonstrated that C(M)IT/MIT induces an irritation of the respiratory tract at the contact site with chromo-rhinorrhea, rhinorrhea, eye squint, bradypnea and dyspnea. Since only local effects have been identified, the NOAEC based on these effects is 2.4 mg/m^3 (corr. to 0.34 mg a.i./m^3).

Genotoxicity

- *In vitro* tests

Several *in vitro* studies of genotoxicity were performed with C(M)IT/MIT. Positive results were observed in three Ames assays and in three tests in mammalian cells (one chromosomal aberration test and two mouse lymphoma assays), with or without S9 activation. In contrast, C(M)IT/MIT was not mutagenic in primary culture of rat hepatocytes (UDS) and in a mouse cell transformation test.

A test was also performed with the major metabolite of C(M)IT/MIT, N-(methyl)malonamic acid (NMMA), which appeared not to be mutagenic when tested in a bacterial gene mutation assay test (Ames assay).

- *In vivo* tests

C(M)IT/MIT was tested in one *in vivo* chromosomal aberrations assay in mice (bone marrow) and one micronucleus test in mice (bone marrow). Negative results were observed in these in vivo studies.

In the studies on tissue distribution of radiolabel in mouse presented in the dossier for MIT and C(M)IT (referenced A6.2.a/03 and A6.2.b/03, respectively in the doc IIIA), radioactivity has been detected in bone marrow tissue following a single oral dose of the test material to adult male and female. This information provides support to the validity of the chromosome aberration test on bone marrow in mice and the micronuclei on bone marrow in mice, since it determines the extent of C(M)IT and MIT distribution to bone marrow of mice after oral exposure.

In the absence of genotoxicity, additional tests were carried out in tissue other than bone marrow. Two UDS assays in rats confirmed the absence of genotoxicity of C(M)IT/MIT when tested *in vivo*.

In conclusion, despite a genotoxic potential *in vitro*, C(M)IT/MIT cannot be considered genotoxic *in vivo*.

The overall conclusion from these studies is that C(M)IT/MIT cannot be considered genotoxic.

Carcinogenicity

C(M)IT/MIT was tested in two chronic/carcinogenicity tests by either the oral route (rat) or dermal route (mouse). C(M)IT/MIT produced no evidence of carcinogenicity (ie., no treatment-related increase in the type or incidence of neoplasms in any group) up to the highest tested doses in these studies : 2140 ppm ai in rat and 2860 ppm ai in mice (corr. to 300 ppm a.i. in rat and 400 ppm a.i. in mice).

Reproductive toxicity

- Developmental toxicity

C(M)IT/MIT was tested in two developmental toxicity studies in rats. None of them revealed a developmental toxicity in pups. In dams, irritating effects at gastric level were principally found, with effects on food consumption and body-weight gain. Based on the study submitted by Thor, the highest tested dose without maternal toxicity was 28.2 mg/kg/day (corr. to 3.95 mg a.i./kg/day). An apparent dose-related increase in mortality of dams was observed in the Dow's study but was eventually deemed as not treatment-related in the absence of mortality in the Thor's study and on the basis of the necropsy data (gross pathological examination showed red areas in the lungs indicating a wrong administration route).

One developmental study in rabbits is also available (Dow). It didn't reveal a developmental toxicity in pups. In dams, irritating effects at gastric level were principally found, with effects on food consumption and body-weight gain. The highest tested dose without maternal toxicity was 14 mg/kg/day (corr. to 2 mg a.i./kg/day).

- Fertility

When tested in both one-generation and two-generation reproductive toxicity studies in the rat, C(M)IT/MIT produced no evidence of reproductive toxicity including no effects on fertility/mating or on post-natal development at any dose.

Neurotoxicity

No studies were requested due to the absence of neurotoxicity alert in the repeated-dose toxicity studies.

Human data

Skin reactions (irritation, chemical burns and sensitisation) are widely reported from medical data but no epidemiological studies are available.
Due to the strong sensitising potential of C(M)IT/MIT, the skin exposure should be reduced as much as possible (closed systems, protective equipment,…)

2.2.1.3 Exposure assessment

Summary of the major intended uses

Table 2.2.1.3-1: Summary of the major intended uses of Kathon™WT and ACTICIDE® SPX

MG/PT	Field of use envisaged	Likely concentration at which active substance (expressed in a.i.) will be used
PT11	Process and cooling water – Used to control the growth of bacteria, algae and fungi in the circulating water of open and closed cooling water systems (e.g., cooling tower - open cooling water system). Kathon™ WT is not used in once-through system.	1 to 6 ppm total a.i. for Kathon™ WT 0.6 to 5 ppm total a.i. for ACTICIDE® SPX
PT11	Air conditioning and air washing systems – The biocide is used for preservation of in-use water based air conditioning, air washing, humidifier, etc., process fluids to control the growth of bacteria, algae and fungi in the recirculating process fluid.[6]	1 to 6 ppm total a.i. for Kathon™ WT
PT11	Preservative for aqueous wood preservative treatment solution – The biocide is used in water based solutions used to pressure treat and dip treat wood. Wood treatment solutions are dosed with biocide to prevent the growth of micro-organisms (mould, slime) in the treatment solutions that could accumulate in storage tanks, block pumps and pipework and prevent the operation of the treatment plant. The biocide is not intended to function as a wood preservative.	3 to 50 ppm total a.i. for Kathon™ WT
PT11	Textile and spinning fluids – The biocide is used for the preservation of textile and spinning fluids, photo processing solutions and print fountain solutions to control the integrity of recirculating fluid by reducing microbial contamination from bacteria, fungi and algae in the bulk solution.	6 to 30 ppm total a.i. for Kathon™ WT
PT11	Paint spray booths and electrodeposition coating systems – The biocide is used for preservation of fluids in paint spray booths and electrodeposition coating systems to control the integrity of recirculating fluid by reducing microbial contamination from bacteria, fungi and algae in the bulk solution.	6 to 30 ppm total a.i. for Kathon™ WT
PT11	Industrial hygiene, clean in place (CIP) – The biocide is used for remediation of industrial water based process fluid streams to control the integrity of recirculating fluid by reducing microbial contamination from	1 to 30 ppm total a.i. for Kathon™ WT

[6] This application is borderline between PT2 and PT11. After consultation of the competent authorities, Rohm and Haas has addressed these uses in a specific dossier for C(M)IT/MIT in PT2. They are mentioned here for completeness, but no risk assessement will be addressed.

	bacteria, fungi and algae.	

In addition to these major uses, minor applications for potential use of Kathon™ WT Biocide include the preservation of process fluids used for non-food pasteurizers/sterilizers/can warmers, reverse osmosis or ultrafiltration membranes [non-food, non potable water, non-medical], wastewater treatment, rinse baths, and conveyor lubricants (outside the food industry). The recommended end use concentration for all of these applications is 1 to 6 ppm active ingredient. These end-use applications for potential PT11 uses (Preservatives for liquid cooling and processing systems) for Kathon™ WT Biocide are considered minor in comparison to the major applications listed in the table above. The major end-use exposure scenarios are sufficiently conservative and broad such that the exposure to Kathon™ WT Biocide in the minor end-use applications will be adequately addressed.

2.2.1.3.1 Kathon™ WT (Dow's product)

Kathon™ WT Biocide may be used directly or formulated as a preservative product for liquid cooling and processing systems, which are ultimately utilized by professionals in industrial applications described in Table 3.1-01 (major uses). These biocidal products are for professional/industrial use only and are not sold to non-professional users (consumers). However, indirect exposure to the general public is possible for certain end-use applications (e.g., handling treated wood in non-industrial applications). A summary of the major PT 11 end-use application(s) and the relevant routes of exposure for potential direct human contact to the treated end-use products are shown in Table below.

PRIMARY EXPOSURE

Professional Users

- Production/formulation of the C(M)IT/MIT active substance and Kathon™ WT biocidal product with 14% a.s. as typical concentration (Professional Users Exposure, Section 3.2.2.1).
- Formulation of Kathon™ WT into biocidal products of lower active substance concentration (Professional Users Exposure, Section 3.2.2.2).
- Application of biocidal product in major fields of use as outlined in Table 3.1-01 (Professional Users Exposure, Section 3.2.2.3).

Non professional Users and consumers

Non-professional and consumer primary exposure to the treated recirculating systems containing C(M)IT/MIT is not relevant since these products are recommended and sold for industrial/professional use only.

INDIRECT AND/OR SECONDARY EXPOSURE

- Indirect exposure to the active substance from its use in major end-use applications (Section 3.2.4.1).
- Indirect exposure to residues via environmental compartments is not considered relevant due to the low potential for bioaccumulation and the rapid biodegradation.

Table 2.2.1.3.1-1: Main paths of human exposure toward active ingredient (C(M)IT/MIT (3:1)) from its major uses in the biocidal product (Kathon™ WT)

End-use application	Exposure path	Industrial use	Professional use	General public	Via the environment *
Process and cooling water	Inhalation	Yes	Yes	Yes	No
	Dermal	Yes	Yes	No	No
	Oral	No	No	No	No
Airconditioning and air washing systems	Inhalation	Yes	Yes	No	No
	Dermal	Yes	Yes	No	No
	Oral	No	No	No	No
Preservative for aqueous wood preservative treatment solution	Inhalation	Yes	Yes	Yes	No
	Dermal	Yes	Yes	Yes	No
	Oral	No	No	Yes	No
Textile and spinning fluids	Inhalation	Yes	Yes	No	No
	Dermal	Yes	Yes	No	No
	Oral	No	No	No	No
Paint spray booths and electrodeposition coating systems	Inhalation	Yes	Yes	No	No
	Dermal	Yes	Yes	No	No
	Oral	No	No	No	No
Industrial hygiene, clean in place (CIP)	Inhalation	Yes	Yes	No	No
	Dermal	Yes	Yes	No	No
	Oral	No	No	No	No

* Exposure to humans via the environment is not considered a relevant route of exposure due to the low production volume of the a.s. (<<1000 MT, see Confidential section for exact value), the low potential for bioaccumulation and the rapid biodegradation.

PRIMARY EXPOSURE

Production of the active substance and formulation into biocidal products (Industrial/Professional users)

The production of biocidal products is not covered by the Regulation (EU) No 528/2012 on the placing of biocidal products on the market. Therefore, this section is not relevant in the Dossier. (Not evaluated).

Formulation of the Biocidal Product Kathon™ WT into end-use treatment concentrates used in PT11 applications

Kathon™ WT Biocide (14 wt % a.i.) is a water treatment preservative that is presently sold to formulators who manufacture their own water treatment biocidal products at active ingredient concentrations of up to 5% C(M)IT/MIT for use in the applications listed in Table above.

As described in Document IIB, the application or use phase includes mixing/loading the biocidal product (14% C(M)IT/MIT a.i.), application and post-application tasks (5% to 14% C(M)IT/MIT a.i).

Table 2.2.1.3.1-2: Exposure estimates for industrial worker using biocidal products in diluting process

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Skin deposit concentration	Systemic dose	Systemic dose
	mg a.i. / m^3 air	mg a.i./kg /d	ppm a.i.	mg a.i./kg /d	mg a.i./kg /d
Task – time frame :	**Automated Loading systems (industrial worker) - daily**				
Tier 1: Without PPE	negligible	negligible	140000	1.29×10^{-1}	1.29×10^{-1}
Tier 2: chemical resistant gloves and impermeable coveralls	negligible	negligible	140000	1.29×10^{-2}	1.29×10^{-2}
Task – time frame :	**Manual Loading (industrial worker) - daily**				
Tier 1: Without PPE	1.65×10^{-2}	2.74×10^{-3}	140000	14.1	14.1
Tier 2: chemical resistant gloves and impermeable coveralls + RPE	1.65×10^{-3}	2.74×10^{-4}	140000	1.41×10^{-1}	1.42×10^{-1}
Task – time frame :	**Cleaning dispensing pumps (industrial worker) - daily**				
Tier 1: Without PPE	negligible	negligible	140000	7.70	7.70
Tier 2a: chemical resistant gloves and impermeable coveralls	negligible	negligible	140000	6.36×10^{-1}	6.36×10^{-1}
Tier 2b: chemical resistant gloves and impermeable coveralls + rinse*	negligible	negligible	1400	3.18×10^{-3}	3.18×10^{-3}

*: the pump is considered to be rinsed before cleaning diluting the a.i. by a factor of 100.

Table 2.2.1.3.1-3: Estimation of combined exposure concerning automated process for industrial worker

Tier	Inhalation exposure	Dermal exposure	Total exposure
	Loading: Tier 1 + Cleaning: Tier 1	**Loading: Tier 2 + Cleaning: Tier 2**	**Loading: Tier 2 + Cleaning: Tier 2* +rinse**
Dermal systemic dose (mg a.i./kg bw/day)	7.83	6.48×10^{-1}	1.61×10^{-2}
Inhaled a.i. concentration (mg a.i./m^3) • 8-hr TWA	negligible	negligible	negligible
Inhalation systemic dose (mg a.i./kg bw/day)	negligible	negligible	negligible
Total systemic dose (mg a.i./kg/day)	7.83	6.48×10^{-1}	1.61×10^{-2}

*: PPE: gloves and impermeable coveralls

Table 2.2.1.3.1-4: Estimation of combined exposure concerning semi-automated process for industrial worker

	Loading: Tier 1 + Cleaning: Tier 1	**Loading: Tier 2 + Cleaning: Tier 2**	**Loading: Tier 2 + Cleaning: Tier 2* +rinse**
Dermal systemic dose (mg a.i./kg bw/day)	21.84	7.77×10^{-1}	1.45×10^{-1}
Inhaled a.i. concentration (mg a.i./m^3) • 8-hr TWA	1.65×10^{-2}	1.65×10^{-3}	1.65×10^{-3}
Inhalation systemic dose (mg a.i./kg bw/day)	2.74×10^{-3}	2.74×10^{-3}	2.74×10^{-3}
Total systemic dose (mg a.i./kg/day)	21.84	7.77×10^{-1}	1.45×10^{-1}

*: PPE: gloves and impermeable coveralls + RPE during mixing and loading

Process and Cooling Water (Cooling Towers)

Kathon™ WT Biocide containing 14% active ingredient is used to control the growth of bacteria, algae and fungi in the recirculating water of open (e.g., cooling tower) and closed cooling water systems. This level represents the highest or worst-case concentration for potential exposure during mixing/loading and certain post application scenarios. Typical treatment concentrations for the recirculating water in cooling towers range from 1 to 6 ppm a.i.

As described in Document IIB, the application or use scenario includes mixing/loading the biocidal product (14% C(M)IT/MIT a.i.) and post-application tasks (6 ppm to 14% C(M)IT/MIT a.i).

Table 2.2.1.3.1-5 - Cooling tower uses professional primary exposure summary

PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Manual Loading in cooling water systems (water treatment service worker) – daily**				
Tier 1: Without PPE	6.58×10^{-3}	1.10×10^{-3}	140000	5.66	5.66
Tier 2: With gloves, RPE and impermeable coveralls	6.58×10^{-4}	1.10×10^{-4}	140000	5.66×10^{-2}	5.67×10^{-2}
Task – time frame:	**Automated Loading in cooling water systems (water treatment service worker) – daily**				
Tier 1: Without PPE	negligible	negligible	140000	5.15×10^{-2}	5.15×10^{-2}
Task– time frame :	**Cleaning dispensing pumps (water treatment service worker) – daily**				
Tier 1: Without PPE	negligible	negligible	140000	7.70	7.70
Tier 2: With gloves and impermeable coveralls	negligible	negligible	140000	6.36×10^{-1}	6.36×10^{-1}
Tier 2 + rinse: With gloves and impermeable coveralls	negligible	negligible	1400	3.18×10^{-3}	3.18×10^{-3}
Task – time frame :	**Cleaning fouled system – every year**				
Tier 1: Without PPE	negligible	negligible	6	9.90×10^{-4}	9.90×10^{-4}
Task – time frame :	**Cooling water monitoring – daily**				
Tier 1: Without PPE	negligible	negligible	6	3.30×10^{-4}	3.30×10^{-4}
Tasks	**Combined exposure – manual loading + cleaning dispensing pump and fouled system + monitoring**				
Tier 1: Without PPE	6.58×10^{-3}	1.10×10^{-3}	Not relevant	13.4	13.4

Tier 2: loading +pump cleaning Tier 1: fouled system cleaning and monitoring	6.58×10^{-4}	1.10×10^{-4}	Not relevant	6.11×10^{-2}	6.12×10^{-2}

Air Washers (Industrial use)

These uses are borderline between PT2 and PT11. They have been included in the PT02 dossier already assessed by FR.

Wood treatment solutions

Kathon™ WT is incorporated into water-based wood treatment solutions to prevent the growth of micro-organisms in the treatment solutions that could accumulate in storage tanks, block pumps and pipework and prevent the operation of the treatment plant. Since Kathon™ WT is not intended to function as a wood preservative but as a preservative for the recirculating wood treatment solution, it has been included in PT 11.02 (Preservatives used in recirculating process systems) and was evaluated in this assessment.

Industrial applications of wood preservative solutions are conducted by a number of application techniques including vacuum pressure, double-vacuum, deluge/flood spray and mechanical or manual dipping. Primary exposure to professionals working in these treatment plants will predominantly occur via the dermal route as a result of direct contact with the surface of treated timber and via inhalation.

The exposure estimates for C(M)IT/MIT in PT 11 (biocidal product containing 14% C(M)IT/MIT a.i. and wood treatment fluid containing a maximum concentration of 50 ppm C(M)IT/MIT a.i.) for the professional users as described in Document IIB. Summaries are shown in the following tables

Table 2.2.1.3.1-6: Wood protective fluids uses professional primary exposure summary

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Manual Loading in wood protective fluids systems (professional worker) – daily**				
Tier 1: Without PPE	2.74×10^{-3}	4.57×10^{-4}	140000	2.36	2.36
Tier 2: With gloves, RPE and impermeable coveralls	2.74×10^{-4}	4.57×10^{-5}	140000	2.36×10^{-2}	2.36×10^{-2}
Task – time frame:	**Automated Loading in wood protective fluids systems (professional worker) – daily**				
Tier 1: Without PPE	negligible	negligible	140000	2.15×10^{-2}	2.15×10^{-2}
Task– time frame :	**Industrial Use of treated wood protective fluids – daily**				
Tier 1: Without PPE	7.13×10^{-5}	1.19×10^{-5}	50	2.41×10^{-2}	2.41×10^{-2}
Task – time frame :	**Cleaning dipping Tank– every year**				
Tier 1: Without PPE	7.13×10^{-5}	1.19×10^{-5}	50	8.04×10^{-3}	8.04×10^{-3}
Tasks	**Combined exposure – manual loading + use of treated wood protective fluid**				
Tier 2: loading + Tier 1: application	3.45×10^{-4}	5.76×10^{-5}	Not relevant	4.77×10^{-2}	4.78×10^{-2}

Textile systems/spinning fluids

Kathon™ WT Biocide is used for the preservation of textile processing fluids to control the integrity of these fluids by reducing microbial contamination from bacteria, fungi and algae in the bulk solution. This biocide is also used in photographic processing operations and print fountain solutions to control the integrity of the process fluids used in these systems. The use of Kathon™ WT Biocide in textile systems was considered representative of the use in photo processing and print fountain solutions since the end-use concentration is identical for these applications (6-30 ppm a.i.) and because it is anticipated that workers will have only short-term, intermittent contact with treated process fluid.

Table 2.2.1.3.1-7: Textile process fluids uses professional primary exposure summary

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Manual Loading in textile process fluid systems (professional worker) – daily**				
Tier 1: Without PPE	2.74×10^{-3}	4.57×10^{-3}	140000	2.36	2.36
Tier 2: With gloves, RPE and impermeable coveralls	2.74×10^{-4}	4.57×10^{-4}	140000	2.36×10^{-2}	2.36×10^{-2}
Task – time frame:	**Automated Loading in textile process fluid systems (professional worker) – daily**				
Tier 1: Without PPE	negligible	negligible	140000	2.15×10^{-2}	2.15×10^{-2}
Task– time frame :	**Industrial Use of treated textile process fluid – daily**				
Tier 1: Without PPE	9.46×10^{-4}	1.58×10^{-4}	30	6.90×10^{-3}	7.06×10^{-3}
Task – time frame :	**Cleaning dispensing pump – every week**				
Tier 1: Without PPE	negligible	negligible	140000	6.42×10^{-1}	6.42×10^{-1}
Tier 2: With gloves and impermeable coveralls	negligible	negligible	140000	5.30×10^{-2}	5.30×10^{-2}
Tasks	**Combined exposure – manual loading + application + cleaning of dispensing pump**				
Tier 2: loading and post-application + Tier 1: application + Tier 2: cleaning	1.22×10^{-3}	2.03×10^{-4}	not relevant	8.34×10^{-2}	8.36×10^{-2}

Paint spray booths and Electrodeposition coating systems (Industrial use)

Kathon™ WT Biocide is used for the preservation of process fluids in paint spray booths and electrodeposition coating systems to control the integrity of recirculating fluid by reducing microbial contamination from bacteria, fungi and algae in the bulk solution. The use of the biocidal product in paint spray booths was considered worst-case since this operation involves aerosolising the treated recirculating paint and because this task may

be conducted manually. The end-use concentration for both of these applications is 6 to 30 ppm C(M)IT/MIT. Therefore, the exposure assessment presented below for paint spray booths is considered sufficiently conservative and broad such that it adequately addressed exposure to electrodeposition coating systems.

The exposure assessment below addresses the use of C(M)IT/MIT in the biocidal product at 14% a.i. and as a preservative for paint spray booth process fluids at a maximum a.i. concentration of 30 ppm. Both of these levels represent the highest or worst-case concentrations for the exposure scenarios to which they apply.

As described in Document IIB, the application or use phase includes mixing/loading the biocidal product (14% C(M)IT/MIT a.i.), application of treated processing fluids (30 ppm C(M)IT/MIT a.i.) and post-application cleaning (30 ppm C(M)IT/MIT a.i.).

The primary exposure scenario for mixing/loading presented in Document IIB for aqueous wood treatment solutions also applies to mixing/loading biocidal products for paint spray booth and electrodeposition applications since these scenarios are essentially similar. Exposure models, inputs and assumptions (e.g., treatment concentrations, exposure duration and frequency, PPE, RPE, dermal absorption) used for mixing/loading wood treatment solutions also apply to the corresponding paint spray booth and electrodeposition mixing/loading scenarios.

Table 2.2.1.3.1-8: Spray booth uses professional primary exposure summary

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Manual Loading in paint spraying systems (professional worker) – daily**				
Tier 1: Without PPE	2.74×10^{-3}	4.57×10^{-3}	140000	2.36	2.36
Tier 2: With gloves, RPE and impermeable coveralls	2.74×10^{-4}	4.57×10^{-4}	140000	2.36×10^{-2}	2.36×10^{-2}
Task – time frame:	**Automated Loading in paint spraying systems (professional worker) – daily**				
Tier 1: Without PPE	negligible	negligible	140000	2.15×10^{-2}	2.15×10^{-2}
Task– time frame :	**Spraying treated paint– daily**				
Tier 1: Without PPE	1.99×10^{-4}	3.32×10^{-5}	30	1.16×10^{-2}	1.16×10^{-2}
Task – time frame :	**Cleaning spray equipment– every week**				
Tier 1: Without PPE	negligible	negligible	30	6.88×10^{-5}	6.88×10^{-5}
Tasks	**Combined exposure – manual loading + use of treated wood protective fluid**				
Tier 2: mixing and loading + Tier 1: spraying and cleaning equipment	4.73×10^{-4}	7.89×10^{-5}	Not relevant	3.52×10^{-2}	3.53×10^{-2}

Industrial Hygiene, Clean in Place (CIP)

Biocidal products containing C(M)IT/MIT are used for remediation of industrial water based process fluid streams to control the integrity of recirculating fluid by reducing microbial contamination from bacteria, fungi and algae. The primary exposure scenario for mixing/loading presented in Document IIB for aqueous wood treatment solutions also applies to mixing/loading in clean in place (CIP) applications since these scenarios are essentially similar. Likewise, the primary exposure scenario for post-application pump maintenance presented in Document IIB for cooling towers also applies to post-application pump maintenance in CIP applications since these scenarios are essentially similar. Exposure models, inputs and assumptions (e.g., treatment concentrations, exposure duration and frequency, PPE, RPE, dermal absorption) used for mixing/loading wood

treatment solutions and post-application pump maintenance for cooling towers also apply to the corresponding CIP scenarios.

As described in Document IIB, the CIP application phase involves circulating an aqueous solution of the biocidal product through a closed system (e.g., pipework) to treat the internal surfaces. Due to the closed and automated nature of the process, exposure to C(M)IT/MIT is not anticipated during this process and therefore the exposure potential is considered negligible.

Table 2.2.1.3.1-9: CIP uses professional primary exposure summary

Tier	**Inhalation exposure**		**Dermal exposure**		**Total exposure**
PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Manual Loading in CIP fluid systems (professional worker) – daily**				
Tier 1: Without PPE	2.74×10^{-3}	4.57×10^{-4}	140000	2.36	2.36
Tier 2: With gloves, RPE and impermeable coveralls	2.74×10^{-4}	4.57×10^{-5}	140000	2.36×10^{-2}	2.36×10^{-2}
Task – time frame:	**Automated Loading in CIP fluid systems (professional worker) – daily**				
Tier 1: Without PPE	negligible	negligible	140000	2.15×10^{-3}	2.15×10^{-2}
Task – time frame :	**Cleaning dispensing pump – every week**				
Tier 1: Without PPE	negligible	negligible	140000	6.42×10^{-1}	6.42×10^{-1}
Tier 2: With gloves and impermeable coveralls	negligible	negligible	140000	5.30×10^{-2}	5.30×10^{-2}
Tasks	**Combined exposure – manual loading + cleaning dispensing sump**				
Tier 2: manual loading and cleaning dispensing sump	2.74×10^{-4}	4.57×10^{-5}	Not relevant	7.65×10^{-2}	7.66×10^{-2}

Others end-use applications

The reasonable worst-case dermal and inhalation exposure potential to C(M)IT/MIT in other potential liquid cooling and processing system preservative (PT11) end-use applications such as non-food pasteurizers/sterilizers/can warmers, reverse osmosis or ultrafiltration membranes [non-food, non potable water, non-medical], wastewater

treatment, rinse baths, and conveyor lubricants is considered to be adequately addressed by the conservative detailed exposure scenarios and risk characterisation provided above for cooling towers, wood, textile, paint spray booth and CIP. Specifically, the reasonable worst-case occupational exposure to C(M)IT/MIT as a preservative for other potential liquid cooling and processing system end-uses would not be higher than the exposure scenarios identified above for cooling towers, air washers, etc. treated with C(M)IT/MIT.

INDIRECT EXPOSURE

Indirect or secondary exposure to bystanders: treated recirculating systems

Bystander exposure to treated recirculating systems is considered negligible or irrelevant since these operations are conducted in closed building or aeras with restricted access.

Indirect or secondary exposure to bystanders: cooling towers

Workers in the proximity of the Cooling towers and bystanders can be exposed to the drift containing the active substance.

In doc IIB a reverse scenario was build to define the characteristics that lead to an acceptable risk of the small / medium / large cooling towers as categorized in the ESD for PT 11. This evaluation is summarized in the risk characterization section (section 2.2.1.4.1.5).

Indirect or secondary exposure to treated wood

Indirect or secondary dermal, inhalation and/or oral exposure to C(M)IT/MIT residues (50 ppm) from treated wood is possible for adults (professionals and non-professionals), children and/or infants who come in contact with treated articles. This scenarios cover the exposure articles covered by treated paint too as they are similar and the concentration of a.i. in wood preservatives is higher than in paint. Reasonable worst-case indirect exposure scenarios are presented in Document IIB and are summarized below in Table 1.4.2-01.

Acute phase reference scenarios

Adult – cutting and sanding treated wood (non-professional)

Infant – chewing wood off-cut

Chronic phase reference scenarios

Adult – cutting and sanding treated wood (professional)

Adult – inhalation of volatilized residues indoors

Child – playing on playground structure outdoors

Infant – playing on weathered structure and mouthing

Table 2.2.1.3.1-10: Indirect Exposure - Acute and Chronic Reference Scenarios

Tier	Inhalation exposure		Dermal exposure		Oral exposure	Total exposure
PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Adult (non-professional) – cutting and sanding treated wood - Acute**					
Tier 1: Without PPE	1.17×10^{-5}	1.95×10^{-6}	Not relevant	1.05×10^{-2}	Not relevant	1.05×10^{-2}
Task – time frame:	**Adult (professional) – cutting and sanding treated wood - Chronic**					
Tier 1: Without PPE	7.03×10^{-5}	1.17×10^{-5}	Not relevant	1.05×10^{-2}	Not relevant	1.05×10^{-2}
Task – time frame:	**Adult – inhalation of volatilized residues indoors - Chronic**					
Tier 1: Without PPE	5.4×10^{-3}	1.66×10^{-3}	Not relevant	Not relevant	Not relevant	1.66×10^{-3}
Task – time frame :	**Infant – chewing wood off-cut - Acute**					
Tier 1: Without PPE	negligible	negligible	Not relevant	Not relevant	1.20×10^{-3}	1.20×10^{-3}
Task – time frame:	**Infant – inhalation of volatilized residues indoors - Chronic**					
Tier 1: Without PPE	5.4×10^{-3}	2.16×10^{-3}	Not relevant	Not relevant	Not relevant	2.16×10^{-3}
Task – time frame:	**Child – playing on playground structure outdoors - Chronic**					
Tier 1: Without PPE	negligible	negligible	Not relevant	2.00×10^{-2}	Not relevant	2.00×10^{-2}
Task – time frame:	**Infant – playing on weathered structure and mouthing – Chronic**					
Tier 1: Without PPE	negligible	negligible	Not relevant	3.00×10^{-2}	3.75×10^{-2}	6.75×10^{-2}

Indirect or secondary exposure to textiles

Secondary exposure to consumers from textiles is considered negligible due to the low treatment levels (6 - 30 ppm a.i.) used to preserved textile processing fluids and because of degradation of the active substance during the manufacturing process.

Indirect or secondary exposure to paint spray booths

Secondary exposure to consumers from dried paint is considered negligible due to the low treatment levels (6 - 30 ppm a.i.) used to preserve these recirculating paint systems and because exposure from dried paint is considered insignificant. Moreover, exposure to treated wood corresponds to a worst-case for this kind of exposure (because the applied dose is higher).

Indirect or secondary exposure to Industrial hygiene, clean in place

Secondary exposure is considered negligible for industrial hygiene CIP applications since this process is conducted on closed systems (e.g., pipework) at industrial facilities.

Indirect exposure to humans via the environment

Exposure to humans via the environment is not considered a relevant route of exposure due to the low production volume of the active substance, its low potential for bioaccumulation and rapid biodegradation.

COMBINED EXPOSURE

Combined exposure is not relevant for this assessment since these PT11 applications involve industrial/professional workers, only and consumers (non-professionals) are not directly exposed. Additionally, exposure estimates for humans via the environment are insignificant when compared to exposure estimates for workplace or occupational exposure.

2.2.1.3.2 Acticide® SPX (Thor's product)

ACTICIDE® SPX is used as preservative for liquid cooling and processing systems which are ultimately utilized by professionals in industrial applications. It is used to control the growth of bacteria, algae and fungi in the recirculating water of open (e.g., cooling tower) and closed cooling water systems. This use represents the worst-case scenario with the highest concentration for potential exposure during mixing/loading and certain post application scenarios.

A summary of the major PT 11 end-use application and the relevant routes of exposure are shown in Table below.

Table 2.2.1.3.2-1: Exposure paths to Acticide® SPX

End use application	Exposure path	Industrial use	Professional use	General public (secondary exposure)	Via the Environment
Process and cooling water	Oral	No	No	Negligible	Negligible
	Dermal	Negligible/ No	Yes	Yes	Negligible
	Inhalation	Negligible/ No	Yes	No	Negligible

PRIMARY EXPOSURE

Professional Users

The significant primary exposure scenarios, described in details in Document IIB 3.2.2, are the following:

- Mixing/Loading: manual loading of the biocidal product (ACTICIDE® SPX containing 1.5% w/w C(M)IT/MIT) to the reservoir for system,
- Post-application (maintenance and disposal): Cleaning the dispensing pump, maintenance of the equipment, monitoring the system and waste disposing.

Combined exposure of professional user doing several tasks in the same day is also calculated. The predicted exposures for each professional user scenario (as calculated in Document IIB) are presented below.

For each exposure scenario, Tier 1 exposure estimates are provided. Tier 2 assessment has been developed only when tier 1 assessment leads to unacceptable risks. Tier 1 estimates assume no Personal Protective Equipment (PPE). Tier 2 estimates assume appropriate PPE and/or risk mitigation measures.
The most relevant paths of exposure to C(M)IT/MIT are the dermal and inhalation routes. The oral route is considered negligible.

Table 2.2.1.3.2-2: Cooling tower uses professional primary exposure summary

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. / m^3 air (8-hrs TWA)	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame:	**Manual Loading in cooling water systems (water treatment service worker) – daily**				
Tier 1: Without PPE	7.05×10^{-4}	1.18×10^{-4}	15 000	6.06×10^{-1}	6.06×10^{-1}
Tier 2: With gloves and impermeable coveralls	7.05×10^{-4}	1.18×10^{-4}	15 000	6.06×10^{-3}	6.18×10^{-3}
Task – time frame:	**Automated Loading in cooling water systems (water treatment service worker) – daily**				
Tier 1: Without PPE	negligible	negligible	15 000	5.52×10^{-3}	5.52×10^{-3}
Task– time frame :	**Cleaning dispensing pumps (water treatment service worker) – daily**				
Tier 1: Without PPE	negligible	negligible	15 000	8.25×10^{-1}	8.25×10^{-1}
Tier 2: With gloves and impermeable coveralls	negligible	negligible	15 000	6.81×10^{-2}	6.81×10^{-2}
Tier 2 + rinse: With gloves and impermeable coveralls	negligible	negligible	150	3.41×10^{-4}	3.41×10^{-4}
Task – time frame :	**Cleaning fouled system – every year**				
Tier 1: Without PPE	negligible	negligible	5	8.25×10^{-3}	8.25×10^{-3}
Task – time frame :	**Cooling water monitoring – daily**				
Tier 1: Without PPE	negligible	negligible	5	2.75×10^{-4}	2.75×10^{-4}
Tasks	**Combined exposure – manual loading + cleaning dispensing pump and fouled system + monitoring**				
Tier 1: Without PPE	7.05×10^{-4}	1.18×10^{-4}	Not relevant	1.4	1.4
Tier 2: loading +pump cleaning Tier 1: fouled system cleaning and monitoring	7.05×10^{-4}	1.18×10^{-4}	Not relevant	7.50×10^{-3}	7.62×10^{-3}

Non Professional users and consumers

Non-professional and consumer primary exposure to the treated process and cooling water systems containing C(M)IT/MIT is not relevant since the product is recommended and sold for industrial/professional use only.

INDIRECT EXPOSURE

Workers and bystanders around the cooling towers can be exposed to the drift containing the active substance.

In doc IIB a reverse scenario was build to define the characteristics that lead to an acceptable risk (a.i. concentration in the drift < long term AEC 0.02 mg a.i./m^3) of the small / medium / large cooling towers as categorized in the ESD for pt 11. This evaluation is summarized in the risk characterization section (section 2.2.1.4.2.4)

COMBINED EXPOSURE

Combined exposure is not relevant for this assessment since these PT11 applications involve industrial/professional workers, only and consumers (non-professionals) are not directly exposed. Additionally, exposure estimates for humans via the environment are insignificant when compared to exposure estimates for workplace or occupational exposure.

2.2.1.4 Risk characterisation

Quantitative risk assessment was performed for both systemic and local effects by inhalation route (irritation), comparing the estimated exposure with relevant reference values (AELs/AECs). The Margin of Exposure (MOE) approach was used as well, comparing the critical NO(A)EL with the estimated exposure.
Concerning the local effects by dermal route, in order to take into account the sensitizing properties of the active ingredient, a qualitative risk assessment was performed comparing the exposure concentrations with the threshold value presented above (15 ppm a.i.).

AELs determination
According to the TNsG on Annex I Inclusion chapter 4.1 (Quantitative Risk Characterisation, September 2009), Acceptable Exposure Levels (AELs) were derived for acute-, medium- and long −term exposures.
These AELs represent the internal (absorbed) dose available for systemic distribution from any route of absorption, and is expressed in mg ai/kg bw/d.

AEL = NO(A)EL * % absorption / assessment factors

An acute- and medium-term AEL can be derived from the 90-day toxicity study in dogs exposed through diet, where a NO(A)EL was identified at 750 ppm ai (corr. to 22 mg ai/kg bw/d) as no systemic effect was observed at the highest tested dose.
A long-term AEL can be derived from the carcinogenicity study in rats exposed through drinking water, where a NO(A)EL was identified at 300 ppm ai (corr. to 17.2 mg ai/kg bw/d) as no systemic effect was observed at the highest tested dose.

The critical studies used for the derivation of AELs were summarised in the table below.

Critical endpoints for the determination of AELs

Study	NO(A)EL	Effects at LO(A)EL
Acute and medium-term AELs		
90-day study in dogs (A6.4.1/02) (Thor)	22 mg ai/kg bw/d	none
Long-term AEL		
2-year study in rats (A6.5/01-A6.7/01) (Dow)	17.2 mg ai/kg bw/d	none

AEL approach

To translate the selected NOAEL into an AEL, the NOAEL is divided by the assessments factors (safety factors). Systemic AELs should be derived using a default factor of 100 corresponding to 10 for inter-species variation and 10 for intra-species variation and an oral absorption factor of 50%.

The following AELs were therefore derived:

- Acute/medium-term AEL= (22/100) x 50% = 0.11 mg ai/kg bw/d
- Long-term AEL= (17.2/100) x 50% = 0.09 mg ai/kg bw/d

In the AEL approach, a risk is considered acceptable if AEL > exposure. In practice, exposure is expressed as a percentage of the AEL (%AEL). The risk is therefore considered acceptable if %AEL < 100.

MOE Approach

To translate the selected NOAEL into an MOE, the systemic NOAEL is divided by the exposure value.

A default factor of 100 corresponding to 10 for inter-species variation and 10 for intra-species variation will be used as reference margin of exposure (MOE_{ref}).

- If the MOE $\leq$ MOE_{ref}, the risk is not considered as acceptable,
- If the MOE > MOE_{ref}, the risk is considered as acceptable

AECs determination

As local toxicity is considered as the critical endpoint associated with exposure, a qualitative approach with the threshold value of 15 ppm (specific concentration limit for sensitizing effect) will be used for dermal route. A quantitative approach will be realized for the inhalation route with the derivation of an Acceptable Exposure Concentrations (AECs); according to the guidance for Human Health Risk Assessment (Volume III, Part B, December 2013).

As well as for the AEL, the AEC corresponds to the NOAEC divided by the assessment factors.

AEC = NOAEC / assessment factors

C(M)IT/MIT induces irritation of the respiratory tract with chromo-rhinorrhea, rhinorrhea, eye squint, bradypnea, dyspnea after inhalation administration. The NOAEC of 0.34 mg ai/m^3/d from the 90-day toxicity study by inhalation route in rat was chosen for the derivation of the $AEC_{inhalation}$.

Critical endpoints for the determination of the AECs

Study	NOAEC	Effects at LO(A)EL/LO(A)EC
Local effects (inhalation)		
90-day inhalation study in rats (A6.4.3/01)	0.34 mg ai/m^3	Irritation of the respiratory tract with chromo-rhinorrhea, rhinorrhea, eye squint, bradypnea, dyspnea

As far as only local effects were observed, a refined inter-species factor is directly proposed. It can actually be assumed that for a local effect at the port of entry, toxicokinetics do not contribute significantly to interspecies differences. In contrast, as the mechanism is not clearly known, it is prudent to assume that the toxicodynamic component should be kept at 2.5.
As well, it is assumed that toxicokinetic does not contribute significantly to intraspecies differences, therefore, this component can be reduced to 1. The intra-species assessment factor is therefore set at 3.2. An additional assessment factor of 2, accounting for the duration extrapolation from subchronic to chronic, is applied for deriving long-term inhalation AEC from medium-term studies.
These values (8 or 16) are used as reference margins of exposure (MOE_{ref}).

The following AECs were therefore derived for inhalation route:

- short/medium-term $AEC_{inhalation}$ = 0.34/8 = 0.04 mg a.i./m^3,
- long-term $AEC_{inhalation}$ = 0.34/16 = 0.02 mg a.i. /m^3.

In the AEC approach, a risk is considered acceptable if AEC > exposure.
In practice, exposure is expressed as a percentage of the AEC (%AEC). The risk is therefore considered acceptable if %AEC < 100.
In the MOE approach, a risk is considered acceptable if MOE > MOE_{ref} (where $MOE = \frac{NOAEC}{Exposure}$).

Other determination

Derivation of ARfD (Acute Reference Dose)

The ARfD can be derived from the NOAEL of 2 mg ai/kg bw/d, based on decreased food consumption and decreased body weight gain (due to gastric irritation), determined in the developmental study in rabbits by applying an overall assessment factor of 100 (10 for interspecies variability and 10 for intraspecies variability).

ARfD = NOAEL/AF = 2/100 = **0.02 mg a.i./kg bw/d**

Derivation of ADI (Acceptable Daily intake)

The ADI for C(M)IT/MIT can be derived from the NOAEC of 0.4 mg a.i./kg bw/d, based on gastric irritation, identified in the 28-days rabbit study, by applying an overall assessment factor of 100 (10 for interspecies variability and 10 for intraspecies variability). An additional assessment factor for extrapolating from sub-acute to chronic is considered not necessary since the chosen NOAEC is already a conservative value, the lowest of the data package.

ADI = NOAEL/AF = 0.4/100 = **0.004 mg/kg bw/d**

Local effects are concentration dependent, therefore for concentrations leading no gastric irritation, no ADI has to a taken into account.

2.2.1.4.1 Risk characterisation for Kathon™ WT (Dow's product)

PRIMARY EXPOSURE

2.2.1.4.1.1 Production / formulation of the active substance and biocidal products

The production of biocidal products is not covered by the Regulation (EU) No 528/2012 on the placing of biocidal products on the market. Therefore, this section is not relevant in the Dossier and the text submitted by the Applicant is removed (see document IIB).

2.2.1.4.1.2 Formulation of the Biocidal Product Kathon™ WT into end-use treatment concentrates used in PT11 applications

Kathon™ WT Biocide (14 wt % a.i.) is a water treatment preservative that is presently sold to formulators who manufacture their own water treatment biocidal products at active ingredient concentrations of up to 5% C(M)IT/MIT for use in the applications listed in document IIB.

- Quantitative risk assessment for systemic effects

Table 2.2.1.4-1**:** Summary of risk assessment for industrial worker using biocidal products in diluting process

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Automated Loading systems (industrial worker) - daily**					
Tier 1 : Without PPE	1.29×10^{-1}	8.6	100	67	0.09	**143**
Tier 2: Chemical gloves and impermeable coveralls	1.29×10^{-2}	8.6	100	667	0.09	14.3
Task– time frame :	**Manual loading systems (industrial worker) - daily**					
Tier 1: Without PPE	14.1	8.6	100	**0.6**	0.09	**15 667**
Tier 2: With gloves and impermeable coveralls+ RPE	1.42×10^{-1}	8.6	100	**61**	0.09	**158**
Task – time frame:	**Cleaning dispensing pumps (industrial worker) - daily**					
Tier 1: Without PPE	7.70	8.6	100	**1.1**	0.09	**8 556**
Tier 2a: With gloves and impermeable coveralls	6.36×10^{-1}	8.6	100	**14**	0.09	**707**
Tier 2b: With gloves, impermeable coveralls and rinse	3.18×10^{-3}	8.6	100	2 704	0.09	3.5
Task – time frame:	**Combined exposure – automated loading + cleaning dispensing pump**					
Tier 1: Without PPE	7.83	8.6	100	**1.1**	0.09	**8 700**
Tier 2: loading Tier 2: cleaning	6.48×10^{-1}	8.6	100	**14**	0.09	**720**
Tier 2: loading Tier 2: cleaning + rinse	1.61×10^{-2}	8.6	100	534	0.09	17.8
Task – time frame:	**Combined exposure – manual loading + cleaning dispensing pump**					
Tier 1: Without PPE	21.84	8.6	100	**0.4**	0.09	**2 427**
Tier 2: loading Tier 2: cleaning	7.77×10^{-1}	8.6	100	**11**	0.09	**867**
Tier 2: loading Tier 2: cleaning + rinse	1.45×10^{-1}	8.6	100	60	0.09	**161**

* NOAEL corrected by the oral absorption factor of 50%.

The risk for systemic exposure during the loading of the biocidal product (14% a.i.) is acceptable for the automated transfer in Tier 2 (with gloves and impermeable coverall). For the manual transfer, the risk is unacceptable even in tier 2 (with gloves and impermeable coveralls and RPE) with a MOE (61) lower than the MOE_{ref} (100) and a %AEL (158) above 100%.
The risk is considered acceptable during the cleaning of the dispensing pumps in Tier 2b (with gloves, impermeable coveralls and a rinse step), with a MOE (2 704) higher than MOE_{ref} (100) and the%AEL (3.5) below 100%.

Concerning the combined exposure (automated loading in Tier 2 + cleaning dispensing pumps in Tier 2b), the risk is deemed acceptable, with a MOE (534) higher than the MOE_{ref} (100) and a %AEL (17.8) below 100%. For the combined exposure (manual loading in Tier 2 + cleaning dispensing pumps in Tier 2b), the risk is deemed unacceptable, with a MOE (60) higher than the MOE_{ref} (100) and a %AEL (161) above 100%.

The risk characterisation for manual transfer and for combined systemic exposure identified an unacceptable risk. When PPE and RMM for local effect are taken into account, no systemic exposure during loading is considered, and the risk can be considered acceptable.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4-2: Summary of risk assessment for industrial worker using biocidal products in diluting process after repeated inhalation exposure

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Automated Loading systems (industrial worker) - daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Semi automated Loading systems (industrial worker) - daily**					
Tier 1: Without PPE	1.65×10^{-2}	0.34	16	20.6	0.02	82.5
Task – time frame:	**Cleaning dispensing pumps (industrial worker) - daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible

No unacceptable risk has been identified during automated, manual transfer and cleaning of the dispensing pumps, since MOEs are higher than MOE_{ref} (16) and associated %AELs are below 100%.

- Qualitative risk assessment for local effects

Dermal exposure

Table 2.2.1.4-3: Summary of risk assessment for industrial worker using biocidal products in diluting process after repeated dermal exposure

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task– time frame :	**Automated Loading systems (industrial worker) - daily**	
Tier 1 : Without PPE	140 000	**15**
Task– time frame :	**Semi automated Loading systems (industrial worker) - daily) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: chemical resistant gloves and impermeable coveralls + RPE	140 000	**15**
Task – time frame:	**Cleaning dispensing pumps (industrial worker) - daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves and impermeable coveralls	140 000	**15**
Tier 2 + rinse: With gloves and impermeable coveralls	1 400	**15**

It should be noted that PPE for dermal protection will not decrease the concentration of exposure but the occurrence of the event of skin contact with the active substance.

The concentrations of C(M)IT/MIT used for these exposure scenarios are above the threshold concentration (15 ppm a.i.).

During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin protection such as gloves, goggles, protective overalls and boots is required under all the identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.

An approval is therefore still possible, provided such risk mitigation measures are implemented.

2.2.1.4.1.3 Professional use of Kathon™ WT under PT 11

A. Process and Cooling Water (Cooling Towers)

- Quantitative risk assessment for systemic effects

Table 2.2.1.4-4: Summary of risk assessment for professionals for cooling tower uses

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Automated Loading in cooling water systems (water treatment service worker) – daily**					
Tier 1 : Without PPE	$5.15\ 10^{-2}$	8.6	100	167	0.09	57.2
Task– time frame :	**Manual Loading in cooling water systems (water treatment service worker) – daily**					
Tier 1: Without PPE	5.66	8.6	100	**1.5**	0.09	**$6.3\ 10^{3}$**
Tier 2: With gloves and impermeable coveralls + RPE	5.67×10^{-2}	8.6	100	152	0.09	63
Task – time frame:	**Cleaning dispensing pumps (water treatment service worker) – daily**					
Tier 1: Without PPE	7.70	8.6	100	**1.1**	0.09	**$8.6\ 10^{3}$**
Tier 2a: With gloves and impermeable coveralls	6.36×10^{-1}	8.6	100	**14**	0.09	**707**
Tier 2b: With gloves, impermeable coveralls and rinse	3.18×10^{-3}	8.6	100	2 705	0.09	3.5
Task – time frame:	**Cleaning fouled system – every year**					
Tier 1: Without PPE	9.90×10^{-4}	8.6	100	$1.8.7\ 10^{3}$	0.09	1.1
Task – time frame:	**Cooling water monitoring – daily**					
Tier 1: Without PPE	3.30×10^{-4}	8.6	100	$2.6\ 10^{4}$	0.09	0.4
Task – time frame:	**Combined exposure – manual loading + cleaning dispensing pump and fouled system + monitoring**					
Tier 1: Without PPE	13.4	8.6	100	**0.7**	0.09	**$1.5\ 10^{4}$**
Tier 2: loading +pump cleaning Tier 1: fouled system cleaning and monitoring	6.12×10^{-2}	8.6	100	141	0.09	68

* NOAEL corrected by the oral absorption factor of 50%.

The risk for systemic exposure during the loading of the biocidal product (14 % a.i.) is acceptable for the automated transfer and the manual transfer in Tier 2 (with gloves and impermeable coveralls) with a MOE (167 and 152, respectively) higher than the MOE_{ref} (100) and a %AEL (57.2 and 63, respectively) below 100%.
The risk is considered acceptable during the cleaning of the dispensing pumps in Tier 2b (with gloves, impermeable coveralls and a rinse step) and the cleaning fouled system in Tier 1 (without PPE), with a MOE (2 705 and 8.7 10^3, respectively) higher than MOE_{ref} (100) and the %AEL (3.5 and 1.1, respectively) below 100%.
The MOE set for the cooling water monitoring scenario (2.6 10^4) is higher than the MOE_{ref} (100) and the associated % AEL (0.4) is below 100 %, therefore the risk is considered as acceptable.
Concerning the combined exposure (loading biocidal product 14 % a.i. with a manual transfer in Tier 2 combined with the cleaning of the dispensing pumps in Tier 2 and a fouled system cleaning and monitoring in Tier 1), the risk is deemed acceptable with a MOE (141) higher than the MOE_{ref} (100) and a %AEL (68) below 100%.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4-5: Summary of risk assessment for professionals for cooling tower uses after repeated inhalation exposure

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Automated Loading in cooling water systems (water treatment service worker) – daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Manual Loading in cooling water systems (water treatment service worker) – daily**					
Tier 1 : Without PPE	6.58 10^{-3}	0.34	16	51.7	0.02	33
Task – time frame:	**Cleaning Kathon WT dispensing pumps (water treatment service worker) – daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task – time frame:	**Cleaning fouled system – every year**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task – time frame:	**Cooling water monitoring – daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible

No unacceptable risk of local effects from inhalation has been identified for the different tasks considered, since MOEs are higher than MOE_{ref} (16) and associated %AELs are below 100%.

- Qualitative risk assessment for local effects

Dermal exposure

Table 2.2.1.4-6: Summary of risk assessment for professionals for cooling tower uses after repeated dermal exposure.

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task– time frame :	**Automated Loading in cooling water systems (water treatment service worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Task– time frame :	**Manual Loading in cooling water systems (water treatment service worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves and impermeable coveralls	140 000	**15**
Task – time frame:	**Cleaning Kathon™ WT dispensing pumps (water treatment service worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves and impermeable coveralls	140 000	**15**
Tier 2 + rinse: With gloves and impermeable coveralls	1 400	**15**
Task – time frame:	**Cleaning fouled system – every year**	
Tier 1 : Without PPE	6	**15**
Task – time frame :	**Cooling water monitoring – daily**	
Tier 1 : Without PPE	6	**15**

The concentrations of C(M)IT/MIT used in these exposure scenarios are below the concentration that would lead to sensitization (15 ppm a.i.) for the cleaning fouled system and for the monitoring, but above 15 ppm a.i. for the automated loading, manual loading and for the cleaning of the dispensing pumps. During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin protection such as gloves, goggles, protective overalls and boots is required under all the identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.

An approval is therefore still possible, provided such risk mitigation measures are implemented.

B. Air Washers (Industrial use)

These systems can be considered borderline between PT2 and PT11. These uses have been included in the PT02 dossier already assessed by FR.

C. Wood treatment solutions

Summaries of the risk characterisation for C(M)IT/MIT in PT 11 (biocidal product containing 14% C(M)IT/MIT a.i. and wood treatment fluid containing a maximum concentration of 50 ppm a.i.) for the professional user scenarios as described in Document IIB are shown in the following tables.

- Quantitative risk assessment for systemic effects

Table 2.2.1.4-7: Summary of risk assessment for professionals using wood treatment solutions

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Automated Loading in wood protective fluids systems (professional worker) – daily**					
Tier 1 : Without PPE	2.15×10^{-2}	8.6	100	400	0.09	23.8
Task– time frame :	**Manual Loading in wood protective fluids systems (professional worker) – daily**					
Tier 1: Without PPE	2.36	8.6	100	**3.7**	0.09	**2 622**
Tier 2: With gloves and impermeable coveralls	2.36×10^{-2}	8.6	100	365	0.09	26.2
Task – time frame:	**Industrial Use of treated wood protective fluids – daily**					
Tier 1: Without PPE	2.41×10^{-2}	8.6	100	357	0.09	26.8
Task – time frame:	**Cleaning dipping Tank– every year**					
Tier 1: Without PPE	8.04×10^{-3}	8.6	100	1 070	0.09	8.9
Task – time frame:	**Combined exposure – manual loading (Tier 2) + use of treated wood protective fluid**					
Tier 2: loading + Tier 1: application	4.78×10^{-2}	8.6	100	180	0.09	53.1

* NOAEL corrected by the oral absorption factor of 50%.

The risk for systemic exposure during the loading of the biocidal product (14 % a.i.) is acceptable for the automated transfer and the manual transfer in Tier 2 (with gloves and impermeable coveralls) with a MOE (400 and 365, respectively) higher than the MOE_{ref} (100) and a %AEL (23.8 and 26.2, respectively) below 100%.
The risk is considered as acceptable during the application and the post-application phases in Tier 1 (without PPE) with a MOE (357 and 1 070, respectively) are higher than MOE_{ref} (100) and the %AEL (6.8 and 8.9, respectively) are below 100%..
Concerning the combined exposure (manual loading of the biocidal product 14 % a.i. in Tier 2 combined with the application phase), the risk is deemed acceptable, with a MOE (180) higher than MOE_{ref} (100) and a % AEL (53.1) below 100 %.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4-8: Summary of risk assessment for professionals using wood treatment solutions after repeated inhalation exposure.

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Automated Loading in wood protective fluids systems (professional worker)**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Manual Loading in wood protective fluids systems (professional worker) – daily**					
Tier 1 : Without PPE	$2.74\ 10^{-3}$	0.34	16	124.1	0.02	13.7
Task – time frame:	**Industrial Use of treated wood protective fluids – daily**					
Tier 1 : Without PPE	$7.13\ 10^{-5}$	0.34	16	4 768.6	0.02	0.36
Task – time frame:	**Cleaning dipping Tank– every year**					
Tier 1 : Without PPE	$7.13\ 10^{-5}$	0.34	16	4 768.6	0.02	0.36

No unacceptable risk has been identified for inhalation exposure during the different tasks considered, with MOEs higher than MOE_{ref} (16) and %AEC below 100%.

- Qualitative risk assessment for local effects

Dermal exposure

Table 2.2.1.4-9: Summary of risk assessment for professionals using wood treatment solutions after repeated dermal exposure.

	Concentration of active ingredient on skin (ppm a.i.)	**Threshold value** (ppm a.i.)
Task– time frame :	**Automated Loading in wood protective fluids systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Task– time frame :	**Manual Loading in wood protective fluids systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves and impermeable coveralls	140 000	**15**
Task – time frame:	**Industrial Use of treated wood protective fluids – daily**	
Tier 1 : Without PPE	50	**15**
Tier 2: With gloves and impermeable coveralls	50	**15**
Task – time frame:	**Cleaning dipping Tank– every year**	
Tier 1 : Without PPE	50	**15**
Tier 2: With gloves and impermeable coveralls	50	**15**

In all phases, the concentrations of C(M)IT/MIT are above the concentration that would lead to sensitisation (15 ppm a.i.).

During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin protection such as gloves, goggles, protective overalls and boots is required under all the identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.

An approval is therefore still possible, provided such risk mitigation measures are implemented.

D. Textile systems/spinning fluids

Kathon™ WT Biocide is used for the preservation of textile processing fluids to control the integrity of these fluids by reducing microbial contamination from bacteria, fungi and algae in the bulk solution. This biocide is also used in photographic processing operations and print fountain solutions to control the integrity of the process fluids used in these systems. The use of Kathon™ WT Biocide in textile systems was considered representative of the use in photo processing and print fountain solutions since the end-use concentration is identical for these applications (6-30 ppm a.i.) and because it is anticipated that workers will have only short-term, intermittent contact with treated process fluid.

The risk characterisation for the textile application phase (textile processing fluids containing 30 ppm C(M)IT/MIT) for the professional user scenario as described in Document IIB is shown in the following table.

- Quantitative risk assessment for systemic effects

Table 2.2.1.4-10: Summary of risk assessment for professionals using textile systems and spinning fluids

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Automated Loading in textile process fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	2.15×10^{-2}	8.6	100	400	0.09	23.9
Task– time frame :	**Manual Loading in textile process fluid systems (professional worker) – daily**					
Tier 1: Without PPE	2.36	8.6	100	**3.7**	0.09	**2 622**
Tier 2: With gloves, impermeable coveralls and RPE	2.36×10^{-2}	8.6	100	365	0.09	26.2
Task – time frame:	**Industrial Use of treated textile process fluid – daily**					
Tier 1: Without PPE	7.06×10^{-3}	8.6	100	1 218	0.09	7.8
Task – time frame:	**Cleaning dispensing pump – every week**					
Tier 1: Without PPE	6.42×10^{-1}	8.6	100	**14**	0.09	**713**
Tier 2: With gloves and impermeable coveralls	5.30×10^{-2}	8.6	100	118	0.09	58.9
Task – time frame:	**Combined exposure – manual loading (Tier 2) + use of treated textile process fluid**					
Tier 2:loading and post-application + Tier 1: application	8.36×10^{-2}	8.6	100	103	0.09	92.9

* NOAEL corrected by the oral absorption factor of 50%.

The risk is considered acceptable in Tier 1 for the loading task (automated transfer) and the textile treatment phase, with a MOE higher than MOE_{ref} (400 and 1 218, respectively) and a %AEL (23.9 and 7.8, respectively) below 100%. For the mixing and loading (manual addition) and the cleaning of pumps, the risk is deemed as acceptable considering the wear of PPE (gloves, impermeable coveralls and RPE), with a MOE higher than the MOE_{ref} (365 and 118, respectively) and a %AEL (26.2 and 58.9, respectively) below 100%.
Concerning the combined exposure (loading biocidal product 14% a.i. with a manual transfer in Tier 2 combined with the application phase in Tier 1 and the cleaning of pumps in Tier 2), the risk is deemed acceptable, with a MOE (103) higher than MOE_{ref} (100) and a %AEL (92.9) below 100%.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4-11: Summary of risk assessment for professionals using textile systems and spinning fluids after repeated inhalation exposure

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Automated Loading in textile process fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Manual Loading in textile process fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	$2.74\ 10^{-3}$	0.34	16	124.1	0.02	13.7
Task – time frame:	**Industrial Use of treated textile process fluid – daily**					
Tier 1 : Without PPE	$9.46\ 10^{-4}$	0.34	16	359.4	0.02	4.7
Task – time frame:	**Cleaning dispensing pump – every week**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible

No unacceptable risk has been identified for inhalation exposure during the different tasks considered, with MOEs higher than MOE_{ref} and %AEC below 100%.

- Qualitative risk assessment for local effetcs

Dermal exposure

Table 2.2.1.4-12: Summary of risk assessment for professionals using textile systems and spinning fluids after repeated dermal exposure

	Concentration of active ingredient on skin (ppm a.i.)	**Threshold value** (ppm a.i.)
Task– time frame :	**Automated Loading in textile process fluid systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Task– time frame :	**Manual Loading in textile process fluid systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves, impermeable coveralls and full face RPE	140 000	**15**
Task – time frame:	**Industrial Use of treated textile process fluid – daily**	
Tier 1 : Without PPE	30	**15**
Task – time frame:	**Cleaning dispensing pump – every week**	
Tier 1 : Without PPE	140 000	**15**
Tier 2a: With gloves and impermeable coveralls	140 000	**15**
Tier 2b: With gloves and impermeable coveralls + rinse	1 400	**15**

The concentrations of C(M)IT/MIT used for these exposure scenarios are above the concentration that would lead to sensitisation (15 ppm a.i.).

During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin protection such as gloves, goggles, protective overalls and boots is required under all the

identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.An approval is therefore still possible, provided such risk mitigation measures are implemented.

E. Paint spray booths and Electrodeposition coating systems (Industrial use)

Summaries of the risk characterisation for the paint spray booth application phase and post-application equipment cleaning (paint containing 30 ppm C(M)IT/MIT a.i.) for the professional user scenarios as described in Document IIB are shown in the following tables.

- Quantitative risk assessment for systemic effects

Table 2.2.1.4-13: Summary of risk assessment for professionals using Paint spray booths and Electrodeposition coating systems

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Automated Loading in paint process fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	2.15×10^{-2}	8.6	100	400	0.09	23.9
Task– time frame :	**Manual Loading in paint process fluid systems (professional worker) – daily**					
Tier 1: Without PPE	2.36	8.6	100	**3.7**	0.09	**2 622**
Tier 2: With gloves, impermeable coveralls and RPE	2.36×10^{-2}	8.6	100	365	0.09	26.2
Task – time frame:	**Spraying treated paint– daily**					
Tier 1: Without PPE	1.16×10^{-2}	8.6	100	742	0.09	12.9
Task – time frame:	**Cleaning spray equipment– every week**					
Tier 1: Without PPE	6.88×10^{-5}	8.6	100	$13\ 10^{4}$	0.09	0.076
Task – time frame:	**Combined exposure – manual loading (Tier 2) + use of treated wood protective fluid**					
Tier 2: mixing and loading + Tier 1: spraying and cleaning equipment	3.53×10^{-2}	8.6	100	244	0.09	39.2

* NOAEL corrected by the oral absorption factor of 50%.

The risk is deemed acceptable for all exposure scenarios considered in Tier 1, except for the manual loading scenario for which an acceptable risk is considered in Tier 2 with the use of PPE. The MOEs are all greater than MOE_{ref} and the %AELs are below 100%.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4-14: Summary of risk assessment for professionals using Paint spray booths and Electrodeposition coating systems after repeated inhalation exposure

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Automated Loading in paint process fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Manual Loading in paint process fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	$2.74\ 10^{-3}$	0.34	16	124.1	0.02	13.7
Task – time frame:	**Spraying treated paint– daily**					
Tier 1 : Without PPE	$1.99\ 10^{-4}$	0.34	16	1 708.5	0.02	0.1
Task – time frame:	**Cleaning spray equipment– every week**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible

No unacceptable risk has been identified for inhalation exposure during the different tasks considered, with the MOEs higher than MOE_{ref} and the %AECs below 100%.

- Qualitative risk assessment for local effects

Dermal exposure

Table 2.2.1.4-15: Summary of risk assessment for professionals using Paint spray booths and Electrodeposition coating systems after repeated dermal exposure

	Concentration of active ingredient on skin (ppm a.i.)	**Threshold value** (ppm a.i.)
Task– time frame :	**Automated Loading in paint process fluid systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Task– time frame :	**Manual Loading in paint process fluid systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves, impermeable coveralls and full face RPE	140 000	**15**
Task – time frame:	**Spraying treated paint– daily**	
Tier 1 : Without PPE	30	**15**
Task – time frame:	**Cleaning spray equipment– every week**	
Tier 1 : Without PPE	30	**15**

The concentrations of C(M)IT/MIT used for these exposure scenarios are above the concentration that would lead to sensitisation (15 ppm a.i.).

During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin protection such as gloves, goggles, protective overalls and boots is required under all the identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.

An approval is therefore still possible, provided such risk mitigation measures are implemented.

F. Industrial Hygiene, Clean in Place (CIP)

Biocidal products containing C(M)IT/MIT are used for remediation of industrial water based process fluid streams to control the integrity of recirculating fluid by reducing microbial contamination from bacteria, fungi and algae. As described in Document IIB, the CIP application phase involves circulating an aqueous solution of the biocidal product through a closed system (e.g., pipework) to treat the internal surfaces. Due to the closed and automated nature of the process, exposure to C(M)IT/MIT is not anticipated during this process and therefore the exposure potential is considered negligible.

- Quantitative risk assessment for systemic effects

Table 2.2.1.4-16: Summary of risk assessment for professionals in industrial hygiene

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Automated Loading in CIP fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	2.15×10^{-2}	8.6	100	400	0.09	23.9
Task– time frame :	**Manual Loading in CIP fluid systems (professional worker) – daily**					
Tier 1: Without PPE	2.36	8.6	100	**3.7**	0.09	**2 622**
Tier 2: With gloves, impermeable coveralls and RPE	2.36×10^{-2}	8.6	100	365	0.09	26.2
Task – time frame:	**Application phase (industrial hygiene CIP) - daily**					
Tier 1: Without PPE	Not relevant due to the closed and automated nature of the application process					
Task – time frame:	**Cleaning dispensing pump – every week**					
Tier 1: Without PPE	6.42×10^{-1}	8.6	100	**13.4**	0.09	**713**
Tier 2a With gloves and impermeable coveralls	5.30×10^{-2}	8.6	100	118	0.09	58.9
Task – time frame:	**Combined exposure – manual loading + cleaning dispensing sump**					
Tier 2: manual loading and cleaning dispensing sump	7.66×10^{-2}	8.6	100	113	0.09	85

* NOAEL corrected by the oral absorption factor of 50%.

The risk is deemed acceptable for the automated loading scenario in Tier 1, with a MOE (400) higher than the MOEref and a %AEL (23.9) below 100%. For the manual loading

scenario and the cleaning of the pumps, an acceptable risk is considered in Tier 2 with the use of PPE. The associated MOEs are greater than MOE_{ref} and the %AELs are below 100%.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4-17: Summary of risk assessment for professionals in industrial hygiene after repeated inhalation exposure

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Automated Loading in CIP fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Manual Loading in CIP fluid systems (professional worker) – daily**					
Tier 1 : Without PPE	2.74 10^{-3}	0.34	16	124.1	0.02	13.7
Task – time frame:	**Application phase (industrial hygiene CIP) - daily**					
Tier 1 : Without PPE	Not relevant due to the closed and automated nature of the application process					
Task – time frame:	**Cleaning dispensing pump – every week**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible

No unacceptable risk has been identified for inhalation exposure during the different tasks considered, with the MOEs higher than MOE_{ref} and the %AECs below 100%.

- Qualitative risk assessment for local effetcs

Dermal exposure

Table 2.2.1.4-18: Summary of risk assessment for professionals in industrial hygiene for after repeated dermal exposure

	Concentration of active ingredient on skin (ppm a.i.)	**Threshold value** (ppm a.i.)
Task– time frame :	**Automated Loading in CIP fluid systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Task– time frame :	**Manual Loading in CIP fluid systems (professional worker) – daily**	
Tier 1 : Without PPE	140 000	**15**
Tier 2: With gloves, impermeable coveralls and full face RPE	140 000	**15**
Task – time frame:	**Application phase (industrial hygiene CIP) - daily**	
Tier 1 : Without PPE	Not relevant due to the closed and automated nature of the application process	
Task – time frame:	**Cleaning dispensing pump – every week**	
Tier 1 : Without PPE	140 000	**15**
Tier 2a: With gloves, impermeable coveralls	140 000	**15**
Tier 2b: With gloves, impermeable coveralls + rinse	1 400	**15**

The concentrations of C(M)IT/MIT used for these exposure scenarios are equal or above the concentration that would lead to sensitisation (15 ppm a.i.).

During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin

protection such as gloves, goggles, protective overalls and boots is required under all the identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.
An approval is therefore still possible, provided such risk mitigation measures are implemented.

G. Risk characterisation for other end-use applications

The reasonable worst-case dermal and inhalation exposure potential to C(M)IT/MIT in other potential liquid cooling and processing system preservative (PT11) end-use applications such as non-food pasteurizers/sterilizers/can warmers, reverse osmosis or ultrafiltration membranes [non-food, non potable water, non-medical], wastewater treatment, rinse baths, and conveyor lubricants is considered to be adequately addressed by the conservative detailed exposure scenarios and risk characterisation provided above for cooling towers, air washers, wood, textile, paint spray booth and CIP. Specifically, the reasonable worst-case occupational exposure to C(M)IT/MIT as a preservative for other potential liquid cooling and processing system end-uses would not be higher than the exposure scenarios identified above for cooling towers, air washers, etc. treated with C(M)IT/MIT.

2.2.1.4.1.4 Risk characterisation for non professional user's applications of preserved product

Kathon™ WT Biocide is used as a biocide in recirculating liquid cooling and processing systems in industrial applications. The biocide functions as a preservative for these water based recirculating systems. Major industrial applications include cooling towers, air conditioning/air washers, wood treatment solutions, textile processing systems, paint spray booth systems, and industrial hygiene CIP operations. Non-professional and consumer exposure to these treated recirculating systems containing C(M)IT/MIT is not relevant since these products are recommended and sold for industrial/professional use only. Bystander exposure to treated recirculating systems is also considered irrelevant since these operations are conducted in closed buildings or areas with restricted access.

SECONDARY EXPOSURE

2.2.1.4.1.5 Indirect exposure as a result of use of the active ingredient in the biocidal product

The most relevant paths of exposure to C(M)IT/MIT in the product from non professional use are from the dermal, oral and inhalation routes as quantified by total systemic exposure.

A. Indirect or secondary exposure to adult bystander (Cooling towers)

Workers and bystanders around the cooling towers can be exposed to the drift containing the active substance.

In doc IIB a reverse scenario was build to define the characteristics that lead to an acceptable risk (a.i. concentration in the drift < long term AEC 0.02 mg a.i./m^3) of the small / medium / large cooling towers as categorized in the ESD for PT 11[7].

Table 2.2.1.4.1.5-1: Reverse calculation to determined exit surface needed for "ESD" cooling towers

	Cooling tower system			Unit
	Large	Medium	Small	
Recirculating Flow rate	9000	100	10	m^3/h
Exit surface needed to have an acceptable risk of the tower (S_{exit})	37.50	4.17×10^{-1}	4.17×10^{-2}	m^2

To verify if this characteristics can be achieved for "real" cooling tower a comparison was made for small and medium models with cooling towers from the catalogue of one of the main fabricant of cooling tower[8] and as large cooling towers are designed specifically for each process, the example of the cooling tower of the hospital of Lens was used[9].

Table 2.2.1.4.1.5-2: Existing cooling towers parameters, air concentration and maximum acceptable water flow calculations

Cooling tower model	Exit surface (m^2)	Maximal acceptable water flow rate (m^3/h)
FXVD closed cooling tower	13.69 to 18.49	3286 to 4438
FXV-E closed cooling tower	6.76 to 12.96	1622 to 3110
HFL closed cooling tower	3.87 to 13.32	930 to 3197
HXI closed cooling tower	2.88 to 6.48	691 to 1555
PFE/PTE opened/closed cooling tower	4.15 to 10.75	997 to 2581
S3000-D opened cooling tower*	5.27 to 14.32	1264 to 3437
Lens Noroxo Plant cooling tower	120	28800

*normal water flow rate: 108-1008 m^3/h
**normal water flow rate: 3000 m^3/h

[7] 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), European Commission, september 2003.
[8] Baltimore Air Coil: http://www.baltimoreaircoil.eu/products
[9] INERIS report February 2004 « Evaluation de la dispersion atmosphérique d'aérosols potentiellement contaminés dans la région de Lens »

The medium cooling towers proposed by the fabricant have exit surfaces greater than the calculated ones required to reach the $AEC_{long-term}$ of 0.02 mg/m^3 according to the ESD parameters.

For the S3000- opening and the Noroxo plant cooling towers, normal water flow rates were available and the following drift a.i. concentrations were calculated:

	Drift a.i; concentration	**Unit**
S3000-D opened cooling tower (Based on min and max water flow rate)	1.71×10^{-3} to 5.87×10^{-3}	mg a.i./m^3
Noroxo plant cooling tower **	2.08×10^{-3}	mg a.i./m^3

The calculated drift a.i. concentrations are below the long term AEC value of 0.02 mg a.i./m^3 therefore the risk is considered as acceptable for secondary exposure to the drift of cooling towers.

B. Indirect or secondary exposure to air washers

These systems can be considered borderline between PT2 and PT11. These uses have been included in the PT02 dossier already assessed by FR.

C. Indirect or secondary exposure to treated wood

Indirect or secondary dermal, inhalation and/or oral exposure to C(M)IT/MIT residues from treated wood is possible for adults (professionals and non-professionals), children and/or infants who manipulate treated articles.

- Quantitative risk assessment for systemic effects

Table 2.2.1.4.1.5-3: Summary of risk assessment for secondary exposure of adult and infant in contact with treated wood articles (systemic effects – acute exposure)

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Adult (non-professional) – cutting and sanding treated wood - Acute						
Tier 1 : Without PPE	1.05×10^{-2}	11	100	1048	0.11	9.5
Adult (professional) – cutting and sanding treated wood - Chronic						
Tier 1 : without PPE	1.05×10^{-2}	8.6	100	819	0.09	11.7
Adult – inhalation of volatilized residues indoors - Chronic						
Tier 1 : Without PPE	1.66×10^{-3}	8.6	100	5 181	0.09	1.8
Infant – chewing wood off-cut - Acute						
Tier 1 : Without PPE	1.20×10^{-3}	11	100	9 167	0.11	1.1
Infant – inhalation of volatilized residues indoors - Chronic						
Tier 1 : Without PPE	2.16×10^{-3}	8.6	100	3 981	0.09	2.4
Child – playing on playground structure outdoors - Chronic						
Tier 1 : Without PPE	2.00×10^{-2}	8.6	100	430	0.09	22.2
Infant – playing on weathered structure and mouthing – Chronic						
Tier 1 : Without PPE	6.75×10^{-2}	8.6	100	128	0.09	75

* NOAEL corrected by the oral absorption factor of 50%.

No unacceptable risk has been identified for secondary exposure as the MOEs are higher than MOEref (100) and the %AELs are below 100%.

- Quantitative risk assessment for local effects

Inhalation exposure

Table 2.2.1.4.1.5-4: Summary of risk assessment for secondary exposure of adult in contact with treated wood articles (local effects by inhalation route)

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Adult (non-professional) – cutting and sanding treated wood - Acute						
Tier 1 : Without PPE	1.17×10^{-5}	0.34	8	29 060	0.04	0.3
Adult (professional) – cutting and sanding treated wood - Chronic						
Tier 1 : Without PPE	7.03×10^{-5}	0.34	16	4 836	0.02	0.4
Adult – inhalation of volatilized residues indoors - Chronic						
Tier 1 : Without PPE	5.4×10^{-3}	0.34	16	63	0.02	27
Infant – inhalation of volatilized residues indoors - Chronic						
Tier 1 : Without PPE	5.4×10^{-3}	0.34	16	63	0.02	27

No unacceptable risk has been identified for inhalation exposure, the MOE exceeds the MOEref and the %AEL is below 100%.

Concerning local effect by dermal route, exposure with freshly treated wood is not expected and is considered irrelevant.

D. Indirect or secondary exposure to air washer systems

Not evaluated in this dossier (see section 2.2.1.4.1.4).

E. Indirect or secondary exposure to textiles

Secondary exposure to consumers from textiles is considered negligible due to the low treatment levels (6 - 30 ppm a.i.) used to preserved textile processing fluids and because of degradation of the active substance during the manufacturing process.

F. Indirect or secondary exposure to paint spray booths

Secondary exposure to consumers from dried paint is considered negligible due to the low treatment levels (6 - 30 ppm a.i.) used to preserve these recirculating paint systems and because exposure from dried paint is considered insignificant.

G. Indirect or secondary exposure to Industrial hygiene, clean in place

Secondary exposure is considered negligible for industrial hygiene CIP applications since this process is conducted on closed systems (e.g., pipework) at industrial facilities.

H. Indirect exposure to humans via the environment

Exposure to humans via the environment is not considered a relevant route of exposure due to the low production volume of the active substance, its low potential for bioaccumulation and rapid biodegradation.

2.2.1.4.2 Risk characterisation for Acticide® SPX (Thor's product)

PRIMARY EXPOSURE

2.2.1.4.2.1 Production / formulation of active substance

The production/formulation of biocidal products is not covered by the Directive 98/8/EC on the placing of biocidal products on the market. Therefore, this section is not relevant in the Dossier.

2.2.1.4.2.2 Professional use of Acticide® SPX under PT 11

A. Process and Cooling Water (Cooling Towers)

ACTICIDE® SPX is used as preservative for liquid cooling and processing systems. It is used to control the growth of bacteria, algae and fungi in the recirculating water of open (e.g., cooling tower) and closed cooling water systems. This use represents worst-case scenario with the highest concentration for potential exposure during mixing/loading and certain post application scenarios.

Summaries of the risk characterization for C(M)IT/MIT in PT 11.01 (biocidal product containing 1.5% C(M)IT/MIT and process water containing up to 5 ppm C(M)IT/MIT) for the professional user scenarios as described below.

- **Quantitative risk assessment for systemic effects**

Table 2.2.1.4.2.2-1 Summary of risk assessment for professionals when loading water systems and post-application tasks

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Manual loading Acticide SPX in cooling water systems (water treatment service worker) - daily**					
Tier 1 : Without PPE	6.06×10^{-1}	8.6	100	**14**	0.09	**673**
Tier 2: With gloves, RPE and impermeable coveralls	6.18×10^{-3}	8.6	100	1 392	0.09	6.9
Task – time frame:	**Automated Loading in cooling water systems (water treatment service worker) – daily**					
Tier 1: Without PPE	5.52×10^{-3}	8.6	100	1 558	0.09	6.1
Task – time frame:	**Cleaning dispensing pumps (water treatment service worker) – daily**					
Tier 1: Without PPE	8.25×10^{-1}	8.6	100	**11**	0.09	**917**
Tier 2: With gloves and impermeable coveralls	6.81×10^{-2}	8.6	100	127	0.09	76
Tier 2 + rinse: With gloves and impermeable coveralls	3.41×10^{-4}	8.6	100	2.5×10^{4}	0.09	0.38
Task – time frame:	**Cleaning fouled system – every year**					
Tier 1: Without PPE	8.25×10^{-3}	8.6	100	1.1×10^{3}	0.09	0.92
Task – time frame:	**Cooling water monitoring – daily**					
Tier 1: Without PPE	2.75×10^{-4}	8.6	100	3.1×10^{4}	0.09	0.31
Task – time frame :	**Combined = loading + cleaning pumps + equipment maintenance + water monitoring - daily**					
Tier 1 : Without PPE	1.4	8.6	100	**6**	0.09	**1591**
Tier 2: loading +pump cleaning Tier 1: fouled system cleaning and monitoring	7.62×10^{-3}	8.6	100	1.1×10^{3}	0.09	8.5

* NOAEL corrected by the oral absorption factor of 50%.

The risk characterisation for systemic exposure during the manual loading is not acceptable in Tier 1, but is the risk became acceptable when PPE are worn with a MOE (1 392) higher than the MOE_{ref} (100) and a %AEL (6.9) below 100.

Concerning the automated loading, the risk for professionals is acceptable, without any PPE, with a MOE of 1 558 and a %AEL of 6.1.
The risk for the cleaning scenario (cleaning of the dispensing pumps) is considered acceptable, in Tier 2 only. But the risk for cleaning fouled system is acceptable in Tier 1.
The risk during process water monitoring is acceptable in Tier 1 (MOE > MOE_{ref} and %AEL<100).
Finally, concerning the combined exposure the risk is considered acceptable in Tier 2 since MOE (1.1×10^3) is higher than the MOE_{ref} (100) and the %AEL (8.5) is lower than 100.

- **Quantitative risk assessment for local effects**

Inhalation exposure

Table 2.2.1.4.2.2-2 Summary of risk assessment for professionals when loading systems and post-application tasks after repeated inhalation exposure

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref} (sum of AFs)	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Task– time frame :	**Manual loading Acticide SPX in process water system (water treatment service worker) - daily**					
Tier 1 : Without PPE	7.05×10^{-4}	0.34	16	482	0.02	3.5
Task– time frame :	**Automated loading Acticide SPX in process water system (water treatment service worker) - daily**					
Tier 1 : without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Cleaning dispensing pump - daily**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Cleaning fouled system – every year**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Cooling water monitoring – every year**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible

The risk characterisation for inhalation exposure during the loading (manual or automated) only, the various post-applications tasks or during loading combined with the post-applications tasks are acceptable, with a MOE higher than the MOE_{ref} (16). This MOE is obtained by comparing the total inhalation exposure as indicated in Tier 1 with the NOAEC of 0.34 mg a.i./m^3 obtained in a 3 months rat inhalation study where irritancy of the respiratory tract was detected. As well, the $\%AEC_{inhalation}$ is below 100 for the different cases.

- **Qualitative risk assessment for local effects**

Dermal exposure

Table 2.2.1.4.2.2-3 Summary of risk assessment for professionals when loading chilled-water systems and cleaning dispensing pumps after repeated dermal exposure

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task– time frame :	**Automated Loading in cooling water systems (water treatment service worker) – daily**	
Tier 1 : Without PPE	15 000	**15**
Task– time frame :	**Manual Loading in cooling water systems (water treatment service worker) – daily**	
Tier 1 : Without PPE	15 000	**15**
Tier 2: With gloves and impermeable coveralls	15 000	**15**
Task – time frame:	**Cleaning Kathon™ WT dispensing pumps (water treatment service worker) – daily**	
Tier 1 : Without PPE	15 000	**15**
Tier 2: With gloves and impermeable coveralls	15 000	**15**
Tier 2 + rinse: With gloves and impermeable coveralls	150	**15**
Task – time frame:	**Cleaning fouled system – every year**	
Tier 1 : Without PPE	5	**15**
Task – time frame :	**Cooling water monitoring – daily**	
Tier 1 : Without PPE	5	**15**

The concentrations of C(M)IT/MIT used for these exposure scenarios are below the concentration that would lead to sensitization (15 ppm a.i.) for the cleaning fouled system and for the monitoring, but above 15 ppm a.i. for the loading, and the cleaning of the dispensing pumps.

During production, exposure to product is limited to loading operations involving automated or manual systems and cleaning tasks. Therefore, this risk of skin sensitization from C(M)IT/MIT active substance is readily controllable through the use of proper risk mitigation measures when handling formulations. Besides, the use of concentrated formulations is restrained to professional operators, the occurrence of exposure should be considered as accidental and manageable as such.

Therefore, packaging, equipments and procedures, e.g. **automated dosing systems**, should be designed to prevent exposure as much as possible. Moreover, effective skin protection such as gloves, goggles, protective overalls and boots is required under all the

identified scenarios for use of C(M)IT/MIT based products. MSDS and product use instructions shall inform the users of the potential risks and prevention measures.

By using adapted processes, protective equipments and respecting good professional practices, the exposure potential to C(M)IT/MIT based products can be avoided and the risk of adverse health effects can be reduced to an acceptable level.

An approval is therefore still possible, provided such risk mitigation measures are implemented.

2.2.1.4.2.3 Risk characterisation for non professional user's applications of preserved product

ACTICIDE®SPX is registered under PT 11 only for professional use.

SECONDARY EXPOSURE

2.2.1.4.2.4 Indirect exposure as a result of use of the active ingredient in the biocidal product

The most relevant paths of exposure to C(M)IT/MIT in the product from non professional use are from the dermal, oral and inhalation routes as quantified by total systemic exposure.

A. Indirect or secondary exposure to adult bystander (Cooling towers)

Workers and bystander around cooling towers can be exposed to the drift containing the active substance.

In doc IIB a reverse scenario was build to define the characteristics that lead to an acceptable risk (a.i. concentration in the drift < long term AEC 0.02 mg a.i./m^3) of the small / medium / large cooling towers as categorized in the ESD for pt 11.

Table 2.2.1.4.2.4-1: Reverse calculation to determined exit surface needed for "ESD" cooling towers

	Cooling tower system			Unit
	Large	Medium	Small	
Recirculating Flow rate	9000	100	10	m^3/h
Exit surface needed to have an acceptable risk of the tower (S_{exit})	31.25	0.35	0.035	m^2

To verify if this characteristics can be achieved for "real" cooling tower a comparison was made for small and medium models with cooling towers from the catalogue of one of the main fabricant of cooling tower[10] and as large cooling towers are designed specifically for each process, the example of the cooling tower of the hospital of Lens was used[11].

[10] Baltimore Air Coil: http://www.baltimoreaircoil.eu/products

[11] INERIS report February 2004 « Evaluation de la dispersion atmosphérique d'aérosols potentiellement contaminés dans la région de Lens »

Table 2.2.1.4.2.3-2: Existing cooling towers parameters, air concentration and maximum acceptable water flow calculations

Cooling tower model	Exit surface (m^2)	Maximal acceptable water flow rate (m^3/h)
FXVD closed cooling tower	13.69 to 18.49	3943 to 5325
FXV-E closed cooling tower	6.76 to 12.96	1947 to 3732
HFL closed cooling tower	3.87 to 13.32	1116 to 3836
HXI closed cooling tower	2.88 to 6.48	829 to 1866
PFE/PTE opened/closed cooling tower	4.15 to 10.75	1197 to 3097
S3000-D opened cooling tower*	5.27 to 14.32	1517 to 4124
Lens hospital cooling tower	120	34560

*normal water flow rate: 108-1008 m^3/h
**normal water flow rate: 3000 m^3/h

The medium cooling towers proposed by the fabricant have exit surfaces greater than the calculated required ones to reach the $AEC_{long-term}$ of 0.02 mg/m^3 based on the characteristics of the ESD.

For the S3000- opening and the Lens hospital cooling towers, normal water flow rates were available and the following drift a.i. concentrations were calculated:

	Drift a.i; concentration	Unit
S3000-D opened cooling tower (Based on min and max water flow rate)	1.42×10^{-3} to 4.89×10^{-3}	mg a.i./m^3
Lens hospital cooling tower **	1.74×10^{-3}	mg a.i./m^3

The calculated drift a.i. concentrations are below the long term AEC value of 0.02 mg a.i./m^3 therefore the risk is considered as acceptable for secondary exposure to the drift of cooling towers.

2.2.1.5 Overall conclusion of the risk characterization for human health

The active substance (3:1 ratio mixture of C(M)IT/MIT) and formulated product are manufactured in closed processes. Potential exposure to the small number of workers involved in production and/or formulation may occur during product sampling, packaging, equipment cleaning and sample analysis. Routine human contact with C(M)IT/MIT, excluding accidental exposure, does not occur because of the closed nature of the

production/formulation process, because the workers are well informed and trained regarding the hazards and risks of the active substance, and appropriate engineering controls and good industrial hygiene practices are implemented.

The workers, which are using biocidal products in PT11 applications, are well informed about potential health hazards of chemicals used to formulate biocidal concentrate products, well trained for working with hazardous chemicals and routinely wear personal protective equipment. Additionally, good engineering controls and industrial hygiene practices are implemented in these plants, therefore, the potential for worker exposure to C(M)IT/MIT is very limited. The risk during the production/formulation of the biocidal products has not been assessed in this dossier, as it is not in the scope of the Directive 98/8/EC.

C(M)IT/MIT is a skin irritant and has skin sensitization potential. In rare situations where exposure to the a.s. may occur (accidental spills, etc.) plant workers must wear the appropriate personal protective equipment (PPE) to prevent over-exposure and to avoid any potential for skin/respiratory irritation or skin sensitisation.

If appropriate PPE is utilized while handling concentrated biocidal products during formulation, mixing/loading and post application tasks, the exposure concentration is not reduced but only the probability of occurrence. However, the exposure to concentrated products should be prevented.

Therefore, as the product is classified and labelled as corrosive (only for Kathon^{TM}WT) and sensitising, C(M)IT/MIT has to be handled with sufficient risk mitigation measures. Manual mixing and loading of Kathon^{TM} WT and ACTICIDE SPX and post application phases to process fluids presents an unacceptable risk for local effects. However, it is concluded that with automated systems of mixing and loading of Kathon^{TM} WT and ACTICIDE SPX and other risk of mitigation measures, leading to avoid exposure during this task, the complete process presents an acceptable risk for local effects.

Therefore, the RMS considers that biocidal products containing up to 14% C(M)IT/MIT can be used in PT11 applications provided that appropriate risk mitigation measures are applied during the loading of the products and the cleaning phases. Possible measures (not exhaustive list) are:

- The containers of the products are designed to prevent spillages during pouring,
- Automated systems preventing contacts with the product are used for mixing and loading,
- Procedures are implemented to prevent contacts and spillages,
- Chemical-resistant coveralls, gloves, shoes and face-mask are worn during the mixing and loading phase,
- Use is restricted to operators informed of the hazards and formed for safe handling of the products.

Labels, MSDS and use instructions of the products shall inform the users of the hazards and of the protective measures. Written procedures and protective equipments shall be available at the places where the products are handled. The RMMs are summarised in the table below.

In conclusion, the use of C(M)IT/MIT as PT11 can be considered as safe for human health on the basis of the available data, provided adequate risk mitigation measures are implemented for avoiding dermal primary exposure.

Table 2.2.1.5-1: Primary Exposure – Use of concentrated product Kathon™WT– Mixing/Loading and Post application for the formulation of the product containing 5% a.i / the cooling water systems / the wood preservative fluids / the textile process fluids / the paint process fluids / the clean in place (CIP) fluids

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	Potential degree of exposure	Relevant RMM&PPE	Conclusion on risk
Automated transfer or manual loading (industrial or professional workers)										

High	Skin Corr 1B (H314) Skin Sens 1A (H317)	-	11	Industrial users	Disconnecting/connecting lines for automated transfer or insert a dip-pipe or lance into the vessel and draw off product (containing up to 14% a.i) into a day tank for manual transfer pouring	Skin	Daily	<u>Manual loading:</u> Small exposure to spills <u>Semi automated and fully automated loading systems:</u> Accidental exposure to spills during connection of container to the pumping system	**Organizational RMM** • Restriction of manual loading to only small quantities. High quantities should be restricted to semi-automated or automated processes. **Personal protective equipment** • Respiratory protection: Wear respiratory protection if ventilation is inadequate. Combination filter for gases/vapours of organic, inorganic, acid inorganic and alkaline compounds (e.g. EN 14387 Type ABEK). • Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber (0.5 mm), butyl rubber (0.7 mm) and other	Acceptable: + Minimization of manual phases; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

				Professional users	Changing out the dip tube (automated systems) and manual dispensing and loading of the biocidal product (containing 14% a.i) to the sump				Manufacturer's directions for use should be observed because of great diversity of types. • Eye protection: Tightly fitting safety goggles (splash goggles) (e.g. EN 166) • Body protection: Chemical protection clothes type 6 (eg EN 13034) **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	
Cleaning the dispensing pumps (industrial worker and professionals)										
High	Skin Corr 1B (H314) Skin Sens 1A (H317)	-	11	Industrial and professional users	Cleaning of dispensing pumps containing the product (up to 14% a.i.)	Skin	Daily	<u>Maintenance:</u> direct contact with residues	**Organisational RMM** • Rinsing of the system before opening and cleaning. **Personal protective equipment** • Respiratory protection: Wear respiratory protection if ventilation is inadequate. Combination filter for gases/vapours	Acceptable: + Minimization of manual phases; + Rinse step with water of the dispensing pump

									of organic, inorganic, acid inorganic and alkaline compounds (e.g. EN 14387 Type ABEK). • Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber (0.5 mm), butyl rubber (0.7 mm) and other Manufacturer's directions for use should be observed because of great diversity of types. • Eye protection: Tightly fitting safety goggles (splash goggles) (e.g. EN 166) • Body protection: Chemical protection clothes type 6 (eg EN 13034) at minimum for maintenance **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be	before cleaning; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

									inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	

Table 2.2.1.5-2: Primary Exposure – Use of diluted concentration of Kathon™WT – Application and post-application for wood preservative fluids (50 ppm) / paint and textile process fluids (30 ppm)

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	Potential degree of exposure	Relevant RMM&PPE	Conclusion on risk
Industrial Use of fluids (application)										
High	Skin Sens 1A (H317)	-	11	Industrial and professional users	Treatment of wood by different methods (vacuum pressure treatment, double vacuum pressure treatment, and deluge/dipping treatment) / Treatment of textile by mixing, diluting, and machine minding / Spray application of paint	Skin	daily	<u>Automated processes:</u> Accidental exposure to spills <u>"Manual" application:</u> maximum exposure will be in case of paint spraying	**Dosing of the treated process fluid** Reduction of the fluid concentration of use below the threshold value of 15 ppm when possible considering the efficacy (e.g detergents, …) **Personal protective equipment** • Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber (0.5 mm), butyl rubber (0.7 mm) and other Manufacturer's directions for use should be observed because of great diversity of types. • Eye / face protection: Tightly fitting safety goggles (splash goggles) (e.g. EN 166) or face shield could be needed for spraying	Acceptable: + Minimization of manual phases; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

									• Body protection: Chemical protection clothes type 6 (eg EN 13034) at minimum for open processes and up to type 3 for paint spraying. **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	
Cleaning of the equipment (post-application)										
High	Skin Sens 1A (H317)	-	11	Industrial and professional users	Post application phases including cleaning of the dipping tank / cleaning the spray equipment	Skin	once a week	<u>Maintenance:</u> direct contact with residues	**Organisational RMM** • Rinsing of the system before opening and cleaning. **Personal protective equipment** • Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber	Acceptable: + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal

									(0.5 mm), butyl rubber (0.7 mm) and other Manufacturer's directions for use should be observed because of great diversity of types. • Eye / face protection: Tightly fitting safety goggles (splash goggles) (e.g. EN 166) or face shield could be needed for maintenance • Body protection: Chemical protection clothes type 6 (eg EN 13034) at minimum for maintenance **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	hygiene.

Table 2.2.1.5-3: Primary Exposure – Use of concentrated product of ACTICIDE SPX – Mixing/Loading and Post application for the cooling water systems

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	Potential degree of exposure	Relevant RMM&PPE	Conclusion on risk
Automated or manual loading in cooling water system (mixing and loading)										
High	Skin Sens 1A (H317)	-	11	Professional users	Changing out the dip tube (automated systems) and manual dispensing and loading of the biocidal product (containing 1.5% a.i) to the sump	Skin	daily	<u>Manual loading:</u> Small exposure to spills <u>Semi automated and fully automated loading systems:</u> Accidental exposure to spills during connection of container to the pumping system	**Organizational RMM** • Restriction of manual loading to only small quantities. High quantities should be restricted to semi-automated or automated processes. **Personal protective equipment** • Respiratory protection: Wear respiratory protection if ventilation is inadequate. Combination filter for gases/vapours of organic, inorganic, acid inorganic and alkaline compounds (e.g. EN 14387 Type ABEK). • Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber (0.5 mm), butyl rubber (0.7 mm) and other Manufacturer's directions for use should be observed because of great	Acceptable: + Minimization of manual phases; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

									diversity of types. ○ Eye protection: Tightly fitting safety goggles (splash goggles) (e.g. EN 166) • Body protection: Chemical protection clothes type 6 (eg EN 13034) **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks)	
Cleaning of the dispensing pump (post-application)										
High	Skin Sens 1A (H317)	-	11	Industrial and professional users	Cleaning the dispensing pump for maintenance, inspecting the interior of cooling tower, sampling the process liquid (dip slide), and	Skin	daily	<u>Maintenance:</u> direct contact with residues	**Organisational RMM** • Rinsing of the system before opening and cleaning. **Personal protective equipment** • Respiratory protection: Wear respiratory protection if ventilation is inadequate. Combination filter for gases/vapours of organic, inorganic, acid inorganic and alkaline compounds (e.g. EN 14387 Type ABEK).	Acceptable: + Professionals using PPE; + Rinse step with water of the dispensing pump before cleaning;

					disposal of waste				• Hand protection: Suitable chemical resistant safety gloves (EN 374) also with prolonged, direct contact (Recommended: Protective index 6, corresponding > 480 minutes of permeation time according to EN 374): E.g. nitrile rubber (0.4 mm), chloroprene rubber (0.5 mm), butyl rubber (0.7 mm) and other Manufacturer's directions for use should be observed because of great diversity of types. • Eye protection: Tightly fitting safety goggles (splash goggles) (e.g. EN 166) • Body protection: Chemical protection clothes type 6 (eg EN 13034) at minimum for maintenance **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks)	+ Professionals following instructions for use; + Good standard of personal hygiene.

2.2.2 Environment risk assessment

2.2.2.1 Fate and distribution in the environment

2.2.2.1.1 Hydrolysis as a function of pH

In the environmental conditions (12°C, pH7), C(M)IT and MIT are considered as stable. C(M)IT and MIT are considered as hydrolytically stable in the test conditions at pH 4, 5 and 7. However at pH 9, C(M)IT hydrolyses at a moderate rate with an extrapolated half-life of 47.81 (Dow Chemical) – 120.6 (Thor) days at 12°C whereas MIT remains stable to hydrolysis..

2.2.2.1.2 Photolysis in water

C(M)IT and MIT photodegrade in water and natural sunlight at a moderate rate with half-lives of 6.6 and 18.2 days, respectively for C(M)IT and MIT.

2.2.2.1.3 Photolysis in air

C(M)IT and MIT photodegrade quickly with a highest DT_{50} of 17.5 hours for C(M)IT. The DT_{50} for MIT corresponds to 16.6 hours. Due to very low production and usage volume, the effect from C(M)IT, MIT and its potential photodegradation products towards global warming is minimal. Therefore, C(M)IT, MIT and its photodegradation metabolites impose no effect to global warming.

2.2.2.1.4 Biodegradation

In the Dow Chemical dossier, the readily biodegradation of the active substance was studied in separate tests for C(M)IT and MIT. C(M)IT is classified readily biodegradable with a failure of the 10-day window and MIT is classified as not readily biodegradable according to the criteria of the test, although significant biodegradation occurred. In the Thor dossier, adaptation of the inoculum used in the ready biodegradation test cannot be excluded and C(M)IT/MIT is therefore considered as not readily biodegradable.

Nevertheless, the biotic degradation of C(M)IT and MIT appears as the major metabolic pathway in simulation tests compared to abiotic degradation which is less rapid than biodegradation.

For the risk assessment, available STP simulation results for C(M)IT, and MIT were considered. For C(M)IT, results show that no parent compound was detected in the effluent phase or in the sludge, C(M)IT was considered to be totally degraded in the STP and no emission of this compound in the different environmental compartments from the STP was foreseen. The only compound considered at the outlet of the STP was MIT. The fractions of MIT emission directed to water through effluents from the STP were 12.2% of MIT. No quantification of MIT in sludge has been carried out. Nevertheless, 6.6% of not identified radioactivity were detected in the sludge, and considered as MIT in a worst case approach. Besides, the half life of MIT has been determined to be 0.04 days.

Provided simulation studies were carried out on C(M)IT and MIT separately. Half life derived for MIT were harmonised with the values available in the MIT dossier by Slovenia. When necessary, other half life have been derived according to FOCUS recommendations leading to different half life for PEC calculations and for persistency assessment when simple first order do not apply to the experimental data. Additionally, in some aquatic

studies, two concentrations of chemicals were tested, leading sometimes to observed toxicity. In this case two half live have been derived for the considered compartment. All these values were reported in the table below.

PBT assessment, DT50, 12°C			
compartment	**C(M)IT**	**MIT**	**C(M)IT/MIT**
Water sediment	2.22 d	2.21 d	2.22 d
Estuarine (<20 µg/L)	1.49 d	2.63 d	2.63 d
Estuarine (>20µg/L)	5.82 d		5.82 d
Marine (<10 µg/L)	3.4 d (4.3 d at 9°C)	6.3 d (8.0 d at 9°C)	6.3 d (8.0 d at 9°C)
Marine (>10µg/L)	32.8 d (41.7 d at 9°C)	23.3 d (29.7 d at 9°C)	32.8 d (41.7 d at 9°C)
Soil	0.21 d	0.51d	0.51 d
PEC calculation, DT50, 12°C			
compartment	**C(M)IT**	**MIT**	**C(M)IT/MIT**
Estuarine (<20 µg/L)	1.49 d	2.63d	2.63d
Estuarine (>20µg/L)	5.82 d		5.82 d
Marine (<10 µg/L)	3.4 d (4.3 d at 9°C)	15.7 d (20.0 d at 9°C)	15.7 d (20.0 d at 9°C)
Marine (>10µg/L)	32.8 d (41.7 d at 9°C)	23.3 d (29.7 d at 9°C)	32.8 d (41.7 d at 9°C)
Soil	1.48 d	0.51 d	1.48 d

In aquatic compartment, no biodegradation test in fresh water was provided by both applicants. Thus, estuarine water was considered as realistic worst case for biodegradation in fresh water. Indeed, for a same range of tested concentration, biodegradation estuarine water, with a lower salinity than marine water, was faster than the biodegradation in marine water and probably slightly slower than in fresh water. Half life in the water sediment system are provided for the whole system which appears as relevant considering the low adsorption capacities of C(M)IT and MIT. This is confirmed in the Thor dossier, where similar half life are observed for the whole system and the water compartment.. Half life derived from the water sediment studies are in the same range than half life from the estuarine studies.

In soil, C(M)IT and MIT rapidly dissipate following a biphasic kinetic. Higher degradation rates are observed during the first 48h of the studies (sometimes less than 2 days, Dow chemical) and after this first rapid degradation, slower degradation rates are observed. Half lives are determined with a value of 1.48 days at 12°C for C(M)IT and a value of 0.51 day at 12°C for MIT.

2.2.2.1.5 Distribution

In adsorption tests, C(M)IT and MIT are weakly adsorbed to soil and activated sludge with Koc values less than 310 for Ka_{oc} and less than 421 for K_{doc}. This indicates that in sewage treatment plant, the active substance would probably be predominant in the water phase. If present in surface water, C(M)IT and MIT will partition mostly in the water column and will probably not accumulate in sediments. In soil, C(M)IT and MIT may have a potential for leaching, but the quick biodegradation of the substances in soil observed in the first 48 h of the biodegradation test in the Dow chemical dossier (half life <2 days) and the similar results reported in the Thor Dossier indicate the risk for groundwater should be low. The Koc values used for risk assessment are 83.2 L/kg for C(M)IT and 7.5 L/kg for MIT (arithmetic mean).

2.2.2.1.6 Metabolites

Identification of metabolites was only carried out in the Dow Chemical Dossier. In the environment, C(M)IT and MIT rapidly dissipate to compounds which are in turn quickly biodegraded, indicating that persistence in the environment should be minimal. Among the principal metabolites of C(M)IT/MIT, a key metabolite has been identified and tested: N-methyl malonamic acid. It has been shown experimentally to be ready biodegradable. The other degradation products are all transient, reach their peak concentration in the first sampling times and quickly become less than 10% of applied radioactivity, generally after 5 to 10 days and in all cases by day 30. To confirm this, QSARs are conducted on these compounds and confirmed these metabolites are expected to be quickly biodegraded.

2.2.2.1.7 Accumulation

With a log Kow value for C(M)IT and MIT below 3 (log Kow = 0.401, C(M)IT –Dow Chemical), the potential of bioaccumulation or biomagnification of C(M)IT and MIT could be considered as negligible. Measured bioconcentration factor for C(M)IT was ≤ 54 which confirms that the bioconcentration potential of C(M)IT/MIT is very low. Furthermore according to the toxicokinetics, metabolism and distribution data provided in the toxicological section (2.2.1), the active substance is rapidly and extensively metabolized and is not considered to have an accumulative potential in food chain. At last, based on log Kow values, metabolites identified in the simulation studies are expeted to have a low potential of bioaccumulation.

2.2.2.2 Effects assessment on environmental organisms (active substance)

For each environmental compartment, the PNECs for active ingredient C(M)IT/MIT are presented in this section. Furthermore, as the risk assessment for the environment is almost based on MIT when releases to STP are considered,, the PNECs for active ingredient MIT issued from the MIT dossier evaluated by Slovenia are also indicated in this section. Experimental data and QSAR have been provided for the metabolites which have been identified in simulation studies and are reported in document IIA. These data indicate that metabolites are less toxic than parent substance.

2.2.2.2.1 Aquatic compartment (including water, sediment and STP)

Aquatic organisms

Available valid aquatic ecotoxicological data provided by the two applicants (Dow Chemical and Thor) have been used to derive the PNEC for the aquatic (freshwater) compartment. Additionally, as the species sensitivity between freshwater and marine fish and algae is within a factor of 10, data from fresh and marine water have been pooled to derive the PNEC for the aquatic (freshwater) compartment.

The most sensitive endpoint is the NOEC value based on geometric mean measured concentration from growth inhibition test performed by Dow Chemical on marine algae, *Skeletonema costatum*.

Hence, **the PNEC $_{\text{fresh surface water}}$ is estimated to be 0.049 µg a.i./L** since a safety factor of 10 according to the TGD[12] should be applied to the lowest endpoint for aquatic environment when chronic data for three trophic levels are available. For marine water, an assessment factor of 50 has been applied as no additional chronic data on marine taxonomic group were provided and as acute data on molluscs indicate that algae are the most sensitive species. **The PNEC$_{\text{marine water}}$ is therefore estimated to be 0.0098 µg a.i./L.**

For **MIT**, the PNEC$_{\text{fresh surface water}}$ is estimated to be **3.9 µg/L**; based on E_rC_{10} value of 0.039 mg/L (geometric mean from two studies on marine algae, *Skeletonema costatum*) divided by an assessment factor of 10.

Inhibition of aquatic microbial activity

In order to prevent adverse effects of C(M)IT/MIT on microbial activity in STPs, a PNEC$_{\text{microorganisms}}$ is derived from the respiration inhibition test according to the OECD guideline 209. The NOEC obtained (0.91 mg a.i./L) divided by an assessment factor of 10 leads to a PNEC$_{\text{microorganisms}}$ of 0.091 mg/L whereas the lowest EC50 (4.5 mg a.i./L) divided by an assessment factor of 100 leads to a lower **PNEC$_{\text{microorganisms}}$ of 0.045 mg/L**. During the WGI2014, it was discussed if, in this case, the lowest PNEC should be selected for the risk assessment. No clear agreement could have been obtained and it was decided to choose the lowest PNEC as the most conservative approach, expecting further discussions on the interpretation of the TGD**.**

The PNEC$_{\text{microorganisms}}$ for MIT is considered (issued from MIT dossier) to be **PNEC$_{\text{microorganisms}}$ = 0.23 mg/L, issued** from an EC_{50} of 2.3 mg/L (growth inhibition test with *Pseudomonas putida*, ISO 10712) and an assessment factor of 10.

Sediment dwelling organisms

The study considered relevant for the risk assessment has been conducted by Dow with *Lumbriculus variegate*s exposed to C(M)IT/MIT spiked sediment and provides a NOEC (28d, survival, initial) of 1.93 mg/kg (equivalent to 0.27 mg a.i./kg) dry $_{\text{weight sediment}}$. A safety factor of 10 is applied, resulting in a **PNEC$_{\text{sed}}$** of 0.027 mg a.i./kg$_{\text{dry sediment}}$ corresponding to **0.0058 mg a.i./kg$_{\text{wet sediment}}$.**

According to the TGD, as the log Kow values of both substances (C(M)IT and MIT) are < 3 and the Koc values for both substances are < 500 L/kg, sediment effects assessment is not considered as relevant for this active substance.

[12] European Commission (2003): Technical Guidance Document on Risk Assessment. European Commission Joint Research Centre, EUR 20418.

2.2.2.3 Atmosphere

No risks are expected due to high degradability and low volatility of C(M)IT/MIT. Additionally, C(M)IT and MIT are not listed on Annex I of Directive 1005/2009 and are therefore not considered to be ozone depleting substances.

2.2.2.4 Terrestrial compartment

For the terrestrial compartment, NOEC values from long-term toxicity tests on soil microorganisms, are available. A NOEC has been derived from the plant study however, as, acutely, plants are the most sensitive species therefore this study could not be considered as chronic according to MOTA v6. Therefore, an assessment factor of 100 is applied to the lowest NOEC, which was the result of respiration test (28d) on microorganisms (NOEC = 1 mg a.i./kg_{dw}, initial) lead to a **$PNEC_{soil}$** of 0.01 mg a.i./$kg_{drysoil}$ corresponding to **0.009 mg a.i./$kg_{wet\ soil}$**.
As stated at the 32nd Competent Authority meeting, as degradation half-life is < 2 days, for the risk assessment the initial PNEC is compared to the initial PEC calculated without taking into account any degradation. Nevertheless, for intended uses leading to continuous release to the soil, PNEC twa has been calculated to be 0.0004 mg a.i./$kg_{wet\ soil}$ taking into account of a half life in soil of 0.78 d at 20°C.

For release through the spreading of STP sludge,, the initial $PNEC_{soil}$ for MIT is considered to be **PNEC soil = 0.0417 mg/$kg_{wet\ soil}$** from EC_{50} of 18 mg/kg $_{dry\ soil}$ issued from a plant tests and an assessment factor of 1000 (issued from MIT dossier).

2.2.2.5 Summary of PNEC values

Table 2.2.2.5-1: Summary of the selected PNEC values used for the risk characterisation part

ENVIRONMENTAL COMPARTMENT	PNEC		Unit
	C(M)IT/MIT	MIT	
$PNEC_{fresh\ surface\ water}$	0.049	3.9	µg a.i./L
$PNEC_{marine\ water}$	0.0098	-	µg a.i./L
$PNEC_{stp}$	0.045	0.23	mg a.i./L
$PNEC_{soil,\ initial}$	0.009	0.0417	mg a.i./kg_{wwt}
$PNEC_{soil,\ TWA}$	0.0004	-	mg a.i./kg_{wwt}

2.2.2.6 Environmental effect assessment (product)

No additional data on the environmental effects of the biocidal products were submitted. The risk assessment is based on the effect of the active substance C(M)IT/MIT.

2.2.2.7 PBT Assessment and endocrine properties

According to the PBT assessment in the Annex XIII from the REACH regulation, substances are classified when they fulfil the criteria for all three inherent properties Persistent, Bioaccumulable, Toxic.

2.2.2.7.1 Persistance criteria

According to the PBT assessment in the Annex XIII from the REACH regulation, criteria for substance to be persistent are fulfilled when:

- T 1/2 in marine water > 60 days or,
- T 1/2 in freshwater > 40days or,
- T 1/2 in marine: sediment > 180 days or,
- T 1/2 in freshwater: sediment > 120 days, or $T_{1/2}$ in soil > 120 days.

In simulation tests, the degradation half-lives of both substances in aerobic estuarine water microcosm and in aerobic and water/sediment are less than 6 days (12°C). Considering these data, the active substance C(M)IT/MIT does not fulfilled the P criteria. Relevant metabolites are shown to be either readily biodegradable or transient and are therefore considered to be not persistent.

2.2.2.7.2 B criteria

According to the PBT assessment in the Annex XIII from the REACH regulation, a substance is considered to fulfill the B criterion when the bioconcentration factor (BCF) exceeds a value of 2 000 L/kg.
The potential of bioaccumulation of C(M)IT measured from a study conducted in fish (Bluegill sunfish) according to OECD 305 guideline is considered as very low ≤ 54. Because of the log Kow value for MIT is lower than the log Kow value for C(M)IT, and taken into account the results of the previous study, the bioaccumulation potential for MIT will be minimal.
Considering these data, the active substance C(M)IT/MIT is no selected according to the B criteria.

2.2.2.7.3 T criteria

According to the PBT assessment in the Annex XIII from the REACH regulation, the toxicity criterion is fulfilled when the chronic NOEC for aquatic organism is less than 0.01 mg/L or when the substance is toxic to mammals and classified as Very Toxic or Toxic after oral dosing.
Based on ecotoxicity data on *Skeletonema costatum*, NOErC (48-hour, growth inhibition) = 0.49 µg a.i./L (static, measured concentrations), T criteria is fulfilled.

As only one of these P, B, T criteria is fulfilled, the active substance C(M)IT/MIT is not classified according the PBT assessment.

2.2.2.8 Environmental exposure

The risk characterisation has been carried out for the representative product of the each applicant: Kathon™ WT (Dow) and ACTICIDE® SPX (Thor). Several metabolites have been

identified in simulation studies. However, based on their lack of persistence, low potential for bioaccumulation and their low toxicity, it is concluded that the potential for adverse environmental effects in response to exposures to the C(M)IT/MIT metabolites is considered negligible. Then no risk assessment on metabolites of C(M)IT/MIT has been conducted.

The main intended uses for Kathon™ WT and ACTICIDE® SPX are applications in the circulating water of open and closed cooling water systems. In the Dow Chemical dossier, several applications in processing systems, other than liquid cooling systems, have been intended: air washing systems and air conditioning, wood preservative treatment solution, photographic processing, print fountain solutions, textile processing, paint spray booths and electrodeposition coating systems (car refinishing and original equipment manufacturing (OEM) car manufacture), industrial hygiene (cleaning in place) and other minor uses (process fluids used for non-food pasteurizers/sterilizers/can warmers, reverse osmosis or ultrafiltration membranes (non-food, non potable water, non-medical), wastewater treatment, rinse baths, and conveyor lubricants (outside the food industry)).
A consumption approach has been applied to assess the environment exposure following the application in cooling systems, using the ESD PT11[13]. Shock and continuous treatments have been intended for these applications. In the absence of reliable data on the biodegradation of the active substance in the systems and considering that only continuous doses have been validated in the efficacy section, only exposure from application of continous doses in cooling systems have been assessed. . Air conditionning and air washing systems have been considered as covered by the scenarios developed for the cooling towers.
For the other uses in processing systems intended by Dow Chemical, a tonnage approach has been developed.

According to the applicant, Kathon™ WT (Dow) is used at concentrations from 1 to 6 mg a.i. L^{-1}) in cooling systems and from 1 to 50 mg a.i. L^{-1}) in the other process fluids. Additionally, the efficacy of the active substance has been demonstrated for a concentration of 1 to 50 mg a.i. L^{-1} in function of the breadth of the disinfection spectrum. Therefore, exposure and risk assessments for cooling systems have been carried out for the intended used concentrations (i.e. 1 to 6 mg a.i. L^{-1}), and information dealing with the risk following the use at higher concentrations is also reported. For the other uses, the maximal intended dose rates were considered for the risk assessment.
ACTICIDE® SPX (Thor) is intended to be used at concentration from 0.2 to 1 mg a.i. L^{-1}; however, since the efficacy has been demonstrated for a concentration of 0.6 to 5 mg a.i. L^{-1} the lowest dose intended by the applicant (0.2 mg L^{-1}) and the highest dose considered as efficient (5 mg L^{-1}) have been taken into account for the exposure and risk assessments for cooling systems.

2.2.2.9 Cooling water systems

The assessment has been focused on the small and large open re-circulating cooling systems since these applications are considered to represent the worst case systems for the environmental compartment compared to the closed systems.
For the large open recirculating systems, discharge to a STP is not considered realistic in view of the large volume of water used and only a direct release to water through the blowdown, to air through the drift and to soil through the deposition have therefore been assumed. For the small open recirculating systems, both direct release to surface water and indirect release via the STP have been considered. For these small systems the

[13] Harmonisation of environmental emission scenarios for biocides used as preservatives for liquid cooling systems, European Commission DG ENV/RIVM, September 2003.

contamination of atmosphere and terrestrial compartment was considered to be only relevant for the indirect releases via the STP, following the assumption from the ESD PT11.

The use of Kathon™ WT Biocide and ACTICIDE® SPX as preservatives in cooling systems has been evaluated via exposure analysis based on the specific Emission Scenario Document for PT11[14]. The ESD provides detailed information on the method of determining the emission rate of C(M)IT/MIT to the environment for both large and small open recirculating cooling systems. To determine the predicted environmental exposure concentrations in water, air, soil and groundwater compartments, equations from the TGD were used.

A tiered approach has been considered when the releases were directed to the STP:

In **Tier I**, considering the STP simulation results based on C(M)IT, showing that no parent compound was detected in the effluent phase or in the sludge, C(M)IT was considered to be totally degraded in the STP and no emission of this compound in the different environmental compartments from the STP was foreseen. The only compound considered at the outlet of the STP was MIT. The fractions of MIT emission directed to water and to sludge from the STP were defined from the simulation tests in aerobic sewage treatment for MIT:

- the fraction of MIT emission directed to water by STP was considered as 0.122,
- the fraction of MIT emission directed to sludge by STP was considered as 0.066.

The Tier I risk assessment has been carried out considering a ratio PEC_{MIT} / $PNEC_{MIT}$.

In **Tier II (only for soil and groundwater compartments),** considering the half-life value of 0.04 days derived of the STP simulation study on MIT and in coherence with the MIT dossier, the fraction of MIT emission directed to sludge by the STP was considered as 7.18E-04.
The Tier II risk assessment has been carried out considering a ratio PEC_{MIT} / $PNEC_{MIT}$.

In fact, the fraction of MIT emission directed to sludge in the STP of 0.066 proposed in the Tier I assessment was considered to be a large overestimation considering the low potential of adsorption of MIT (Koc = 7.5 $L.kg^{-1}$). In the simulation study in STP, the fraction of 6.6% in the sludge represented the total radioactivity measured in this compartment and not the parent compound only. The default value of the fraction adsorbed onto sludge given by Simple Treat model (Fstp sludge = 0.0718%) seems to be more realistic for the active ingredient MIT.

According to the TGD, as the log Kow values of both substances (C(M)IT and MIT) are < 3 and the Koc values for both substances are < 500 L/kg, sediment effects assessment is not considered as relevant for this active substance. No sediment risk assessment is needed.

Risk characterisation

To carry out a quantitative risk assessment for the environment when Kathon™ WT and ACTICIDE® SPX are used as a preservative to control microbial contamination in cooling

[14] Harmonisation of environmental emission scenarios for biocides used as preservatives for liquid cooling systems, European Commission DG ENV/RIVM, September 2003.

systems (PT11), the PEC values were compared to the respective PNEC values for the different compartments, resulting in the following PEC/PNEC ratios.

When direct releases to the environment occur, the $PEC_{C(M)IT/MIT}/PNEC_{C(M)IT/MIT}$ ratios have been considered whereas the $PEC_{MIT}/PNEC_{/MIT}$ have been derived when releases occur through the STP.

Table 2.2.2.9-1: PEC/PNEC values for Kathon™ WT and ACTICIDE® SPX use – Large cooling tower process fluids, not connected to a STP, direct release to surface water

Large cooling tower process fluids	**$PEC_{C(M)IT/MIT}$ / $PNEC_{C(M)IT/MIT}$ ratio**			
	0.2 mg a.i L^{-1} ACTICIDE® SPX (Thor)	1 mg a.i L^{-1} Kathon™ WT (Dow Chemical)	5 mg a.i L^{-1} ACTICIDE® SPX (Thor)	6 mg a.i L^{-1} Kathon™ WT (Dow Chemical)
Sewage treatment plant	n.r.	n.r.	n.r.	n.r.
Surface water[a]	**4.1**	**20**	**102**	**122**
Sediment	n.r.	n.r.	n.r.	n.r.
Grassland Soil[b]	**8.9**	**45**	**223**	**268**
Groundwater	**>> 0.1 µg/L**	**>> 0.1 µg/L**	**>> 0.1 µg/L**	**>> 0.1 µg/L**
Air	n.r	n.r	n.r	n.r

n.r. = not relevant

[a] Considering the maximum dilution factor of 1000

[b] steady state PECs, considering deposition derived from total amount in the system. Higher PEC were derived from deposition as a function of air releases.

Table 2.2.2.9-2: PEC/PNEC values for Kathon™ WT and ACTICIDE® SPX use – Small cooling tower process fluids, not connected to a STP, direct release to water

Small cooling tower process fluids, not connected to a STP	**$PEC_{C(M)IT/MIT}$ / $PNEC_{C(M)IT/MIT}$ ratio**			
	0.2 mg a.i L^{-1} ACTICIDE® SPX (Thor)	1 mg a.i L^{-1} Kathon™ WT (Dow Chemical)	5 mg a.i L^{-1} ACTICIDE® SPX (Thor)	6 mg a.i L^{-1} Kathon™ WT (Dow Chemical)
Sewage treatment plant	n.r.	n.r.	n.r.	n.r.
Surface water[a]	**10.9**	**54**	**272**	**326**
Sediment	n.r.	n.r.	n.r.	n.r.
Agricultural Soil	n.r.	n.r.	n.r.	n.r.
Groundwater	n.r.	n.r.	n.r.	n.r.
Air	n.r.	n.r.	n.r.	n.r.

n.r. = not relevant

[a] Considering the maximum dilutin factor of 1000

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Table 2.2.2.9-3: - PEC/PNEC values for Kathon™ WT and ACTICIDE® SPX use – Small cooling tower process fluids, connected to a STP

TIER 2- Small cooling tower process fluids, connected to a STP	**PEC_{MIT} / $PNEC_{MIT}$ ratio**			
	0.2 mg a.i L^{-1} ACTICIDE® SPX (Thor)	1 mg a.i L^{-1} Kathon™ WT (Dow Chemical)	5 mg a.i L^{-1} ACTICIDE® SPX (Thor)	6 mg a.i L^{-1} Kathon™ WT (Dow Chemical)
Sewage treatment plant	0.0006	0.003	0.016	0.019
Surface water	0.004	0.02	0.09	0.11
Sediment	n.r.	n.r.	n.r.	n.r.
Agricultural Soil	0.01	0.039	0.20	0.236
Groundwater	< 0.1 µg/L	< 0.1 µg/L	**0.134 µg/L** (0.001 µg/L*)	**0.160 µg/L** (0.002 µg/L*)
Air	n.r	n.r	n.r	n.r

n.r. = not relevant

* Tier 2 exposure assessment

2.2.2.9.1 Aquatic compartment

In the case of large open recirculating system and small open recirculating system with direct release into the river, estimated risks from use of Kathon™ WT or ACTICIDE® SPX as preservative are considered as unacceptable for the aquatic organisms, whatever the dose rates applied. For the large open recirculating tower, it is worth noting that the exposure assessment has been carried out considering a dilution factor of 1000 which is, according to the TGD, the highest dilution factor which can been applied.

For the small open recirculating systems connected to a STP, in Tier 1 approach, estimated risks from use of Kathon™ WT or ACTICIDE® SPX as preservative are considered as unacceptable for the aquatic organisms, whatever the dose rates.
Estimated risks from use of Kathon™ WT or ACTICIDE® SPX as preservative in small open recirculating systems connected to a STP are considered as acceptable at minimal and maximal intended dose rates. Additionally, it should be noted that acceptable risk would have been obtained with the highest dose validated in the efficacy section of the Dow Chemical dossier (50 mg a.i. L^{-1}); the risk remains acceptable only up to a dose of 15.4 mg a.i. L^{-1}.

2.2.2.9.2 Sewage treatment plant

Estimated risks from the use of Kathon™ WT or ACTICIDE® SPX as preservative in small open recirculating systems connected to a STP are considered as acceptable for the organisms involved in the biological processes of the sewage treatment works.

2.2.2.9.3 Atmosphere

The proposed uses of C(M)IT/MIT biocidal products in the EU (i.e. as preservative in open recirculating cooling systems) are predicted to result in no or low concentrations in air in the case of the small open recirculating systems (see Document IIB, Section 3). Moreover, the degradation rate in air for C(M)IT/MIT, indicates a rapid degradation of CMIT and MIT and the resulting concentrations in air are expected to be low. Additionally, according to the Reference Document on the application of Best Available Techniques to Industrial

Cooling Systems (European Commission December 2001), the use of standard droplet separators allow to limit the fraction of water loss by drift to 0.01% and lower initial concentrations of active substance in air are thus expected.

2.2.2.9.4 Terrestrial compartment

The terrestrial compartment is exposed through two different ways: direct contamination through the drift deposition, and indirect contamination through the spreading of the STP sludge.

Direct contamination only occurs after the use of Kathon™ WT or ACTICIDE® SPX as preservative in large open recirculating cooling systems. In this case, the values calculated for the grassland are twice higher than those calculated for agricultural soils and have therefore been chosen for the risk assessment. Additionally, a steady state PEC value has been calculated because of the continuous drift deposition and the lack of accumulation of the active substance in soil. The steady state PECs are compared to a time weighted average PNEC value. According to the ESD, deposition to the soil can be calculated either directly from the total amount in the system applying a deposition factor of 0.025 or from the predicted release in air according to equations from TGD. The latter method of calculation appears as a worst case, even considering the use of a standard droplet separator as a mitigation measure which could lead to a decrease of emission to air by a factor 100. Even with the method of calculation leading to the lowest PECs (deposition of 0.025%), the risk coefficient ratios are high (from 9 to 268) andindicate unacceptable risk for terrestrial organisms.

Indirect contamination results from use of Kathon™ WT or ACTICIDE® SPX as preservative in small open recirculating cooling systems only. Initial PECs are calculated in soil and compared to an initial PNEC value. The risk can be considered as acceptable for a the use of Kathon™ WT or ACTICIDE® SPX as preservative in small open recirculating cooling systems whatever the dose rates considered for the assessment. Additionally, it should be noted that unacceptable risk would have been obtained with the highest dose validated in the efficacy section of the Dow Chemical dossier (50 mg a.i. L^{-1}); the risk remains acceptable only up to a dose of 25.6 mg a.i. L^{-1}. Nevertheless, acceptable risk would have been obtained when considering the fraction of MIT adsorbed on sludge according to Simple treat model (Tier II).

2.2.2.9.5 Groundwater

Direct contamination soil through air drift deposition following use of Kathon™ WT or ACTICIDE® SPX as preservative in large open recirculating cooling systems results in unacceptable risks for groundwater whatever the dose rates and the method of calculation of deposition and of groundwater concentration including FOCUS assesssment.

Considering the simulation studies in STP demonstrating that only MIT is released in the sludge of the STP, the concentration in porewater under agricultural soil (surrogate for groundwater) is < 0.1 µg/L set up for directive 98/83/EC only for the Kathon™ WT or ACTICIDE® SPX as preservative in small open recirculating cooling systems at the minimal concentrations of 0.2 and 1 mg L^{-1}. For the maximal concentrations (5 and 6 mg L^{-1}), the concentration in porewater under agricultural soil is slightly higher than 0.1 µg/L (0.16 µg/L and 0.13 µg/L) set up for directive 98/83/EC. Nevertheless, due to the low potential of adsorption of MIT and the ready biodegradability of the molecule, the risk is probably overestimated by the use of a fraction adsorbed onto sludge of 6.6%. In fact in the simulation study in STP with radoilabelled MIT, the fraction of 6.6% in the sludge represented the total radioactivity measured in this compartment and not the parent compound MIT only. Therefore, the default value of the fraction adsorbed onto sludge given by Simple Treat model considering the degradation rate from the simulation study

has been used in a Tier 2 approach (Fstp sludge = 7.18E-04). The resulting risk for groundwater should be considered as acceptable for maximal concentrations following application in the small open recirculating cooling systems..

2.2.2.9.6 Conclusion for cooling water systems

The use of ACTICIDE® SPX or Kathon™ WT as preservative in large open recirculating systems results in unacceptable risk for the aquatic and terrestrial organisms whatever the dose rates considered. Refinement of some assumptions of the assessment, such as a higher flow rate for the river, or a lower emission to the air thanks to use of standard droplet separators[15] do not allow to decrease the PEC values sufficiently to obtain acceptable risk.

The use of ACTICIDE® SPX or Kathon™ WT as preservative in small open recirculating system with direct release into the river also results in unacceptable risk for the surface water, whatever the dose rate in the systems.

The use of ACTICIDE® SPX or Kathon™ WT as preservative in small open recirculating system with release to STP results in acceptable risk for all the environmental compartments. As the scenario for small open recirculating system covers the use of the substance in closed systems and in air cleaning and washing systems, the risks are also considered acceptable for these two uses.

2.2.2.10 Other uses in processing systems

Several uses as preservatives in liquid processing systems, other than cooling systems have been intended by Dow. The environmental risk assessment following these specific uses has been carried out through a tonnage approach following the TGD[16]. Risks resulting from the addition of the active substance to these systems (called "formulation") and from the industrial use in these systems have been assessed. Additionally, the in-use phase of the wood treated with a solution containing C(M)IT/MIT has been evaluated.
Concerning the formulation and the industrial use of the substance, direct emissions to the air and to the STP through the waste water have been considered..
Emissions to the air result in very low or no concentrations of the active substance in the air and no further risk assessment has thus been performed.
Concerning the in-use phase of treated wood, the three worst case scenarios have been assessed: house (worst case for soil), noise barrier (worst case for the STP) and sheet piling (worst case for water) considering two types of treatment (by impregnation and by surface treatment).
The tables below present the results of these evaluations for each relevant environmental compartment.

Table 2.2.2.10-1 : PEC/PNEC indication for Kathon™ WT used in liquid processing systems different from cooling systems, formulation and industrial use stages

[15] According to the Reference Document on the application of Best Available Techniques to Industrial Cooling Systems (European Commission December 2001), the use of standard droplet separators allows to limit the fraction of water loss by drift to 0.01%

[16] Technical Guidance Document in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC of the European Parliament and of the Council concerning the placing of biocidal products on the market. EUR 20418 EN/2. Italy, April 2003.

Stage	Aquatic compartment (via the STP)		Terrestrial compartment (via the STP)		Conclusion
	STP PEC/PNEC	**Surface water PEC/PNEC**	**Soil PEC/PNEC**	**Groundwater Porewater concentration, µg/L**	
Wood Treatment Solution Preservative					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	<1	<0.1	Acceptable
Photographic Processing Solutions					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	**>1**	**> 0.1** <0.1*	**Non acceptable**
Print Fountain Solutions					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	<1	<0.1	Acceptable
Textile Processing Fluids					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	<1	**> 0.1** <0.1*	Acceptable
Car Refinishing					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	<1	<0.1	Acceptable
OEM Car Manufacture					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	<1	<0.1	Acceptable
Industrial Hygiene					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial use	<1	<1	<1	<0.1	Acceptable
Minor uses/Conveyor Lubricant					
Formulation	<1	<1	<1	<0.1	Acceptable
Industrial	<1	<1	<1	**> 0.1**	Acceptable

use				<0.1*	

* Tier 2 exposure assessment

Table 2.2.2.10-2: PEC/PNEC indication for Kathon™ WT used in wood treatment solution preservative, in- use phase of treated wood

Scenario	Treatment	Aquatic compartment		Terrestrial compartment		Conclusion
		STP	Surface water	Soil	Ground water	
House	Impregnation	n.r.	n.r.	**> 1**	**> 0.1 µg/L**	**Non acceptable**
	Surface treatment	n.r.	n.r.	< 1*	**> 0.1 µg/L**	**Non acceptable**
Noise barrier	Impregnation	< 1	< 1	< 1 (direct and indirect release)	**> 0.1 µg/L (direct release)** < 0.1 µg/L (indirect release)	**Non acceptable**
	Surface treatment	< 1	< 1	< 1 (direct and indirect release)	**> 0.1 µg/L (direct release)** < 0.1 µg/L (indirect release)	**Non acceptable**
Sheet piling	Impregnation	n.r.	**> 1**	n.r.	n.r.	**Non acceptable**
	Surface treatment	n.r.	< 1*	n.r.	n.r.	Acceptable*

n.r. : not relevant
*: considering release over 365 days and degradation

For the application in the wood treatment solution, risks following formulation, industrial use and in-use phase have been assessed. Acceptable risks result from the use of Kathon™ 886F Biocide as preservative in wood treatment solution following the formulation and the industrial use stages.

For the in-use phase of the treated wood, three worst case scenarios have been considered:

- House scenario (worst case for the terrestrial compartment),
- Noise barrier scenario (worst case for the STP),
- Sheet piling scenario (worst case for the aquatic compartment).

The emissions to the environment have been calculated for these 3 scenarios considering two time scale (Time 1 = 30 days and Time 2 = 365 days) and considering that the total

quantity of substance applied in wood could leach during the service life of the wooden device.

The in-use phase of wood treated by impregnation or surface treatment induces unacceptable risk for the environment. Only the sheet piling scenario using a wood treated by surface treatment leads to an acceptable risk to all the compartments, which is not sufficient to conclude to an acceptable risk for the in-use phase.

According to the environmental risk assessment carried out through a tonnage approach, the use of Kathon™ WT Biocide as preservative in print fountain solutions, textile processing fluids, car refinishing, OEM car manufacture fluids, industrial hygiene, and other minor uses results in acceptable risk for the environment, whatever the compartment considered. Use of Kathon™ WT Biocide as preservative in photographic processing solution results in unacceptable risk for the terrestrial compartment at the industrial stage. Details are reported in the confidential part of Doc IIC.

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

Since C(M)IT and MIT have log Kow values less than 3 (0.401 and -0.486, respectively) their potentials for bioaccumulation is considered to be very low. This was confirmed by either measurement or QSAR modeling of the BCF for aquatic and terrestrial organisms.
In addition, toxicokinetic and metabolism studies showed that both C(M)IT and MIT are rapidly excreted and highly metabolized in mammals. This confirms that their potential to accumulate is low and it can be considered that there is no significant risk of secondary poisoning to birds and mammals. In conclusion, the risk of secondary poisoning associated with the use of C(M)IT/MIT to prevent microbial contamination in the process water and conveyor lubrication fluids in food industry applications is considered to be negligible.

2.2.3 Assessment of endocrine disruptor properties

Neither C(M)IT nor MIT are included in the priority list of substances for further evaluation of their role in endocrine disruption established within the Community Strategy for Endocrine Disrupters (COM (1999) 706, COM (2007) 1635).

2.2.4 Overall conclusions of the assessment

Thor:

Uses	Human risk assessment		Environmental risk assessment	
	Conclusions*	**Conditions**	**Conclusions***	**Conditions**
Process and cooling water				
	Acceptable	With gloves, impermeable coveralls, RPE and rinse of dispensing pumps	Acceptable	Closed and small open recirculating cooling systems, only when release from the systems are directed to a STP and at a doses rates range from 0.2 to 6 mg L^{-1},

***acceptable/ not acceptable / Not relevant (NR)**

Dow:

Uses	Human risk assessment		Environmental risk assessment	
	Conclusions*	**Conditions**	**Conclusions***	**Conditions**
Process and cooling water				
	Acceptable	With gloves, impermeable coveralls, RPE and rinse of dispensing pumps	Acceptable	Closed and small open recirculating cooling systems, only when release from the systems are directed to a STP and at a doses rates range from 0.2 to 6 mg L^{-1},
Preservative for aqueous wood preservative treatment solution				
	Acceptable	With gloves, impermeable coveralls and RPE	Not acceptable	
Textile and spinning fluids				
	Acceptable	With gloves and impermeable coveralls	Acceptable	

Uses	Human risk assessment		Environmental risk assessment	
	Conclusions*	**Conditions**	**Conclusions***	**Conditions**
Paint spray booths and electrodeposition coating systems (including car refinishing and manufacture)				
	Acceptable	With gloves, impermeable coveralls and RPE	Acceptable	
Industrial hygiene, clean in place (CIP)				
	Acceptable	With gloves, impermeable coveralls and RPE	Acceptable	
Photographic Processing Solutions				
	Acceptable	*Covered by others uses evaluation*	Not acceptable	
Print Fountain Solutions				
	Acceptable	*Covered by others uses evaluation*	Acceptable	

*__acceptable/ not acceptable / Not relevant (NR)__

2.2.5 Data requirement for the representative product

- Acidity, relative density and compatibility with other products of Acticide SPX are required and should be provided by Thor at the product authorization stage. Moreover details on the "UV resistant" packaging should be provided by Thor at the product authorisation stage.

2.3 OVERALL CONCLUSIONS

The outcome of the assessment for C(M)IT/MIT in product-type 11 is specified in the BPC opinion following discussions at the 9th meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

Appendix I: List of endpoints

Listing of end points to be included in the document Overall Summary and Assessment - Doc. I

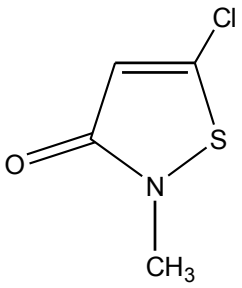
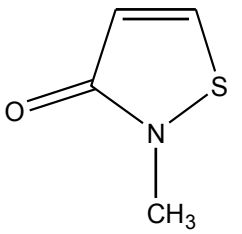
Note: The owner of data is marked before or after endpoints where relevant: T = THOR, DOW (previously Rohm & Haas)..
In case of several values in each toxicological endpoints, the value used in risk assessment is indicated in bold. Concerning the environmental risk assessment two values per endpoint are given in most cases.

Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

Active substance (ISO Common Name)	No ISO name accepted or proposed. The active ingredient common name used is:C(M)IT/MIT (3:1)
Function (*e.g.* fungicide)	Broad spectrum preservative biocide. Bactericide and fungicide.
Rapporteur Member State	France

Identity (Annex IIA, point II.)

Chemical name (IUPAC)	Mixture of 5-chloro-2-methylisothiazol-3(2H)-one and 2-methylisothiazol-3(2H)-one
Chemical name (CA)	Mixture of 5-chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one
CAS No	55965-84-9 for the mixture C(M)IT/MIT, 26172-55-4 for C(M)IT (5-chloro-2-methyl-4-isothiazolin-3-one) 2682-20-4 for MIT (2-methyl-4-isothiazolin-3-one)
EC No	There is no EC-N° for the mixture. The EC Nrs for both individual substances are: 247-500-7 for C(M)IT 220-239-6 for MIT.
Other substance No.	No
Minimum purity of the active substance as manufactured (g/kg or g/l)	C(M)IT/MIT (3:1) is manufactured as a TK Min purity of the TC (expressed in dry weight): 57.9% Range of purity of the TK: 139.4-148.5 g/kg of C(M)IT/MIT (3:1), including 105.9-108.8 g/kg of C(M)IT and

	33.5-39.7 g/kg of MIT (DOW) 122.1-157.8 g/kg of C(M)IT/MIT (3:1), including 94.7-116.6 g/kg of C(M)IT and 27.4-41.2 g/kg of MIT (DOW) 258.9-300.7 g/kg of C(M)IT/MIT (3:1), including 193.2-228.5 g/kg of C(M)IT and 65.7-72.2 g/kg of MIT (DOW) 138-144 g/kg of C(M)IT/MIT (3:1), including 104-107 g/kg of C(M)IT and 34-37 g/kg of MIT (T
Identity of relevant impurities and additives (substances of concern) in the active substance as manufactured (g/kg)	Magnesium nitrate and magnesium chloride
Molecular formula	C_4H_4ClNOS for C(M)IT C_4H_5NOS for MIT
Molecular mass	149.6 g/mol for C(M)IT 115.2 g/mol for MIT
Structural formula	 C(M)IT  MIT

Physical and chemical properties (Annex IIA, point III., unless otherwise indicated)

Melting point (state purity)	C(M)IT: melting onset at 51.3°C, with a peak at 54.9°C (purity = 99.86%) (DOW) 46.6-48.9°C (purified) (T) MIT: 46.7-48.3°C (purity = 99.7%) (DOW) 44.2-47.7°C (purity = about 100%) (T) C(M)IT/MIT (3:1): melting onset at 22.2°C, with a peak at

	35.1°C (purity = 98.7 %) (DOW) < -25 °C (concentration = 14.05 % in water) (DOW) -23°C (concentration not stated, ~14% C(M)IT/MIT in water) (T)
Boiling point (state purity)	C(M)IT: no boiling point observed until decomposition (purity > 98%) (T) MIT: no boiling point observed until decomposition (purity > 99%) (T) C(M)IT/MIT (3:1): boiling did not occur until decomposition at 97.3°C (purity = 98.7%) (DOW) 100.1 ± 0.2°C (concentration = 13.7-13.8 % in water) (DOW) 106.5°C (concentration not stated, ~14% in water) (T)
Temperature of decomposition	C(M)IT: above 167°C (purity > 98%) (T) MIT: above 236°C (purity > 99%) (T) C(M)IT/MIT (3:1): 97.3°C (purity = 98.7%) (DOW)
Appearance (state purity)	C(M)IT/MIT (3:1): Solid, pale yellow to yellow at 20 °C, weakly sweet and pungent (purity = 97.8-99.3 %) (DOW) Clear liquid pale yellow at 20°C (concentration = 14.05 % in water) (DOW) Liquid, colorless to pale yellow, mild odor (concentration not stated, ~14% C(M)IT/MIT in water) (T)
Relative density (state purity)	C(M)IT: 1.6g/cm^3 at 20.8°C (purity > 98%) (T) MIT: 1.39g/cm^3 at 20°C (purity > 99%) (T) C(M)IT/MIT (3:1): 1.396 g/cm^3 at 38°C (molten phase), 1.420 g/cm^3 at 25°C (solid phase) (purity = 98.7 %) (DOW) 1.296 g/mL at 25ºC (concentration = 13.7-13.8 % in water) (DOW) 1.256g/ml at 20°C (concentration not stated, ~14% C(M)IT/MIT in water) (T)
Surface tension	C(M)IT/MIT (3:1): 72.3 mN/m at 20.0ºC (1g/L C(M)IT/MIT 3:1) (DOW) 73.0 mN/m at 19.5ºC (1g/L C(M)IT/MIT 3:1) (DOW) 72.6mN/m (concentration 1.106g/L) (T)
Vapour pressure (in Pa, state temperature)	C(M)IT: 0.9Pa at 20°C and 1.3Pa at 25°C (purity =

	99.86%) (DOW) 1.6Pa at 20°C (extrapolated) and 2.8Pa at 25°C(measured) (purity = 98.4%) (T) MIT: 2.1Pa at 33°C, measured ; 0.4Pa at 20°C and 0.7 Pa at 25°C, extrapolated (purity = 99.7%) (DOW) 0.99Pa at 20°C and 1.6Pa at 25°C (extrapolated) (purity = 98.5%) (T) C(M)IT/MIT (3:1): 2.2Pa at 20°C and 3.8Pa at 25°C, extrapolated (purity = 98.7%) (DOW) 2080Pa at 20°C, actually the vapor pressure of water (concentration not stated, ~14% C(M)IT/MIT in water) (T)
Henry's law constant (Pa m^3 mol^{-1})	C(M)IT: k< 4.26×10^{-4} Pa m^3 mol^{-1} at 20°C and k< 7.07×10^{-4} Pa m^3 mol^{-1} at 25°C (purity = 98.4%) (T) MIT: k< 2.72×10^{-5} Pa m^3 mol^{-1} at 20°C and k< $4.39.10^{-5}$ Pa m^3 mol^{-1} at 25°C (purity = 98.5%) (T) C(M)IT/MIT (3:1): k< 10^{-4} Pa.m^3.mol^{-1} at 20°C (estimated) (purity = 98.7%) (DOW)
Solubility in water (g/l or mg/l, state temperature)	C(M)IT and MIT (separately tested): extremely soluble in water: 1g of C(M)IT and 4g of MIT are completely dissolved in 1mL of water (respectively 100% and 400% w/v solutions). Solubility not depending on temperature and pH. (T) C(M)IT/MIT (3:1): It was not possible to achieve full saturation at nominally 3g/mL. The test sample is therefore of very high solubility (>3000g/l). There is not a significant effect on solubility on increasing the pH from 5 to 9 or increasing the temperature from 9.3 to 20.4ºC. The pH of the solution was below 3, even if buffered solutions were used. (purity = 98.7%) (DOW)
Solubility in organic solvents (in g/l or mg/l, state temperature) (Annex IIIA, point III.1)	C(M)IT: (T) n-heptane: 14.5g/L xylene: 393g/L Acetonitrile: 1g in 1mL at 10°C and 3.8g in 1mL at 30°C MIT: (T) n-heptane: 1.46g/L xylene: 143.6g/L Acetonitrile: 1.4g in 1mL at 10°C and 7.2g in 1mL at 30°C

	C(M)IT/MIT (3:1): (purity = 95.78-95.51%) (DOW) At 25°C: n-Hexane: 22.5 g/L Ethyl acetate: >763 g/L (not saturated)
Stability in organic solvents used in biocidal products including relevant breakdown products (IIIA, point III.2)	Not applicable; biocidal products do not include organic solvents. (DOW and T)
Partition coefficient (log P_{OW}) (state temperature)	Measured on active ingredients individually: (DOW) C(M)IT: 0.401 at 24 °C (purity = 98.1%) MIT: - 0.486 at 24 °C (purity = 97.8%) These values will not vary as a function of pH and/or temperature. (DOW) Measured on C(M)IT/MIT (3:1), 13.9% in water: (T) C(M)IT: 0.75 MIT: -0.71 Test item is not considered ionisable. Therefore investigation of the pH effect on the partition coefficient is not necessary. (T)
Hydrolytic stability (DT_{50}) (state pH and temperature) (point VII.7.6.2.1)	**DOW :** CMIT, RH-651: pH__5____: > 60 days at 25±0.1°C pH__7____: >60 days at 25±0.1°C pH___9___: 22 days at 25±0.1°C, pH__5____: > 170 days at 12°C pH__7____: >170 days at 12°C pH___9___: 62.24 days at 12°C MIT, RH-573: In pH 5, 7, and 9 buffers (24.1 ± 0.4°C) no significant hydrolysis of MIT was observed as the compound was stable for more than 30 days. **Thor :** pH__4____: > 365 days at 20°C pH__7____: >365 days at 20°C pH___9___: 63.6 days at 20°C,
Dissociation constant (not stated in Annex IIA or IIIA; additional data requirement from TNsG)	Not applicable, C(M)IT and MIT do not dissociate. (DOW and T)
UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)	C(M)IT: (T)

Solvent	Wavelength	Molar absorption coefficient (L/mol.cm)

Water	274nm	6600
	223nm	4980
HCl (0.1M)	273nm	7280
	222nm	5510
Methanol	279nm	6540
	218nm	5020

MIT: (T)

Solvent	Wavelength	Molar absorption coefficient (L/mol.cm)
Water	273nm	7600
	<200nm	Maximum below range
HCl (0.1M)	273nm	7630
	<200nm	Maximum below range
Methanol	277nm	7420
	205nm	2140

C(M)IT/MIT (3:1):

purified: (DOW)

Neutral (pH 5.3): λ_{max} at 273nm, $\in$ =7780; λ_{max} at 220nm, $\in$ =4430

Acid (pH 1.3): λ_{max} at 273nm, $\in$ = 7300; λ_{max} at 218nm, $\in$ = 4320

Basic (pH 8.4): λ_{max} at 276nm, $\in$ = 7080; 200nm, $\in$ > 7080

14% in water: (DOW)

Neutral (pH 7): λ_{max} at 272.7nm, $\in$ =9879; λ_{max} at 207.8nm (due to nitrate anion)

Acid (pH 2): λ_{max} at 272.9 nm, $\in$ = 9567; λ_{max} at 209.9nm (due to nitrate anion)

Basic pH: not applicable; C(M)IT/MIT (3:1) is not stable in alkaline conditions.

Photostability (DT_{50}) (aqueous, sunlight, state pH)
(point VII.7.6.2.2)

DOW :

CMIT, RH-651: DT_{50} = 6.6 days at pH 7 and at 24.8±0.5°C

MIT, RH-573: DT_{50} = 11.1 days at pH 7 and at 24.9±0.8°C

Thor :

	CMIT,: DT_{50} = 6.3 days at pH 7 and at 25±1°C MIT,: DT_{50} = 18.2 days at pH 7 and at 25±1°C
Quantum yield of direct phototransformation in water at Σ > 290 nm (point VII.7.6.2.2)	Not determined.
Flammability	C(M)IT and MIT: Not highly flammable (T) C(M)IT/MIT (3:1): purified: not highly flammable (DOW) 14% in water: not flammable (DOW) 14% in water: not flammable (T)
Explosive properties	C(M)IT and MIT: do not have explosive properties (T) C(M)IT/MIT (3:1): purified: not explosive (DOW) 14% in water: not explosive (DOW)

Classification proposed by the RMS according to the regulation 1272/2008 for C(M)IT/MIT 14% and C(M)IT/MIT 100%

	C(M)IT/MIT 14%	C(M)IT/MIT 100%
Hazard classes and categories	Acute Tox 4 for acute oral hazard Acute Tox 3 for acute dermal hazard Acute Tox 4 for inhalation hazard Skin Corr. 1B Skin Sens. Cat 1A STOT SE 3 Aquatic acute 1 Aquatic Chronic 1	Acute Tox. 3 for acute oral hazard Acute Tox 2 for acute dermal hazard Acute Tox 2 for acute inhalation hazard Skin Corr. 1B Skin Sens. Cat 1A STOT SE 3 Aquatic acute 1 Aquatic Chronic 1
Hazard statements	H332: Harmful if inhaled H312: Harmful in contact with skin H302: Harmful if swallowed H 314: Causes severe skin burns and eye damage H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=10 H410 very toxic to aquatic life M-factor = 10	H 330: Fatal if inhaled H 310: Fatal in contact with skin H 301: Toxic if swallowed H 314: Causes severe skin burns and eye damage H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=100 H410 very toxic to aquatic life M-factor=100
Specific concentration limit	Skin Corr. 1B; H314: Causes severe skin burns and eye damage C ≥ 0.6%** Eye Irrit. 2; H319: Causes serious eye irritation Skin Irrit. 2; H315: Causes skin irritation 0.06% ≤ C < 0.6% Skin Sens.Cat 1A/H317: May cause an allergic skin reaction C ≥ 0.0015% This specific concentration limit is considered as relevant for this dossier.	

****** A classification as Skin Corr. 1C H 314: Causes severe skin burns and eye damage should be required due to the study results, however a harmonised classification as Skin Corr. 1B has been set, and therefore this classification is retained in the dossier.

Classification proposed by the RMS according to the directive 67/548/EEC for C(M)IT/MIT 14% and C(M)IT/MIT 100%

	C(M)IT/MIT 14%	C(M)IT/MIT 100%
Class of danger	Xn - Harmful C: Corrosive Xi: Irritant N: Dangerous to the environment	T+ - very Toxic C: Corrosive Xi: Irritant N: Dangerous to the environment
R phrases	R20/21/22: Harmful by inhalation, in contact with skin and if swallowed R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	R26/24/25: Very toxic by inhalation, toxic in contact with skin and if swallowed. R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact. R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S phrases	S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.	
Specific concentration limit	C, R34: Causes burns C ≥ 0.6% Xi, R36/38: Irritating to eyes and skin 0.06% ≤ C < 0.6% Xi; R43: May cause sensitization by skin contact C ≥ 0.0015% This specific concentration limit is considered as relevant for this dossier.	

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	DOW: Reversed Phase High Performance Liquid Chromatography with UV detection (254 nm) T: HPLC-UV (275 nm)
Impurities in technical active substance (principle of method) (Annex IIA, point 4.1)	DOW: Titration and GC-FID Validation data are missing on some impurities and should be provided T: Titration and NMR-spectroscopy Validation data are missing on the impurities and should be provided

Analytical methods for residues

Soil (principle of method and LOQ) (Annex IIA, point 4.2)	DOW: Extraction and purification followed by reversed phase HPLC with UV detection (275 nm); LOQ=0.05µg/g of soil or sediment (for both C(M)IT and MIT) A confirmatory method should be provided if the use which induces a continuous rejection of C(M)IT and MIT in soil is claimed and acceptable at the product authorisation stage, T: No method submitted. Must be provided for C(M)IT and MIT in soil if the use which induces a continuous rejection of C(M)IT and MIT in soil is claimed and acceptable at the product authorisation stage,
Air (principle of method and LOQ) (Annex IIA, point 4.2)	DOW: Trap airborne C(M)IT and MIT on OVS tube, extract and analyze by HPLC/MS/MS; LOQ=2.6µg/m^3 MIT; 7.5µg/m^3 C(M)IT T: GC-MSD, LOQ=0.0025 mg/m3 for C(M)IT and 0.0008 mg/m3 for MIT for 12 L of sampled air
Water (principle of method and LOQ) (Annex IIA, point 4.2)	DOW: Solid phase extraction followed by HPLC/MS/MS; LOQ=0.05 µg/L (for both C(M)IT and MIT) T: C(M)IT and MIT are extracted from water with SPE columns, eluted with ethyl acetate/acetone, and quantified using HPLC-MS/MS analysis; LOQ=0.1µg/L (for both C(M)IT and MIT)
Body fluids and tissues (principle of method and LOQ) (Annex IIA, point 4.2)	DOW and T: Not required C(M)IT/MIT is classified toxic based on local effect rather than systemic effects. Moreover C(M)IT/MIT is readily absorbed, extensively metabolised and rapidly excreted. Parent

	compound is not detected in urine, bile or faeces. C(M)IT/MIT does not bioaccumulate in the mammal. Moreover, none of the metabolites are considered of concern.
Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	DOW: Simulated foods (acidic water, water + ethanol, olive oil): Liquid extraction and/or dilution extraction followed by HPLC/MS/MS LOQ: MIT 2.5µg/L, C(M)IT 7.5µg/L T: No method submitted. Not necessary due to intended uses.
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes) (Annex IIIA, point IV.1)	DOW: Simulated foods (acidic water, water + ethanol, olive oil): Liquid extraction and/or dilution extraction followed by HPLC/MS/MS LOQ: MIT 2.5µg/L, C(M)IT 7.5µg/L T: No method submitted. Not necessary due to intended uses.

Chapter 3: Impact on Human Health

Absorption, distribution, metabolism and excretion in mammals (Annex IIA, point 6.2)

	DOW	THOR
Rate and extent of oral absorption:	**C(M)IT: 49 %** MIT: 78%	C(M)IT: 44-47% MIT: 67-69%.
Rate and extent of dermal absorption:	➔ **50%** for aqueous solution below corrosive concentration**;** ➔ **100%** for corrosive concentration (> 0.6% the specific concentration limit)	➔ **50%** for aqueous solution below corrosive concentration; ➔ **100%** for corrosive concentration (> 0.6% the specific concentration limit)
Tissue Distribution study:	4 days after exposure: 4.72% of dosed radioactivity found in tissues (rat) Highest amount of radioactivity in blood	
Potential for accumulation:	After oral administration, no evidence of accumulation in the animal body	After dermal exposure C(M)IT/MIT is largely (>80%) absorbed. However, a large part

		remains tightly bound to the skin
Rate and extent of excretion:	Following oral administration, C(M)IT and MIT are both rapidly excreted: - C(M)IT: urine and faeces are equal major routes of excretion whereas bile is a minor (4.74%) - MIT: largely excreted in urine and in a lesser extent in faeces of which the major part came from bile (29.09%) No parent compound in excreta.	All the C(M)IT/MIT is rapidly metabolized after oral absorption: no parent compound is found in the excreta. The first step in metabolism was glutathione conjugation, resulting in four major metabolites for MIT and two major metabolites for C(M)IT. The open literature points to the formation of malonic acid, malonamic acid, *N*-methylmalonamic acid and other small polar organic acids.
Toxicologically significant metabolite	None of the metabolites are considered to be of concern.	None of the metabolites are considered to be of concern.

Acute toxicity (Annex IIA, point 6.1)

	DOW	THOR
Rat LD_{50} oral C(M)IT/MIT 14% (values for C(M)IT 100% between brackets)	**457 mg/kg bw (corr. to 64 mg a.i./kg bw)**	472 mg/kg bw (corr. to 66 mg a.i./kg bw)
Rat LD50 oral, N-(methyl) malonamic acid (NMMA)	3550 mg NMMA/kg b.w. in males 4100 mg NMMA/kg b.w. in females	
Rat; Rabbit LD_{50} dermal C(M)IT/MIT 14% (values for C(M)IT 100% between brackets)	**Rabbit= 660 mg/kg bw (corr. to 92.4 mg a.i./kg bw)**	Rat > 1007 mg/kg bw (corr. to 141 mg a.i./kg bw)
Rat LC_{50} inhalation C(M)IT/MIT 14% (values for C(M)IT 100% between	2.36 mg/L (corr. to 0.33 mg a.i./L)	**1.23 mg/L (corr. to 0.171 mg a.i./L)**

brackets)		
Skin irritation (rabbit) C(M)IT/MIT 14% (and C(M)IT/MIT 100%)	Irritant	**Corrosive**
Eye irritation (rabbit) C(M)IT/MIT 14% (and C(M)IT/MIT 100%)	**Corrosive**	Not tested, but C(M)IT/MIT is considered to pose a risk of serious damage to the eyes
Airway irritation C(M)IT/MIT 14%	RD_{50}= 69µg/L (corr. to 9.66 µg a.i/L)	
Skin sensitization (test method used and result) C(M)IT/MIT 14% (and C(M)IT/MIT 100%)	**Sensitizing**	**Sensitizing**
N-(Methyl) malonamic acid (NMMA)	Not sensitising	

Repeated dose toxicity (Annex IIA, point 6.3)

C(M)IT/MIT 14% (values in a.i. between brackets for C(M)IT/MIT 100%)

	DOW	**THOR**
Species/ target / critical effect	Rabbit-rat / Irritation at site of administration.	Rabbit-rat-dog / Irritation at site of administration.
Lowest relevant oral NOAEL / LOAEL	Rabbit, 28 days - NOAEL = 27.9 mg/kg bw/ day based on no systemic effects (corr. to 3.9 mg a.i./kg bw/d) - NOAEC = 2.9 mg/kg bw/ day based on the fundus irritation (corr. to 0.4 mg a.i./kg bw/d) **Rat, 90 days** - NOAEL = 116/176 mg/kg bw/d based on no signs of systemic effects (corr. to 16.3/24.7 mg a.i./kg bw/d) (for males / females respectively) **- NOAEC = 536 ppm based on gastric irritation toxic effects (corr. to 75 ppm a.i.)**	**Rat, 90 days (Letter of access)** - NOAEL = 116/176 mg/kg bw/d based on no signs of systemic effects (corr. to 16.3/24.7 mg a.i./kg bw/d) (for males / females respectively) **- NOAEC = 536 ppm based on gastric irritation toxic effects (corr. to 75 ppm a.i.)** Dog, 90 days

	Rat, 2 years -NOAEL = 123/184 mg/kg bw/d (corr. to 17.2/25.7 mg a.i./kg bw/d) (for males/females respectively) **-NOAEC = 210 ppm (corr. to 30 ppm a.i. or 2– 3.1 mg ai/kg bw/d male and female resp.)**	NOEL = 157 mg/kg bw/d (corr. to 22 mg a.i./kg bw/ day) **Rat, 2 years (Letter of access)** -NOAEL = 123/184 mg/kg bw/d (corr. to 17.2/25.7 mg a.i./kg bw/d) (for males/females respectively) **-NOAEC = 210 ppm (corr. to 30 ppm a.i. or 2 – 3.1 mg ai/kg bw/d male and female resp.)**
Lowest relevant dermal NOAEL / LOAEL	Rabbit, 90 days LO(A)EL = 710 ppm (corr. to 100 ppm a.i. based on systemic and local effects observed at this dose. Mouse, 30 months NOAEL = 2857 ppm (corr. to 400 ppm a.i. corr. to 0.25 mg a.i./kg.bw/d)	**Rat, 90 days** - NOEL = 18.75 mg/kg/d (corr. to 2.61 mg a.ikg bw/day) based on no systemic effects **- NOAEC = 12500 ppm (corr. to 1740 ppm a.i) based on local effects**
Lowest relevant inhalation NOAEL / LOAEL	**Rat, 90 days** **NOAEC = 2.4 mg/m^3 (corr. to 0.34 mg a.i./m^3 based on irritation to the respiratory tract)**	**Rat, 90 days (Letter of access)** **NOAEC = 2.4 mg/m^3 (corr. to 0.34 mg a.i./m^3 based on irritation to the respiratory tract)**

Repeated dose toxicity of C(M)IT/MIT metabolites (Annex IIA, point 6.3)

	DOW	**THOR**
Species/ target / critical effect	Rat/-	
Lowest relevant oral NOAEL / LOAEL	N-methyl malonamic acid (NMMA): 90 days NOEL (diet, rat) = 13-15 mg NMMA/kg bw/day (110-220 ppm), the highest dose tested. Malonamic acid (MA): 90 days NOEL (diet, rat) = 2.6-3.0 mg MA/kg bw/day (22-44 ppm), the highest dose tested.	

Genotoxicity (Annex IIA,	Genotoxic *in vitro* (Ames,	Genotoxic *in vitro* (Ames,

point 6.6)	mammalian cell gene mutation test) Not a genotoxic *in vivo* (*in vivo* unscheduled DNA synthesis, *in vivo* chromosome aberration assay)	mammalian chromosome aberration test, mammalian cell gene mutation test) Not a genotoxic *in vivo* (*in vivo* unscheduled DNA synthesis, *in vivo* bone marrow micronucleus test)

Genotoxicity of C(M)IT/MIT metabolites (Annex IIA, point 6.6)	N-methyl malonamic acid (NMMA): **Not mutagenic** (Bacterial Gene Mutation Assay test)	

Carcinogenicity (Annex IIA, point 6.4)

	DOW	THOR
Species/type of tumour	<u>Rat, 2 years, oral drinking water</u> **No evidence of carcinogenicity**: no effects on type or incidence of neoplasms at up to and including 2140 ppm (corr. to 300 ppm a.i.) equivalent to 17.2 and 25.7 mg a.i./kg bw/d for systemic effects for males and females respectively <u>Mice, 30-months study</u> **No evidence of carcinogenicity**: results of histopathology didn't show any indication of a treatment-related increased incidence of neoplasm of any type was seen either locally (at the application site) or systemically	<u>Rat, 2 years, oral drinking water (Letter of access)</u> **No evidence of carcinogenicity**: no effects on type or incidence of neoplasms at up to and including 2140 ppm (corr. to 300 ppm a.i.) equivalent to 17.2 and 25.7 mg a.i./kg bw/d for systemic effects for males and females respectively
lowest dose with tumours	No evidence of carcinogenicity	No evidence of carcinogenicity

Reproductive toxicity (Annex IIA, point 6.8)

For C(M)IT/MIT 14% (values in a.i. between brackets for C(M)IT/MIT 100%)

	DOW	THOR
Species/ Reproduction target / critical effect	No effects on reproductive capability in rats.	No effects on reproductive capability in rats.

Lowest relevant reproductive NOAEL / LOAEL	Rat: no effects on fertility/mating, post-natal development (one-generation and two-generation)	Rat: no effects on fertility/mating, post-natal development (one-generation and two-generation)
Species/Developmental target / critical effect	Rat, rabbit: no developmental effects	Rat: no developmental effects
Lowest relevant developmental NOAEL / LOAEL	Rat: NOAEL maternal = 100 mg/kg bw/d (corr. to 15 mg a.i./kg bw/day) **NOAEL developmental = 100 mg/kg/d (corr. to 15 mg a.i./kg bw/day)** Rabbit: NOAEL maternal = 57.1 mg/kg bw/d (corr. to 8 mg a.i./kg bw/day) based on no systemic effects = NOAEL developmental NOAEC maternal = 14.3 mg/kg bw/d (corr. to 2 mg a.i./kg/day) based on decreased body weight and food consumption due do gastric irritation	Rat **NOAEL maternal = 28 mg/kg bw/d (corr. to 3.95 mg a.i./kg bw/day)** NOAEL developmental = 139 mg/kg bw/d (corr. to 19.6 mg a.i./kg bw/day) Rabbit (Letter of access): NOAEL maternal = 57.1 mg/kg bw/d (corr. to 8 mg a.i./kg bw/day) based on no systemic effects = NOAEL developmental NOAEC maternal = 14.3 mg/kg bw/d (corr. to 2 mg a.i./kg/day) based on decreased body weight and food consumption due do gastric irritation

Neurotoxicity / Delayed neurotoxicity (Annex IIIA, point VI.1)

	DOW	**THOR**
Species/ target/critical effect	No evidence of neurotoxicity in multiple dose studies (rat, rabbit, mouse, dog)	No evidence of neurotoxicity in multiple dose studies (rat, rabbit, mouse, dog)
Lowest relevant developmental NOAEL / LOAEL.	No evidence of neurotoxicity in multiple dose studies (rat, rabbit, mouse, dog)	No evidence of neurotoxicity in multiple dose studies (rat, rabbit, mouse, dog)

Other toxicological studies (Annex IIIA, VI/XI)

....	none

Medical data (Annex IIA, point 6.9)

....	Despite some incidents over the years, no worker has experienced any continuing skin problems and none has had to be transferred to other duties due to exposure to chemicals.

Summary (Annex IIA, point 6.10)

AEL (Acceptable Exposure Level (C(M)IT/MIT 3:1)	NO(A)EL	Study	Safety factor
Acute, mid-term AEL= 0.11 mg ai/kg bw/d	22 mg ai/kg bw/d	90-day	100
Long-term AEL= 0.09 mg ai/kg bw/d	17.2 mg ai/kg bw/d	24-month	100
AEC (Acceptable Exposure Concentration (C(M)IT/MIT 3:1)	NOAEC	Study	Safety factor
Oral route:	NR	NR	NR
Dermal route(irritation):	Specific concentration limit for sensitising effect: 15 ppm		
Inhalation route:			
Acute, mid-term $AEC_{inhalation}$ = 0.04 mg a.i./m^3	0.34 mg a.i./m^3	90-day	8
Long-term $AEC_{inhalation}$ = 0.02 mg a.i./m^3	"	"	16
ARfD (acute reference dose) = 0.02 mg a.i/kg bw/d	2 mg ai/kg bw/d	Developmental study in rabbit	100
ADI (Acceptable Daily Intake) = 0.004 mg a.i/kg bw/d	0.4 mg ai/kg bw/d	28-day	100

Chapter 4: Fate and Behaviour in the Environment

Route and rate of degradation in water (Annex IIA, point 7.6, IIIA, point XII.2.1, 2.2)

	DOW	THOR
Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	CMIT, pH 5: stable pH 7: stable pH 9 : 16.9 and 22 days at 25 °C (47.8 and 62.2 days at 12°C)	tested as ACTICIDE® 14 pH 4: MIT and CIT stable pH 7: MIT and CIT stable pH 9: MIT stable pH 9: CIT : 63.6 days at 20°C (120.6 days at 12°C) and 15.8

	MIT, pH 5, 7, and 9 : stable	days at 30°C (66.7 days at 12°C)
	CMIT: pH 4, 5, 7: stable, pH 9 : 62.4-120.6 days at 12°C **MIT: pH 4, 5, 7, 9 : stable** **C(M)IT/MIT : stable to hydrolysis at environmental pH**	
Photolytic / photo-oxidative degradation of active substance and resulting relevant metabolites	CMIT, DT_{50} = 6.6 days at 24.8°C, pH 7 and sunlight	CIT DT_{50} = 6.3 days at 25°C pH 7 and sunlight
	MIT, DT_{50} = 11.1 days at 24.9°C, pH 7 and sunlight	MIT DT_{50} = 18.2 days at 25°C, pH 7 and sunlight
	CMIT DT_{50} = 6.6 days at pH 7 (sunlight) **MIT DT_{50} = 18.2 days at pH 7 (sunlight)** **C(M)IT/MIT: DT_{50} = 18.2 days (endpoint for the risk assessment)**	
Readily biodegradable (yes/no)	CMIT, Readily biodegradable with a failure of the 10 day window	Tested as ACTICIDE® 14 Not readily biodegradable
	MIT, Not readily biodegradable	
	C(M)IT/MIT: not readily biodegradable	
Biodegradation in Sewage Treatment Plant	CMIT, $DT_{50\ (dissipation)}$ = 0.27 day at 22°C $DT_{50\ (mineralisation)}$ = 0.36 day at 22°C MIT, $DT_{50\ (dissipation)}$ = 0.03-0.04 day at 22°C $DT_{50\ (mineralisation)}$ = 1.69 days at 22°C	Tested as ACTICIDE® 14 CIT: elimination >96% MIT: elimination >80% Tested on MIT only MIT: $DT_{50\ (dissipation)}$ = 0.02 day
	Sewage Treatment Plant **CMIT DT_{50} = 0.27 day at 22°C** **MIT DT_{50} = 0.04 day at 22°C**	
Biodegradation in Sewage Treatment Plant (metabolites)	Not relevant	No relevant

Biodegradation in surface water	Estuarine water CMIT, DT_{50} = 0.81 (22 µg/L) - 3.17 days (115 µg/L) at 19.6 °C DT_{50} = 1.49 (22 µg/L) – 5.82 days (115 µg/L) at 12 °C MIT, DT_{50} = 1.38 (22 µg/L) -1.24 days (112 µg/L) at 20 °C DT_{50} = 2.63 (22 µg/L) – 2.35 days (112 µg/L) at 12 °C Marine water CMIT, DT_{50} = 1.8 (10 µg/L) – 17.3 days (100 µg/L) at 20°C DT_{50} = 3.4 (10 µg/L) – 32.8 days (100 µg/L) at 12 °C DT_{50} = 4.3 (10 µg/L) – 41.7 days (100 µg/L) at 9 °C MIT, DT_{50} = 3.6 for threshold and 8.3 for PEC calculation (10 µg/L) – 12.3 days (100 µg/L) at 20°C DT_{50} = 6.8 for threshold and 15.7 for PEC calculation (10 µg/L) – 23.3 days (100 µg/L) at 12 °C DT_{50} = 8.7 for threshold and 20.0 for PEC calculation (10 µg/L) –29.7 days (100 µg/L) at 9 °C	Estuarine water Not available Marine water CIT (20µg/L): DT_{50} = >2 days and < 7 days at 15°C DT_{50}>2.5 and < 8.9 days at 12°C DT_{50} > 3.2 and <11.3 days at 9°C MIT (87.5 µg/L): DT_{50} = 3.9 days at 15°C DT_{50} = 5.0 days at 12°C DT_{50} = 6.3 days at 9°C
	Estuarine water **CMIT DT_{50} = 5.82 days at 12°C** **MIT DT_{50} = 2.63 days at 12°C** **C(M)IT/MIT: DT_{50} = 5.82 days at 12°C (endpoint for the risk assessment)**	
	Marine water **CMIT DT_{50} = 41.7 days at 9 °C**	

	MIT DT_{50} = 29.7days at 9 °C **C(M)IT/MIT: DT_{50} = 41.7 days at 9 °C (endpoint for the risk assessment if necessary)**	
Distribution in water sediment systems	CMIT, Aerobic conditions: $DT_{50\ whole\ system}$ = 0.38-1.33 days at 20°C $DT_{50\ whole\ system}$ = 0.72-2.47 days at 12°C MIT, Aerobic conditions: $DT_{50\ whole\ system}$ = 0.46-1.44 days at 20°C $DT_{50\ whole\ system}$ = 0.87-2.7 day at 12°C	CIT: Aerobic conditions: $DT_{50\ whole\ system}$ = 1.86-2.04 days at 20°C $DT_{50\ whole\ system}$ = 3.53-3.86 days at 12°C MIT: Aerobic conditions: $DT_{50\ whole\ system}$ = 1.28-2.2 days at 20°C $DT_{50\ whole\ system}$ = 2.43-4.17 days at 12°C
	Aerobic Freshwater/sediment **CMIT DT_{50} whole system = 2.22 days at 12°C (geometric mean)** **MIT DT_{50} whole system = 2.21 days at 12°C (geometric mean)**	
Distribution in water sediment systems (metabolites)	Aerobic, CMIT Not relevant Aerobic, MIT <1% of applied radioactivity except for 2-(methylcarbamoyl)ethane sulfonic acid and 2-hydroxyethane sulfonic acid. maximum 23.5% in Almhouse water:sediment system (0.9 at day 30) and maximum 20.5% in the Cedar Hill water: sediment system, (3.3% at day 30).	Aerobic, CMIT Only detected in the water sediment system with high organic carbon - a polar degradation product (10.1% of applied activity by day 6, 4.6% by day 58) - a degradation product of polarity similar to C(M)IT (13.6% of applied activity by day 13, 3.0% by day 58). Their identity was not elucidated, despite efforts with LC/MS analysis Aerobic, MIT One metabolite detected but not identified in both water:sediment system: - low organic matter water: sediment system, maximum 48.5% by day 4 and 11.4% by day 38 - high organic matter water: sediment system, maximum 36.9% by day 8 and not

		detected by day 58.
Non-extractable residues	C(M)IT, aerobic: 45.4-69.5 % of the applied ^{14}C-activity with 60.4 % at study termination (30 days) and 34.6-44.4 % with 42.2 % at study termination (30 days) for the Almhouse and Cedar Hill water:sediment systems, respectively). MIT, aerobic: 45.2-60.2 % of the applied ^{14}C-activity with 57.7 % at study termination (30 days) and 27.2-62.6 % with 62.6 % at study termination (30 days) for the Almhouse and Cedar Hill water:sediment systems, respectively).	C(M)IT, aerobic: - low organic matter water: sediment system, from 17.0% of applied activity by day 1 to 43.9% by day 58 - high organic matter water: sediment system, from 17.8% of applied activity by day 1 to 51.4% by day 31.5 MIT, aerobic: - low organic matter water: sediment system, from 12.6% of applied activity by day 1 to 53.7% by day 38 - high organic matter water: sediment system, from 15.8% of applied activity by day 1 to 42.0% by day 39

Route and rate of degradation in soil (Annex IIIA, point VII.4, XII.1.1, XII.1.4; Annex VI, para. 85)

	DOW	**THOR**
Mineralization (aerobic)	CMIT, CO_2 was present at 75% of the applied activity after 100 days of incubation.	CIT Not available
	MIT, CO_2 was present at 46.6% of the applied activity after 100 days of incubation.	MIT 25.2% mineralisation after 51 days
Laboratory studies (range or median, with number of measurements, with regression coefficient)	CMIT, DT_{50} = 0.11 day for threshold and 0.78 day for PEC calculation at 20°C DT_{50} = 0.21 day for threshold and 1.48 days for PEC calculation at 12°C	CIT Not available.

	MIT, DT_{50} = 0.27 day at 20°C DT_{50} = 0.51 day at 12°C	MIT DT_{50} < 0.08 day at 20°C DT_{50} < 0.15 day at 12°C
	CMIT DT_{50} = 1.48 days at 12°C **MIT DT_{50} = 0.51 days at 12°C** **C(M)IT/MIT: DT_{50} = 1.48 days at 12°C (endpoint for the risk assessment, PEC calculations)**	
Field studies (state location, range or median with number of measurements)	DT_{50f}: not available	DT_{50f}: not available
	DT_{90f}: not available	DT_{90f}: not available
Anaerobic degradation	Not available	Not available
Soil photolysis	Not available	Not available
Non-extractable residues	CMIT, *Non extractable residues:* from 1.62 % to 76.49 % after 48 hours 58.70% after 64 days MIT, *Non extractable residues:* from 6.2 % to 39.7 % after 30 days and 38.8 % after 100 days.	CIT Not available MIT from approximately 33% of the applied activity at t=2h to approximately 55% of the applied activity at the end of the incubation
Relevant metabolites - name and/or code, % of applied a.i. (range and maximum)	CMIT, CO_2 was the only metabolite detected and identified that was greater than 10% of the applied radioactivity. The presence of $^{14}CO_2$ demonstrates that the isothiazolone ring is cleaved and significant metabolism of the resulting alkyl metabolites has occurred. While definitive identification of the metabolites could not be achieved, they can be characterized as a mixture of malonic acid, malonamic acid,	Not applicable (all compounds <10% of the applied activity)

	N-methyl malonamic acid, and N-methyl oxamic acid. MIT, Besides CO_2 , two metabolites were quantified above 10% but were transient. They were isolated and identified by LC-MS as N-methyl-2-oxo-propionamide, and 2-methylcarbamoyl-ethene sulfonic acid. CO_2 increased continually throughout the study reaching 46.6% after 100 days of incubation.	
Soil accumulation and plateau concentration	Based on degradation studies, no accumulation is expected.	Based on degradation studies, no accumulation is expected.

Adsorption/desorption (Annex IIA, point XII.7.7; Annex IIIA, point XII.1.2)

	DOW	**THOR**
Ka , Kd	CMIT, Kf (sludge) = 55.6 Ka_{oc} (sludge) = 79.9-107.1 Ka_{oc} (soil and sediment) = 30-310 Kd_{oc} (soil and sediment) = 39-421	CIT, Ka_{oc} = 11.75 CIT (OECD 106): Ka_{oc} (soil and sediment) = 26-69
Ka_{oc} , Kd_{oc}	MIT, Kf (sludge) = 6.12 Ka_{oc} (sludge) = 54.1-152.7 Ka_{oc} (soil and sediment) = 6.4-10 Kd_{oc} (soil and sediment) not determined	MIT Ka_{oc} << 5.6
pH dependence (yes / no) (if yes type of dependence)	Not expected.	
	CMIT Ka_{oc} (soil and sediment) = 26-310 ; Ka_{oc} (arithmetic mean) = 83.2 **MIT Ka_{oc} (soil and sediment) = 6.4-10; Ka_{oc} (arithmetic mean) = 7.5**	

Fate and behaviour in air (Annex IIIA, point VII.3, VII.5)

	DOW	THOR
Direct photolysis in air	The phototransformation half-lifes in air calculated with OH radicals are 16.4 and 16.6 hours for CMIT and MIT, respectively. For the observed metabolites and degradates of CMIT and MIT the half-lives range from 24.2 to 31.8 hours. The phototransformation half-lifes in air calculated with NO_3 radicals are 29 and 29.9 hours for CMIT and MIT, respectively	The calculated phototransformation half-lifes in air with OH radicals are 17.5 and 14.3 hours for CMIT and MIT, respectively. The calculated phototransformation half-lifes in with ozone air are 45.8 days and 6.55 days for CMIT and MIT, respectively.
	CMIT DT_{50} = 17.5 hours **MIT DT_{50} = 16.6 hours** **C(M)IT/MIT: DT_{50} = 17.5 hours**	
Quantum yield of direct photolysis	Not available	
Photo-oxidative degradation in air	Not available	
Volatilization	Low potential due to low vapour pressure.	

Monitoring data, if available (Annex VI, para. 44)

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
A.i.r (indicate location and type of study)	Not available

Chapter 5: Effects on Non-target Species

Toxicity data of C(M)IT/MIT for aquatic species (most sensitive species of each group)
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	**DOW**	**THOR**
		Endpoint	Endpoint
Freshwater Fish			
Rainbow trout (*Oncorhynchus mykiss*)	Acute-96 hr US-EPA 72-1 Flow through	96 hr LC_{50} 1.36 mg/L (eq. to 0.19 mg a.i./L) 96 hr NOEC 0.93 mg /L (eq. to 0.13 mg ai/L) (mean measured concentration)	
	Acute-96 hr OECD 203 Static		96 hr LC_{50} 1.57 mg /L (eq. to 0.22 mg ai/L) (nominal concentration)
Bluegill sunfish (*Lepomis macrochirus*)	Acute-96 hr US-EPA 72-1 Flow through	96 hr LC_{50} 2.00 mg /L (eq. to 0.28 mg ai/L) 96 hr NOEC 1.57 mg /L (eq. to 0.22 mg ai/L) (mean measured concentration)	
Rainbow trout (*Oncorhynchus mykiss*)	Prolonged Toxicity Test -14 Day OECD 204 Flow through	14 d NOEC 0.36 mg /L (eq. to 0.05 mg ai/L) (mean measured concentration)	
	Mortality test -28 Days OECD 215 Semi Static		28d NOEC 0.70 mg /L (eq. to 0.098 mg ai/L) (nominal concentration)

Fathead minnow (*Pimephales promelas*)	Early life stage toxicity-36 days US-EPA 72-4 Flow through	NOEC, egg hatch, survival, length 0.86 mg /L (eq. to 0.12 mg ai/L) NOEC, weight 0.14 mg /L (eq. to 0.02 mg ai/L) (mean measured concentration)	
Saltwater Fish			
Sheepshead minnow (*Cyprinodon variegatus*)	Acute-96 hr Static	96 hr LC_{50} 2.14 mg ./L (eq. to 0.30 mg ai/L) 96 hr NOEC 1.29 mg /L (eq. to 0.18 mg ai/L) (nominal concentration)	
	Acute-96 hr Flow through		96 hr LC_{50} 3.43 mg /L (eq. to 0.48 mg ai/L) (nominal concentration)
Freshwater Invertebrates			
Daphnia magna	Acute-48 hr US-EPA 72-2 Flow through	48 hr EC_{50} 1.14 mg /L (eq. to 0.16 mg ai/L) 48 hr NOEC 0.86 mg ./L (eq. to 0.12 mg ai/L) (mean measured concentration)	
	Acute-48 hr OECD 202 Static		48 hr LC_{50} 4.71 mg ./L (eq. to 0.71 mg/L C(M)IT /MIT 14% a.i. and 0.10 mg ai/L) (issued from 2.1% source) (nominal concentration)

Daphnia magna	Chronic-21 days US-EPA 72-4	NOEC, survival of first generation[1], 0.71 mg ./L (eq. to 0.10 mg ai/L) EC_{50}, survival of first generation[1], > 1.29 mg ./L (eq. to 0.18 mg ai/L) (mean measured concentration)	
	Chronic-21 days OECD 202		NOEC reproduction 0.172 mg./L (eq. to 0.026 mg/L C(M)IT /MIT 14% a.i. and 0.0036 mg ai/L,issued from 2.1% source) (mean measured concentration)

[1]: most sensitive parameter

Saltwater Invertebrates			
Mysid (*Americamysis bahia*)	Acute-96 hr US-EPA OPPTS 850.1035 Flow through	96 hr EC_{50} 2.01 mg ./L (eq. to 0.282 mg a.i./L) 96 hr NOEC 0.21 mg./L (eq. to 0.030 mg a.i./L) (mean measured concentration)	
	Acute-96 hr US-EPA FIFRA 72-3 Flow through		96 hr EC_{50} 2.36 mg ./L (eq. to 0.33mg ai/L) (nominal concentration)
(Acartia tonsa)	Acute-48 hr ISO TC 147/SC 5 WG 2: and PARCOM Ring Test Protocol Static	48 hr EC_{50} 0.05 mg ./L (eq. to 0.007 mg ai/L) (nominal concentration)	
Crassostrea virginicia (Eastern oyster)	Acute-96 hr US-EPA FIFRA 72-3 Flow through		96 hr LC_{50} 0.29 mg ./L (eq. to 0.041mg ai/L) (nominal concentration)
Freshwater Algae			

Selenastrum capricornutum	120 hr OECD 201 US-EPA FIFRA 122-2 Static	24 hr NOErC 35.3 µg/L (eq. to 4.955 µg ai/L) (Initial measured concentration (LOQ/2))	
	72 hr OECD 201 US-EPA OPPTS 850.5400 Static		72 hr NOErC 8.29 µg ./L (eq. to 1.16 µg ai/L) 72 hr EbC50 69.50 µg /L (eq. to 9.73 µg ai/L) 72 hr ErC50 382.1 µg /L (eq. to 53.5 µg ai/L) (mean measured concentration)
Saltwater Algae			
Skeletonema costatum	48 hr OECD 201 US EPA OPPTS 850.5400 Static	48 hr NOE_rC 3.5 µg/L (eq. to 0.49 µg a.i./L) 48 hr ErC50 37.1 µg/L (eq. to 5.2 µg a.i./L) (mean measured concentration)	Available but no reliable
Freshwater sediment dwelling organisms			
Midge larvae (Chironomus riparius)	Chronic-28 days OECD 218	28 d NOEC, survival 23.79 mg/kg (eq to 3.33 mg a.i./kg) dry sediment 28 d LC_{50}, survival 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment 28 d NOEC, adult emergence 27 mg/kg (eq to 3.78 mg a.i./kg) dry sediment 28 d EC_{50}, adult emergence 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment 28 d NOEC, developmental rate > 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment 28 d EC_{50}, developmental rate > 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment (mean measured concentration)	Not Available

Lumbriculus variegatus	Chronic-28 days Draft OECD	28d EC50 survival 2.64-3.29 mg/kg dry sediment (eq to 0.37 - 0.46 mg a.i./kg dry sediment) 28d NOEC survival 1.93 mg/kg (eq to 0.27 mg a.i./kg) dry sediment (mean measured concentration)	Not Available
Hyalella azteca	Chronic-28 days US-EPA OPPTS 850.1735	28d EC50 survival 13.07-45.39 mg/kg dry sediment (eq to 1.83- 6.34 mg a.i./kg dry sediment) 28d NOEC survival 7.93 mg/kg (eq to 1.11mg a.i./kg) dry sediment (mean measured concentration)	Not Available

Saltwater sediment dwelling organisms - not available			
Microorganisms			
Activated sludge respiration inhibition	Acute-3 hr OECD 209	3 hr NOEC 6.50 mg ./L (eq. to 0.91 mg a.i./L) 3 hr EC_{50} 32.14 mg ./L (eq. to 4.5 mg a.i./L)	3 hr EC_{50} 56.57 mg /L (eq. to 7.92 mg ai/L) 3h EC_{20} 6.93 mg /L (eq. to 0.97 mg a.i./L)

Toxicity data of C(M)IT/MIT metabolites for aquatic species (most sensitive species of each group))
(Annex IIA, point 8.2, Annex IIIA, point 10.2)

Species	Time-scale	DOW*	
		Endpoint	Toxicity
Freshwater Fish- N-methyl malonamic acid			
Rainbow trout (*Oncorhynchus mykiss*)	Acute-96 hr	96 hr LC_{50} 96 hr NOEC	> 1000 mg /L ≥ 1000 mg /L (nominal concentration)
Freshwater Fish- N-methyl acetamide			
Rainbow trout (*Oncorhynchus mykiss*)	Acute-96 hr	96 hr LC_{50} 96 hr NOEC	> 694 mg /L ≥ 694 mg /L (mean measured concentration)
Freshwater Fish- Malonamic acid			
Rainbow trout (*Oncorhynchus mykiss*)	Acute-96 hr	96 hr LC_{50} 96 hr NOEC	> 1000 mg /L ≥ 1000 mg /L (nominal concentration)
Freshwater Invertebrates- N-methyl malonamic acid			
Daphnia magna	Acute-48 hr	48 hr EC_{50} 48 hr NOEC	> 986 mg /L ≥ 986 mg /L (mean measured concentration)
Freshwater Invertebrates- N-methyl-acetamide			
Daphnia magna	Acute-48 hr	48 hr EC_{50} 48 hr NOEC	> 863 mg /L not available (mean measured concentration)

Freshwater Invertebrates- Malonamic acid			
Daphnia magna	Acute-48 hr	48 hr EC_{50} 48 hr NOEC	> 1000 mg /L ≥ 1000 mg /L (nominal concentration)
Freshwater Algae- N-methyl malonamic acid			
Selenastrum Capricornutum	96 hr EC_{50}	96 hr NOEC 96 hr E_bC_{50} 96 hr E_rC_{50}	36 mg /L 58 mg ./L 128 mg /L (nominal concentration)
Freshwater Algae- N-methyl-acetamide			
Selenastrum Capricornutum	96 hr EC_{50}	72 hr NOEC 72 hr E_bC_{50} 72 hr E_rC_{50}	0.51 mg /L 1.6 mg /L 5.8 mg /L (nominal concentration)
Freshwater Algae- Malonamic acid			
Selenastrum Capricornutum	96 hr EC_{50}	96 hr NOEC 96 hr E_bC_{50} 96 hr E_rC_{50}	519 mg /L > 1080 mg /L > 1080 mg /L (initial measured concentration)

***No data provided by THOR**

Effects on earthworms or other soil non-target organisms

	DOW	**THOR**
	OECD 207, 14-days mortality	OECD 207, 14-days mortality
Acute toxicity to Earthworm (*Eisenia foetida*) (Annex IIIA, point XIII.3.2)	- Nominal : LC_{50}(survival)= 618.6 mg /kg dw (eq. to 86.6 mg a.i./kg dw) NOEC(survival)=63.1 mg/kg dw (eq. to 8.83 mg a.i./kg dw) - Twa: LC_{50}(survival)= 49.7 mg /kg dw (eq. to 6.96 mg a.i./kg dw) NOEC(survival)=5.07 mg/kg dw (eq. to 0.71 mg a.i./kg dw)	- Nominal : NOEC (survival) = 180 mg/kg (eq to 26 mg a.i/kg) dw LC_{50} (survival) > 1000 mg/kg (eq to > 143 mg a.i/kg) dw - Twa: NOEC (survival) = 14.47 mg/kg (eq to 2.09 mg

		a.i/kg) dw LC_{50} (survival) > 80.38 mg/kg (eq to >11.49 mg a.i/kg) dw
Reproductive toxicity to Earthworm (*Eisenia foetida)* (Annex IIIA, point XIII.3.2)	Not available	Not available

Effects on soil micro-organisms (Annex IIA, point 7.4)

	DOW	THOR
	OECD 216, OECD 217, 28 days	OECD 216, OECD 217, 28 days
Nitrogen mineralization	- Nominal : EC_{50} = 266.4 mg /kg dw (eq. to 37.3 mg a.i. /kg dw) NOEC = 71.4 mg /kg dw (eq. to 10 mg a.i. /kg dw) - Twa: EC_{50} = 10.71 mg /kg dw (eq. to 1.50 mg a.i. /kg dw) NOEC = 2.87mg /kg dw (eq. to 0.402 mg a.i. /kg dw)	- Nominal : EC_{50} = 214.3 mg / kg d.w (eq. to 30 mg a.i. /kg dw) NOEC = 114.3 mg / kg d.w (eq. to16 mg a.i /kg dw) - Twa: EC_{50} = 8.14 mg / kg d.w (eq. to 1.14 mg a.i. /kg dw) NOEC = 4.34 mg / kg d.w (eq. to 0.61 mg a.i /kg dw)
Carbon mineralization	- Nominal : EC_{50} = 275.7 mg /kg dw (eq. to 38.6 mg a.i. /kg dw) NOEC (nominal) = 7.14 mg /kg dw (eq. to 1 mg a.i. /kg dw) - Twa: EC_{50} = 11.08 mg /kg dw (eq. to 1.55 mg a.i. /kg dw) NOEC (nominal) = 0.287 mg /kg dw (eq. to 0.0402 mg a.i. /kg dw)	- Nominal : EC_{50} = 180.71 mg /kg d.w (eq. to 25.3 mg a.i. /kg dw) NOEC = 114.3 mg / kg d.w (eq. to 16 mg a.i /kg dw) - Twa: EC_{50} = 6.87 mg /kg d.w (eq. to 0.96 mg a.i. /kg dw) NOEC = 4.34 mg / kg d.w (eq. to 0.61 mg a.i /kg dw)

Effects on terrestrial vertebrates

	DOW	THOR
Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	LD_{50} oral : 457 mg/kg bw (rat) (eq. to 64 mg a.i. /kg bw) LD_{50} dermal : 660 mg./kg bw (rabbit) (eq. to 92.4 mg a.i./kg bw)	LD_{50} oral : 472 mg/kg bw (rat) (eq. to 64 mg a.i. /kg bw) LD_{50} dermal > 1 007 mg./kg bw (rat) (eq. to 141 mg

	LC_{50} inhalation : 2.36 mg./L air (rat) (eq. to 0.33 mg a.i./L) Skin irritation : Irritant (rabbit) Eye irritation : Corrosive (rabbit) Skin sensitization : Sensitising	a.i./kg bw) LC_{50} inhalation : 1.23 mg./L air (rat) (eq. to 0.171 mg a.i./L) Skin irritation : Corrosive (rabbit) Eye irritation : Corrosive (rabbit) Skin sensitization : Sensitising
Acute toxicity to birds (Annex IIIA, point XIII.1.1)	Bobwhite quail : LD_{50} = 460.71 mg /kg bw (eq. to 64.5 mg a.i./kg bw) (nominal concentration)	Not available
Dietary toxicity to birds (Annex IIIA, point XIII.1.2)	Bobwhite quail : LC_0 = 10357 mg /kg (eq. to1450 mg /kg a.i.) in diet NOEC = 1614 mg /kg (eq. to 226 mg /kg a.i.) based on weight and food consumption LC_{50} = 25257 mg /kg (eq. 3536 mg /kg a.i.) Mallard Duck: LC_0 = 1614 mg /kg (eq. to 226 mg /kg a.i.) LC_{50} = 6750 mg /kg (eq. to 945 mg /kg a.i.) (mean measured concentrations)	Not available
Reproductive toxicity to birds (Annex IIIA, point XIII.1.3)	Not available	Not available

Effects on honeybees (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not available
Acute contact toxicity	Not available

Effects on other beneficial arthropods (Annex IIIA, point XIII.3.1)

Acute oral toxicity	Not available
Acute contact toxicity	Not available
Acute toxicity to	Not available

Bioconcentration (Annex IIA, point 7.5)

	DOW	THOR
Bioconcentration factor (BCF)	CMIT- Bluegill sunfish: Steady state BCF = 41-54 (total ^{14}C-residues, parent and metabolites) The log P (log octanol:water partition coefficient) for CMIT is 0.401. MIT: not available The log P (log octanol:water partition coefficient) for MIT is -0.486.	EPIWIN: CIT BCF = 3.16 MIT BCF = 3.16
Depuration time (DT_{50}) (DT_{90})	CMIT- Bluegill sunfish: D_{T50} = 0.64-1.6 days MIT: not available	NA
Level of metabolites (%) in organisms accounting for > 10 % of residues	Not applicable	NA

Chapter 6: Other End Points

Effects on Terrestrial plants (Document IIIA, point 7.5)

Terrestrial Plants			DOW
Canola, Red Clover, and Rice	OECD 208 21 days Seedling emergence and seedling growth Soil incorporation	Canola : - Nominal : EC_{50}, emergence EC_{50}, survival EC_{50}, shoot weight NOEC, emergence NOEC, survival NOEC, shoot weight - Twa: EC_{50}, emergence EC_{50}, survival EC_{50}, shoot weight NOEC, emergence NOEC, survival NOEC, shoot weight Red Clover :	 660 mg /kg dry soil (eq. to 92.4 mg ai/kg) 218.57 mg /kg dry soil (eq. to 30.6 mg ai/kg) 68.9 mg /kg dry soil (eq. to 9.65 mg ai/kg) 214.3 mg /kg dry soil (eq. to 30 mg ai/kg) 64.3 mg /kg dry soil (eq. to 9.0 mg ai/kg) 19.3 mg /kg dry soil (eq. to 2.7 mg ai/kg) 28.04 mg /kg dry soil (eq. to 3.93 mg ai/kg) 9.29 mg /kg dry soil (eq. to 1.30 mg

		- Nominal : EC_{50}, emergence EC_{50}, survival EC_{50}, shoot weight NOEC, emergence NOEC, survival NOEC, shoot weight - Twa: EC_{50}, emergence EC_{50}, survival EC_{50}, shoot weight NOEC, emergence NOEC, survival NOEC, shoot weight Rice : - Nominal : EC_{50}, emergence EC_{50}, survival EC_{50}, shoot weight NOEC, emergence NOEC, survival NOEC, shoot weight - Twa: EC_{50}, emergence EC_{50}, survival EC_{50}, shoot weight NOEC, emergence NOEC, survival NOEC, shoot weight	ai/kg) 2.93 mg /kg dry soil (eq. to 0.41 mg ai/kg) 9.11 mg /kg dry soil (eq. to 1.27 mg ai/kg) 2.73 mg /kg dry soil (eq. to 0.38 mg ai/kg) 0.82 mg /kg dry soil (eq. to 0.11 mg ai/kg) 230.71 mg /kg dry soil (eq. to 32.3 mg ai/kg) 85 mg /kg dry soil (eq. to 11.9 mg ai/kg) 48.36 mg /kg dry soil (eq. to 6.77 mg ai/kg) 64.3 mg /kg dry soil eq. to 9.0 mg ai/kg) 19.3 mg /kg dry soil (eq. to 2.7 mg ai/kg) 19.3 mg /kg dry soil (eq. to 2.7 mg ai/kg) 9.80 mg /kg dry soil (eq. to 1.37 mg ai/kg) 3.61 mg /kg dry soil (eq. to 0.51 mg ai/kg) 2.05 mg /kg dry soil (eq. to 0.29 mg ai/kg) 2.73 mg /kg dry soil eq. to 0.38 mg ai/kg) 0.82 mg /kg dry soil (eq. to 0.11 mg ai/kg) 0.82 mg /kg dry soil (eq. to 0.11 mg ai/kg) > 714.3 mg /kg dry soil (eq. to 100 mg ai/kg dry soil) > 714.3 mg /kg dry soil (eq. to 100 mg ai/kg dry soil) 120 mg /kg dry soil (eq. to 16.8 mg ai/kg) 214.3 mg /kg dry soil (eq. to 30 mg ai/kg) 214.3 mg /kg dry soil (eq. to 30 mg ai/kg)

			64.3 mg /kg dry soil (eq. to 9.0 mg ai/kg) > 30.35 mg /kg dry soil (eq. to 4.25 mg ai/kg dry soil) > 30.35 mg /kg dry soil (eq. to 4.25 mg ai/kg dry soil) 5.10 mg /kg dry soil (eq. to 0.71 mg ai/kg) 9.11 mg /kg dry soil (eq. to 1.27 mg ai/kg) 9.11 mg /kg dry soil (eq. to 1.27 mg ai/kg) 2.73 mg /kg dry soil (eq. to 0.38 mg ai/kg)
Canola, Red Clover, and Rice	Vegetative vigor Foliar spray	<u>Canola , Red Clover, Rice :</u> NOEC, biomass EC_{50}, biomass	7143 mg /L (eq. to1000 mg a.i./L) > 7143 mg /L (eq. to1000 mg a.i./L)

Appendix II: List of intended uses

Summary of intended uses (Thor)

Object and/or situation (a)	Product name	Organisms controlled (c)	Formulation		Application			Applied amount per treatment		
			Type (d-f)	Conc. of as (i)	method kind (f-h)	number min max (k)	interval between applications (min)	g as/L min max	water L/m^2 min max	g as/m^2 min max
PT 11: Liquid-cooling/ processing systems	ACTICIDE®MV	Bacteria and Fungi	solution	1,5 % CIT/MIT	Automatic dosing device	Continuous dosing	Continuous dosing	Continuous dosing: 0, 6 – 5, 0 mg a.i/L	NA	NA

Summary of intended uses (Dow)

Object and/or situation	Product name	Organisms controlled	Formulation		Application			Applied amount per treatment			Remarks:
			Type	Conc. of as	method kind	number min max	interval between applications (min)	g as/L min max	water L/m^2 min max	g as/m^2 min max	

Preservation of liquid cooling and industrial processing systems: (open and closed recirculating cooling towers, industrial process water, air washers, air conditioning systems, humidifiers, non-food pasteurizers/sterilizers/can warmers, non-medical/non-potable reverse osmosis (RO) and ultrafiltration (UF) membranes, wastewater treatment systems, water rinse baths, and conveyor lubricants). Preservation of photo-processing systems, print fountain solutions, textile systems/spinning fluids, electrodeposition coating systems, paint spray booths, wood treatment solutions, and industrial cleaning in place.	C(M)IT/MIT containing biocidal products Kathon™886F (Kathon™WT)	bacteria, fungi and algae.	Kathon™886F: aqueous concentrate	14% (Kathon™ 886F). This product may also be diluted to obtain 3% or 1.5% aqueous formulations.	Add to a central reservoir or suitable location to provide adequate mixing using manual addition or a metered pump and repeat as needed.	Single dose. Dose C(M)IT/MIT weekly to maintain microbial control.	N/A	1 - 50 ppm total a.i.depending on the intended uses.	N/A	N/A	-

Appendix III: List of acceptable intended uses

Thor:

Uses	Human risk assessment	Environmental risk assessment
	Conditions	Conditions
Process and cooling water		
	With gloves, impermeable coveralls, RPE and rinse of dispensing pumps	Closed and small open recirculating cooling systems, only when release from the systems are directed to a STP and at a doses rates range from 0.2 to 6 mg L^{-1},

Dow:

Uses	Human risk assessment	Environmental risk assessment
	Conditions	Conditions
Process and cooling water		
	With gloves, impermeable coveralls, RPE and rinse of dispensing pumps	Closed and small open recirculating cooling systems, only when release from the systems are directed to a STP and at a doses rates range from 0.2 to 6 mg L^{-1},

Uses	Human risk assessment	Environmental risk assessment
	Conditions	**Conditions**
Textile and spinning fluids		
	With gloves and impermeable coveralls	
Paint spray booths and electrodeposition coating systems (including car refinishing and manufacture)		
	With gloves, impermeable coveralls and RPE	
Industrial hygiene, clean in place (CIP)		
	With gloves, impermeable coveralls and RPE	
Print Fountain Solutions		
	Covered by others uses evaluation	

Appendix IV: List of Studies

Reference list sorted by section: Dow

Section No / Reference No	Author(s)	Year	Title. Source (if different from company) Company, Report No. GLP (where relevant) / (Un)Published	Data Protection Claimed (Y/N)	Owner
A2.10/01	Popendorf W., Selim M. S. and Lewis M. Q.	1995	Exposure while applying industrial antimicrobial pesticides. American Industrial Hygiene Association Journal, 56:993-1001.	N	/
A3/01	Petigara, R.B.	2001	Biocides product directives common core data set for active (chemical) substances, Parts 2 and 3: identity, and physical and chemical properties of Kathon™ 886F Biocide. Rohm and Haas Company, Report N° TR-01-058 (December 20, 2001), GLP, Unpublished.	Y(ii)[17]	Rohm and Haas
A3/02	Petigara, R.B.	2003	Biocides product directives common core data set for active (chemical) substances, Parts 2 and 3: identity, and physical and chemical properties of SF-886 Technical. Rohm and Haas company, Report N° GLP-2003-040 (August 12, 2003), GLP, Unpublished.	Y(ii)	Rohm and Haas

[17] Y(ii) : Data protection claimed in accordance with Article 12.1(c) (ii) : Active substance already on the market on 14 May 2000. Data submitted for the first time in support of the first inclusion in Annex I or IA **or** Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA (data generated/submitted after the entry into force of the Directive).

A3/03	Derbyshire, R.L.	1990	Product chemistry Kathon™ 886F microbicide, Report N° TR-90-29 (November 26,1990), GLP, Unpublished.	Y(ii)	Rohm and Haas
A3/04	Broughton, H.S.	1993	Characterization of test substance Kathon™ 886F, an MUP, to be used for submission to regulatory agencies in Europe, (December 15, 1993), GLP, Unpublished.	Y(ii)	Rohm and Haas
A3/06	Betteley, J.; Petigara, R.	2001	Kordek™ 573T Industrial Microbicide Physicochemical Properties, (August 13, 2001), GLP, Unpublished.	Y(ii)	Rohm and Haas
A3/07	Broughton, H.S.	1992	Product chemistry –Series 63: SF-886 Tech Technical grade of active ingredient, (February 19, 1992), GLP, Unpublished.	Y(ii)	Rohm and Haas
A3/08	Padmanaban, A.	2008	High AI Kathon™ 886: Determination of Physico-Chemical Properties – Part 1; International Institute of Biotechnology and Toxicology (IIBAT); Rohm and Haas Company; Report N° GLP-2008-129; GLP / Unpublished	Y(ii)	Rohm and Haas
A3/09	Pandisolvi, S.	2008	High AI Kathon™ 886: Determination of Physico-Chemical Properties – Part 2; International Institute of Biotechnology and Toxicology (IIBAT); Rohm and Haas Company; Report N° GLP-2008-128; GLP / Unpublished	Y(ii)	Rohm and Haas
A3/10	Tremain, S.P.	2008	High A.I. Kathon™ 886: Determination of Hazardous Physico-Chemical Properties; SafePharm Laboratories Ltd.; Rohm and Haas Company; Report N° GLP-2008-133; GLP / Unpublished	Y(ii)	Rohm and Haas
A3/11	Berrios, E.	2008	High AI Kathon 886: Determination of Accelerated Storage Stability; Rohm and Haas Company; Report N° GLP-2008-126; GLP / Unpublished	Y(ii)	Rohm and Haas

A3/12	Berrios, E.	2008	High AI Kathon 886: Determination of Long-Term Storage Stability, three months interim report; Rohm and Haas Company; Report N° GLP-2008-134; GLP / Unpublished	Y(ii)	Rohm and Haas
A4.1.a/01:	Berrios, Efrain	2006	"CIS Dept. Test method #06-111-01, Reverse phase HPLC analysis of Kathon™ 886 Technical for active ingredients" July 20, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.a/02:	Berrios, Efrain	2006	"CIS Dept. Test method #06-111-02, Reverse phase HPLC analysis of Kathon™ 886 Technical for active ingredients" October 3, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.a/03:	Berrios, Efrain	2006	"GLP validation of CIS analytical test method #06-111-01 for the analysis of Kathon™ Tech for active ingredient" under protocol # GLP 24P-2006-106" Rohm and Haas Report # GLP-2006-085, September 12, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/01:	Doshi, Deepak,	2001	"CIS Dept. Test method #89-03-03, Reverse phase HPLC analysis of Kathon™ Formulations for active ingredients" March 5, 2001, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/02:	Doshi, Deepak	2001	"GLP report on validation of CIS test method #89-03-03 (Draft) for the analysis of Kathon™ formulations for active ingredients under protocol # GLP 24P-2000-026" Rohm and Haas Report # GLP-2001-006, February 15, 2001, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/03:	Doshi, Deepak	2003	"Round robin study for the analysis of active ingredients in Kathon™ formulations in support of European Biocidal Product Directives", Rohm and Haas Report # GLP-2002-072, April 1, 2003, Unpublished.	Y(ii)	Rohm and Haas

A4.1.b/04:	Eisenschmied, Mark A	2006	"GLP LC-MS peak identity verification of AI in Kathon™ CG and Kathon™ 886F as detected by CIS TM 89-03-03", CAs Technical document # TD2006-182. July 19, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/05:	Eisenschmied, Mark A,	2006	"GLP LC-MS peak identity verification of AI in Kathon™ 39FG as detected by CIS TM 89-03-03", CAS Technical Document # TD2006-096, May 1, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/06 :	Berrios, Efrain	2006	"CIS Dept. Test Method #06-105-01, Reverse phase HPLC analysis of Kathon™ 39FG for active ingredients" May 15, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/07:	Berrios, Efrain	2006	"GLP validation of CIS analytical test method #89-03-03 for the analysis of Kathon™ 39FG for active ingredients" Protocol # GLP 24P-2006-027" Rohm and Haas Report # GLP-2006-016, May 15, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.c/01:	Bluder, David	1997	Test Method # 96-53-02,"Ion-pair HPLC method to determine magnesium nitrate in Kathon™ formulations", January 15, 1997, Unpublished.	Y(ii)	Rohm and Haas
A4.1.c/02:	Berrios, Efrain	2006	2006, CIS Dept. Test method #96-53-03, Ion-pair HPLC method to determine magnesium nitrate in Kathon™ formulations" June 15, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.c/03:	Berrios, Efrain	2006	"GLP validation of BRAG analytical test method #96-53-02 for the analysis of Kathon™ 886F for magnesium nitrate", protocol # GLP 24P-2006-083, Rohm and Haas Report # GLP-2006-021, June 08, 2006, Unpublished.	Y(ii)	Rohm and Haas

A4.1.d/01:	Berrios, Efrain	2006	CIS Dept. Test method #06-110-01, "Analysis of Kathon™ 886F for % magnesium chloride using potentiometric titration" June 26, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.d/02:	Berrios, Efrain	2006	CIS Dept. Test method #06-110-02, "Analysis of Kathon™ 886F for % magnesium chloride using potentiometric titration", August 2, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.d/03:	Berrios, Efrain	2006	"GLP validation and revision of of CIS analytical test method #06-110-01 for the determination of magnesium chloride in Kathon 886F ", protocol # 24P-2006-097, Rohm and Haas Report # GLP-2006-046, July 25, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.2.a/01:	Marbo, M	2005	Validation of CIS analytic methods to determine RH-886 and RH-573 in soil and sediment Samples. Performed at Rohm and Haas Technical Center, Spring House, PA, USA, Technical Report N°. GLP-2005-009, December 12, 2005, Unpublished.	Y(ii)	Rohm and Haas
A4.2.b/01:	Dr. Krainz Alexander	2006	Test method for the determination of 2-methyl-4-isothiazolin-3-one (RH-573) and 5-chloro-2-methyl-4-isothiazolin-3-one (RH-651) the active ingredients in RH-886 and RH-573 formulations, in air, Test method 857665, June19, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.2.b/02:	Dr. Krainz, Alexander	2006	Development and validation of residue analytical methods for determination of 2-methyl-4-isothiazolin-3-one (RH-573) and 5-chloro-2-methyl-4-isothiazolin-3-one (RH-651) the active ingredients in RH-886 and RH-573 formulations, in air, RCC Ltd., Study # 857665, Rohm and Haas Study # GLP-2005-012, June19, 2006, Unpublished.	Y(ii)	Rohm and Haas

A4.2.c/01:	Dr. Stefan Wolf	2004	Development and validation of a residue analytical method for 5-chloro-2-methyl-4-isothiazolin-3-one (CMIT or RH-651) and 2-methyl-4-isothiazolin-3-one (MIT or RH-573) in Drinking, Surface and Sea Water, RCC Ltd., Study # 852129, Rohm and Haas Report # GLP-2004-042, November 01, 2004, Unpublished.	Y(ii)	Rohm and Haas
A4.2.c/02:	Dr. Stefan Wolf	2004	Test Method for the determination of 5-chloro-2-methyl-4-isothiazolin-3-one (CMIT or RH-651) and 2-methyl-4-isothiazolin-3-one (MIT or RH-573) in Drinking, Surface and Sea Water, RCC Ltd., Study # 852129, Rohm and Haas Report # GLP-2004-042, November 01, 2004, Unpublished.	Y(ii)	Rohm and Haas
A4.3/01:	Dr. Krainz A.	2007	Validation of a residue analytical method for the determination of 2-methyl-4-isothiazoin-3-one (RH-573) and 5-chloro-2-methyl-4-isothiazolin-3-one (RH-651), the active ingredients in Kathon™ 886 in acetic acidic water, water containing ethanol and olive oil (food stimulants), RCC Ltd, Study # B25626, Rohm and Haas Report # GLP-2007-070, August 29, 2007, Unpublished.	Y(ii)	Rohm and Haas
A4.3/02:	Dr. Krainz A.	2007	Test method for the determination of 2-methyl-4-isothiazoin-3-one (RH-573) and 5-chloro-2-methyl-4-isothiazolin-3-one (RH-651), the active ingredients in Kathon™ 886 in acetic acidic water, water containing ethanol and olive oil (food stimulants), RCC Ltd, Study # B25626, August 29, 2007, Unpublished.	Y(ii)	Rohm and Haas

A5.3.1/01	Diehl M A	2005	The Antimicrobial Activity of Chloromethylisothiazolinone + Methylisothiazolinone (CMIT/MIT): "Minimum Inhibitory Concentration (MIC) Studies versus Algae, Fungi, and Bacteria." Rohm and Haas Company, Technical Report Nº TR-05-026 (April 20, 2005), unpublished.	Y(ii)	Rohm and Haas
A5.3.1/02	Diehl M A	2006	Speed of kill (SOK) and multiple challenge efficacy test with Chloromethylisothiazolinone + Methylisothiazolinone (CMIT/MIT) in an in-can model preservative system. Rohm and Haas Company, Technical Report NºBPD-06-017 (May 23, 2006), unpublished.	Y(ii)	Rohm and Haas
A5.4.1/01	Williams T.M	2006	The Antimicrobial Mechanism of Action of Chloromethylisothiazolinone-Methylisothiazolinone (CMIT/MIT) Biocide. Rohm and Haas Company, Technical Report Nº TR-06-064 (July 26, 2006), unpublished.	Y(ii)	Rohm and Haas
A6.1.1/01:	[redacted]	1993	Kathon™ 886 all-magnesium formulation: acute oral toxicity study in male rats, Rohm and Haas Company, Rohm and Haas Report N° 77R-038A, July 23, 1993, Unpublished.	Y(i)[18]	Rohm and Haas
A6.1.1/02:	[redacted]	2006	N-Methyl-malonamic acid acute oral toxicity study in male and female rats (metabolite), Rohm and Haas Company Report N°: 72R-1039 (November 13, 1972 original report; April 13, 2006 additional data), unpublished.	Y(ii)	Rohm and Haas

[18] Y(i) : Data protection claimed in accordance with Article 12.1(c) (i), as data already submitted in member states before the entry into force of the Directive. Data submitted to the MS before 14 May 2000 on existing a.s. for the purpose of its entry into Annex I/IA.

A6.1.2/01:	[redacted]	1993 b	Kathon™ 886 all-magnesium formulation: acute dermal toxicity study in male rabbits, Rohm and Haas Company, Rohm and Haas Report N° 76R-056A, July 23, 1993, unpublished.	Y(i)	Rohm and Haas
A6.1.3.a/01:	[redacted]	1991 a	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 91R-018, July 10, 1991, Unpublished.	Y(i)	Rohm and Haas
A6.1.3.a/02:	[redacted]	1991 b	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018A, August 12, 1991, Unpublished.	Y(i)	Rohm and Haas
A6.1.3.a/03:	[redacted]	1992	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018B, June 9, 1992, Unpublished.	Y(i)	Rohm and Haas
A6.1.3.b/01:	Papagiannis C.N.	1993	Kathon™ 886F biocide: evaluation of the upper airway irritation potential (RD50), International Research and Development Corporation Project ID: 285-047, Rohm and Haas Report N° 91RC-047, April 23, 1993, Unpublished.	Y(i)	Rohm and Haas
A6.1.4.a/01:	[redacted]	1986	Kathon™ 886 – 13.9 %: determination of the acute dermal irritation or corrosion in male rabbits, [redacted] Protocol N° BT0102, Rohm and Haas Report N° 86RC-1005, November 26, 1986, Unpublished.	Y(ii)	Rohm and Haas
A6.1.4.a/03:	[redacted]	1985	Kathon™ 886 1.5 % Biocide: skin irritation study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 84R-244A, B, C, D, January 16, 1985, Unpublished.	Y(i)	Rohm and Haas

A6.1.4.b/01:	Longacre, S.L.	1995	Kathon™ 886 Biocide: revised acute toxicity reports, Rohm and Haas Company, Rohm and Haas Report N° 76-56B, March 20, 1995, Unoublished.	Y(i)	Rohm and Haas
A6.1.5/01:	House R.V.	2000 a	Murine local lymph node assay with Chloromethylisothiazolinone and Methylisothiazolinone, Covance Laboratories Study ID: 6228-145, Rohm and Haas Report N° 00RC-148A, November 7, 2000, Unpublished.	Y(ii)	Rohm and Haas
A6.1.5/02:	[redacted]	2001	Chloromethylisothiazolinone/Methylisothiazolinone 3:1 - Open epicutaneous test in guinea pigs, [redacted] Project ID N 31H0367/002132, US Ref N° 01RC-1030, July 12, 2001, Unpublished.	Y(ii)	
A6.1.5/03:	House R.V.	2000 b	Murine local lymph node assay to evaluate Chloromethylisothiazolinone/Methylisothiazolinone, Covance Laboratories Study ID: 6228-146, Rohm and Haas Report N° 00RC-148B, November 7, 2000, Unpublished.	Y(ii)	Rohm and Haas
A6.1.5/04:	[redacted]	2000	Chloromethylisothiazolinone and Methylisothiazolinone 3:1: Dermal sensitization study in guinea pigs Maximization test, Rohm and Haas Company Report N° 00R-140, September 28, 2000, Unpublished.	Y(i)	Rohm and Haas
A6.1.5/06:	[redacted]	1982	Kathon™ 886: a study of the concentration-dependent delayed contact hypersensitivity in guinea pigs, Rohm and Haas Company, Rohm and Haas Report N° 81R-66, August 24, 1982, Unpublished.	Y(i)	Rohm and Haas

A6.1.5/06bis:	[redacted]	1983	KathonTM Biocide: Manifestation of delayed contact hypersensitivity in guinea pigs is dependent on the concentration for induction and challenge, The Journal of Investigative Dermatology, 81:409-411, 1983, Unpublished, Published.	N	Rohm and Haas
A6.1.5/07:	Chapdelaine J.M.	2003	N-(Methyl) malonamic acid: Local lymph node assay, Calvert Laboratories Report No. 0787XR07.001, Rohm and Haas Report N°: 02RC-049 (August 8, 2003), Unpublished.	Y(ii)	Rohm and Haas
A6.2.a/01:	[redacted]	2005a	Metabolism and pharmacokinetics of 14C-RH-573 in the rat, [redacted] Study N°: XBL01057, Rohm and Haas Report N°: 03RC-043, June 13, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.2.a/02:	[redacted]	2005b	Metabolism of 14C-RH-573 in the biliary cannulated rat, [redacted] Report N°: RPT01215, Rohm and Haas Report N°: 04RC-056, July 14, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.2.a/03:	[redacted]	2003	Tissue distribution of 14C-RH-573 in the mouse. [redacted], unpublished report, XBL Report N° XBL00994, Rohm and Haas Company Report N° 03RC-042, August 27, 2003, Unpublished.	Y(ii)	Rohm and Haas
A6.2.a/04:	[redacted]	2003	2-Methyl-4-isothiazolin-3-one: In vitro percutaneous absorption through rat skin, Rohm and Haas Company, Rohm and Haas Company Report No. 00R-066, August 22, 2003, Unpublished.	Y(ii)	Rohm and Haas

A6.2.a/05:	Ward R.J.	2005	2-Methyl-4-isothiazolin-3-one (MI): in vitro absorption from water and three formulations through human epidermis, Central Toxicology Laboratory Study No: JV1839, Rohm and Haas Report N° 04RC-066 (August 16, 2005), Unpublished.	Y(ii)	Rohm and Haas
A6.2.b/01:	[redacted]	2005c	Metabolism of 14C-RH-651 in the rat, [redacted] Study N°: RPT01224, Rohm and Haas Report N°: 04RC-053, August 4, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.2.b/02:	[redacted]	2005d	Metabolism of 14C-RH-651 in the biliary cannulated rat, [redacted] Report N°: RPT01229, Rohm and Haas Report N°: 04RC-057, August 4, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.2.b/03:	[redacted]	2004	Tissue distribution of 14C-RH-651 in the mouse. [redacted] unpublished report, XBL Report N° XBL01156, Rohm and Haas Company Report N° 04RC-054, August 31, 2004, Unpublished.	Y(ii)	Rohm and Haas
A6.2.b/04:	Ward RJ	2005	5-Chloro-2-methyl-4-isothiazolin-3-one (CMIT) and 2-Methyl-4-isothiazolin-3-one (MIT) in a 3:1 w/v mixture: in vitro absorption of CMI from aqueous solutions through human epidermis, Central Toxicology Laboratory Study N°: JV1858, Rohm and Haas Report N°: 04RC-067, August 16, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.2.b/05:	Ward RJ	2005	5-Chloro-2-methyl-4-isothiazolin-3-one (CMIT)/2-Methyl-4-isothiazolin-3-one (MIT): in vitro absorption of CMIT from an aqueous solution and three formulations through human epidermis, Central Toxicology Laboratory Study N°: JV1870, Rohm and Haas Report N°: 05RC-055, October 20, 2005, Unpublished.	Y(ii)	Rohm and Haas

A6.2.c/01:	[redacted]	1997	14C-Kathon biocide toxicokinetic study in rats, Rohm and Haas Company, Rohm and Haas Report N° 97R-1058, March 14, 1997, Unpublished.	Y(i)	Rohm and Haas
A6.3.1/01:	[redacted]	1984	Kathon™ 886 MW: one month oral toxicity study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 84R-095, August 31, 1984, Unpublished.	Y(i)	Rohm and Haas
A6.4.1.a/01:	[redacted]	1982	Kathon™ 886 NAR three month rat drinking water study and one generation reproduction study, Rohm and Haas Company, Rohm and Haas Report N° 81R-162, September 9, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.4.1.a/02:	[redacted]	1975	RH-886T, RH-35,375 and RH-00,345: three month subchronic oral safety evaluation study in rats (metabolite). [redacted] Study N°: 285-010, Rohm and Haas Report N°: 75RC-1001 (February 17, 1975), Unpublished.	Y(ii)	Rohm and Haas
A6.4.1.b/01:	[redacted]	1975	RH-886: Three month subchronic oral safety evaluation study in Beagle dogs, International Research and Development Corporation Study N° 285-008, Rohm and Haas Report N° 75RC-1002, February 19, 1975, Unpublished.	Y(ii)	Rohm and Haas
A6.4.2/01:	[redacted]	1982	Kathon™ 886 MW: 90-day percutaneous toxicity study in rabbits. Rohm and Haas Company, Rohm and Haas Report N° 80R-119, August 31, 1982, Unpublished.	Y(i)	Rohm and Haas

A6.4.3/01:	[redacted]	1984	Kathon™ 886 MMPA Process: thirteen-week inhalation toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 82R-245, December 10, 1984, Unpublished.	Y(i)	Rohm and Haas
A6.5/01:	[redacted]	1994	Kathon biocide: 24-month drinking water chronic/oncogenic study in rats, Rohm and Haas Company, Rohm and Haas Report N° 90R-149, January 24, 1994, Unpublished.	Y(i)	Rohm and Haas
A6.5/02:	[redacted]	1983	Kathon™ CG: 30-month dermal carcinogenesis study in male mice, Rohm and Haas Company, Rohm and Haas Report N° 81R-288, January 14, 1983, Unpublished.	Y(ii)	Rohm and Haas
A6.6.1/01:	Fujii M. and Sugita N.	1982	Microbial mutagenicity study on Kathon WT, Takeda Chemical Industries, Japan, Rohm and Haas Report N° 82RC-1019, January 1982, Unpublished.	Y(ii)	Rohm and Haas
A6.6.1/02:	Sames J.L., Frank J.P.	1990	Kathon™ 886: Salmonella typhimurium gene mutation assay, (Screening test in TA98 and TA1537), Rohm and Haas Company, Rohm and Haas Report N° 90R-0142, July 24, 1990, Unpublished.	Y(ii)	Rohm and Haas
A6.6.1/03:	San R.H.C. and VanDyke M.R.	2005	N-Methyl Malonamic Acid: bacterial reverse mutation (Ames) assay, BioReliance Study N°: AB13CE.503.BTL, Rohm and Haas Report N°: 05RC-045, September 9, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.6.2/01:	McGlynn A.M. and McCarthy K.L.	1981	Kathon™ 886 mammalian cell transformation test, Rohm and Haas Company, Rohm and Haas Report N° 81R-110, June 29, 1981, Unpublished.	Y(i)	Rohm and Haas

A6.6.3/01:	[redacted]	1981	Mutagenicity evaluation of TD-81-155 in the mouse lymphoma forward mutation assay, [redacted] Project N° 20989, Rohm and Haas Report N° 81RC-153, December 1981, Unpublished.	Y(i)	Rohm and Haas
A6.6.3/02:	[redacted]	1991	Kathon™ 886 M.W. biocide: Test for chemical induction of unscheduled DNA synthesis in rat primary hepatocyte cultures by autoradiography, [redacted] Study N° 0159-5100, Rohm and Haas Report N° 90RC-168, April 24, 1991, Unpublished.	Y(i)	Rohm and Haas
A6.6.4/01:	[redacted]	1997	Kathon™ 886F biocide: measurement of unscheduled DNA synthesis in rat liver using an in vivo/in vitro procedure, [redacted] Report N° 616/21-1052, Rohm and Haas Report N° 97RC-055, October 1997, Unpublished.	Y(i)	Rohm and Haas
A6.6.4/02:	[redacted]	1992	Acute test for chemical induction of chromosome aberration in mouse bone marrow cells in vivo, [redacted] Study N° 0202-1541, Rohm and Haas Report N° 92RC-0054, October 15, 1992, Unpublished.	Y(i)	Rohm and Haas
A6.6.5/01:	Valencia R.	1982	Drosophila sex-linked recessive lethal test on Kathon biocide, Zoology Department, University of Wisconsin, Madison, WI, USA, Laboratory Project N° 100, Rohm and Haas Report N° 82RC-94, December 22, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.7/01:			Refer to the A6.5.1/01 study above.		
A6.7/02:			Refer to the A6.5.2/01 study above		

A6.8.1.a/01:	[redacted]	1980	Kathon™ 886: Teratology study in rats, [redacted] Project N° 417-399, Rohm and Haas Report N° 80RC-81, September 25, 1981, Unpublished.	Y(i)	Rohm and Haas
A6.8.1.b/01:	[redacted]	1992	Kathon™ biocide: oral (gavage) developmental toxicity study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 91R-074, April 28, 1992, Unpublished.	Y(i)	Rohm and Haas
A6.8.2.a/01:	[redacted]	1982	Kathon™ 886 NAR three month rat drinking water study and one generation reproduction study, Rohm and Haas Company, Rohm and Haas Report N° 81R-162, September 9, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.8.2.b/01:	[redacted]	1998	Kathon™ 886F biocide: two-generation reproductive toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 96R-189, August 7, 1998, Unpublished.	Y(i)	Rohm and Haas
A6.12.6/05:	Scott F.	1979	Repeated Insult Patch Test of Kathon™ 886, Hill Top Research Report No 78-1011-70 and 79-0129-70, Rohm and Haas Report No 79RC-0014 (February 1, 1979), Unpublished.	Y(ii)	Rohm and Haas
A6.12.6/06:	Maibach H.I.	1984 d	Repeated insult patch test with Kathon™ CG 50 ppm active ingredient, University of California, San Francisco Study N° HIM 83 – R&H D-1, Rohm and Haas Report No 84RC-011 (February 29, 1984), Unpublished.	Y(ii)	Rohm and Haas
A6.12.6/07:	Maibach H.I.	1984 e	Human repeat insult patch test Kathon™ CG 100 ppm active ingredient, University of California, San Francisco Study No HIM 83 – R-H D-2, Rohm and Haas Report No 84RC-051 (September 21, 1984), Unpublished.	Y(ii)	Rohm and Haas

A6.12.6/08:	Schwartz S.R.	1990	A double-blind study to determine the topical contact sensitization potential of three test products, International Research Services, Inc. Study N° 743RH1289, Rohm and Haas Report N° 90RC-0017 (May 11, 1990), Unpublished.	Y(ii)	Rohm and Haas
A6.12.6/09:	Maibach H.I.	1990	Modified Draize Skin Sensitization Study, University of California, San Francisco Study N° HIM 89-R&H-D-1&2, Rohm and Haas Report N° 90RC-016 (July 6, 1990), Unpublished.	Y(ii)	Rohm and Haas
A6.15/01	Quérou R. and Lévy R.	2007	Calculation of the maximum loading of CMIT/MIT in food contact packaging materials in a worst case situation Rohm and Haas Company, Report N° 0704_RQ (13 March 2007), unpublished.	Y(ii)	Rohm and Haas
A6.16/01:	[redacted]	2005	Neutral red uptake phototoxicity assay in BALB/C 3T3 mouse fibroblasts, [redacted] Study No 04AF51.140058, Rohm and Haas Report No 04RC-059 (May 11, 2005), Unpublished.	Y(ii)	Rohm and Haas
A7.1.1.1.1/01:	Jalali-Araghi, K and Shepler, K.	1993	Hydrolysis of 14C RH-651 (the major component of RH-886) at pH 5, 7, and 9; Pharmacology and Toxicology Research Laboratory-West, Richmond, CA USA, PTRL Report N° 225W-1 Rohm and Haas Company, Technical Report N° 34-93-07 (18 February 1993), unpublished.	Y(i)	Rohm and Haas
A7.1.1.1.1/02:	Mazza, L.	1998	Identification of Hydrolytic Degradates of 14C RH-651 at pH 9; Rohm and Haas Company Technical Report N° Biocides TR-98-039 (11 November 1998), Unpublished.	Y(ii)	Rohm and Haas

A7.1.1.1.1/03:	Marx, M, Castle, S, and Shepler, K.	1992	Hydrolysis of 14C RH-573 at pH 5, 7, and 9; Pharmacology and Toxicology Research Laboratory-West, Richmond, CA USA, PTRL Report N° 223W-1 Rohm and Haas Company, Technical Report N° 34-92-63 (6 November 1992), unpublished.	Y(i)	Rohm and Haas
A7.1.1.1.2/01:	Concha, M., Ruzo, L.O., and Shepler, K..	1994	Sunlight Photodegradation of 14C RH-651 (the major component of RH-886) in a Buffered Aqueous Solution at pH 7; PTRL West, Inc. Richmond, CA, USA, PTRL Report N° 226W-1, Rohm and Haas Technical Report N° 34-94-17 (December 8, 1994), Unpublished.	Y(i)	Rohm and Haas
A7.1.1.1.2/02:	Shepler, K..	1995	Sunlight Photodegradation of 14C RH-573 (the Minor Component of RH-886) in a Buffered Aqueous Solution at pH 7; PTRL West, Inc. Richmond, CA, USA, PTRL Project N° 224W, Rohm and Haas Technical Report N° 34-94-78 (May 4, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.1.1.2.1/01:	Bashir, M.	1998 a	Ready Biodegradation of 14C-RH-651: Modified Sturm Test, Covance Laboratories, Inc., Madison, WI, USA, Covance Study N° 6228-125, Rohm and Haas Biocide Technical Report N° TR97-15 (February 27, 1998), Unpublished.	Y(i)	Rohm and Haas
A7.1.1.2.1/02:	Bashir, M.	1998 b	Ready Biodegradation of 14C-RH-573: Modified Sturm Test, Covance Laboratories, Inc., Madison, WI, USA, Covance Study N° 6228-141, Rohm and Haas Biocide Technical Report N° TR97-076 (March 26, 1998), Unpublished.	Y(i)	Rohm and Haas

A7.1.1.2.3/01:	Oteyza, T.	2008a	[14C]RH-573: Aerobic mineralisation in marine surface water; Brixham Environmenal Laboratory, Devon, UK. BEL Report N° BL8607/B and Rohm and Haas Technical Report N° TR-08-046 (6 October 2008), Unpublished.	Y(i)	Rohm and Haas
A7.1.1.2.3/02	Oteyza, T.	2008b	[14C]RH-651: Aerobic mineralisation in marine surface water; Brixham Environmenal Laboratory, Devon, UK. BEL Report N° BL8608/B and Rohm and Haas Technical Report N° TR-08-044 (15 October 2008), Unpublished.	Y(i)	Rohm and Haas
A7.1.2.1.1/01:	Daniel, M. and Roberts, G.C.	2007	RH-651 : Simulation test for aerobic sewage treatment by activated sludge. Brixham Environmental Laboratories, Brixham, Devon, UK. Brixham Report N°. BL8438/B, Rohm and Haas Technical Report N° 07-011 (July 11, 2007). Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.1.1/02:	Oteyza, T., Gillings, E. and Roberts, G.C.	2007	RH-573 : Simulation test for aerobic sewage treatment by activated sludge. Brixham Environmental Laboratories, Brixham, Devon, UK. Brixham Report N°. BL8162/B, Rohm and Haas Technical Report N° TR-07-012 (August 20, 2007). Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.2.1.a/01:	Guo I., Marbo M., Jacobson A.	2007a	Aerobic Transformation of RH-651 in Surface Water; Rohm and Haas Technical Report N° GLP-2007-017 (April 30, 2007), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.2.1.a/02:	Guo I., Marbo M., Jacobson A.	2007b	Aerobic Transformation of RH-573 in Surface Water; Rohm and Haas Technical Report N° GLP-2007-041 (April 10, 2007), Unpublished.	Y(ii)	Rohm and Haas

A7.1.2.2.2.a / 01:	Reynolds, J. L.	1994	Aerobic Aquatic Metabolism of 14C RH-651; XenoBiotic Laboratories, Inc. Plainsboro, NJ, USA. XenoBiotic Report N° RPT 00172, Rohm and Haas Technical Report N° 34-94-64 (30 September 1994), Unpublished.	Y(i)	Rohm and Haas
A7.1.2.2.2.a / 02:	Schuck, H.	2002	Aerobic Transformation of RH-651 in Aquatic Sediment Systems, Rohm and Haas Research Laboratories, Spring House, PA, USA, Rohm and Haas Technical Report N° TR-02-011 (August 01, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.2.2.a / 03:	Reynolds, J. L.	1994	Aerobic Aquatic Metabolism of 14C RH-573; XenoBiotic Laboratories, Inc. Plainsboro, NJ, USA. XenoBiotic Report N° RPT 00170, Rohm and Haas Technical Report N° 34-94-122 (30 September 1994), Unpublished.	Y(i)	Rohm and Haas
A7.1.2.2.2.a / 04:	Schuck, H.	2002	Aerobic Transformation of RH-573 in Aquatic Sediment Systems, Rohm and Haas Research Laboratories, Spring House, PA, USA, Rohm and Haas Technical Report N° TR-02-010 (July 31, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.2.2.c / 01:	Liu, P. and Reynolds J. L.	1994	Anaerobic Aquatic Metabolism of 14C RH-651; XenoBiotic Laboratories, Inc. Plainsboro, NJ, USA. XenoBiotic Report No. RPT 00169, Rohm and Haas Technical Report N° 34-94-63 (07 October 1994), Unpublished.	Y(i)	Rohm and Haas
A7.1.2.3/01:	Seyfried, B.	2003 a	Ready Biodegradation of N-methyl Malonamic Acid in a CO2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study N°.: 843966, Rohm and Haas Report N° GLP-2002-081 (April 22, 2003), Unpublished.	Y(ii)	Rohm and Haas

A7.1.2.3/02:	Seyfried, B.	2003 b	Ready Biodegradation of N-methyl Acetamide in a CO2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study No.: 843967, Rohm and Haas Report N° GLP-2003-031 (November 5, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.3/03:	Seyfried, B.	2003 c	Ready Biodegradation of Malonamic Acid in a CO2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study No.: 843968, Rohm and Haas Report N° GLP-2003-032 (November 5, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.3/04:	Jacobson A.	2007	Memo: Status of ready biodegradation study of metabolite. Support section A7.1.2.3. Not GLP, Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.3/05:	Seyfried B.	2007	Study plan (Protocol) : Sodium salt of 2-(methylcarbamoyl) ethene sulfonic acid, RCC Ltd. B44098, Rohm and Haas company GLP24P-2007-068 (2007), Unpublished.	Y(ii)	Rohm and Haas
A7.1.3.a/01:	Swales, S.	2002 a	14C-RH-651: Activated Sludge Adsorption Isotherm; Covance Laboratories Ltd., North Yorkshire England, Covance Report N°: 616/32-D2149, Rohm and Haas Report N°: 02RC-0030 (December 23, 2002a), Unpublished.	Y(ii)	Rohm and Haas
A7.1.3.a/02:	Swales, S.	2002 b	14C-RH-573: Activated Sludge Adsorption Isotherm; Covance Laboratories Ltd., North Yorkshire England, Covance Report No. 616/31-D2149, Rohm and Haas Report N° 02RC-0031 (December 23, 2002b), Unpublished.	Y(ii)	Rohm and Haas

A7.1.3.b/01:	Wang, W.W.	1991	Soil Adsorption and Desorption of 14C RH-651 in Four Soils and One Sediment; XenoBiotic Laboratories, Inc., Princeton, NJ, USA. XBL Report No. RPT0046, Rohm and Haas Technical Report N° 31-91-09 (May 31, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.1.3.b/03:	Gillings, E.	2006	RH-573: Adsorption and Desorption to Soil; Brixham Environmental Laboratories, Brixham, Devon, UK. Brixham Report N°. BL8308/B, Rohm and Haas Technical Report N° 06-058 (29 August 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.2.1.a/01:	Guo, I and Eisensch mid, M.	2006	Aerobic Transformation of RH-651 in Soil. Performed at Rohm and Haas Technical Center, Spring House, PA, USA, Technical Report N°. GLP-2006-024, (December 18, 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.2.1.a/02:	Wang, W.W.	1991	Aerobic Soil Metabolism of 14C RH-651; Xenobiotic Laboratories, Inc (XBL), Plainsboro, New Jersey, USA, XBL Report N°. RPT0045, Rohm and Haas Technical Report N°. 34-91-03 (April 11, 1991), Unpublished.	Y(ii)	Rohm and Haas
A7.2.1.b/01:	Guo, I	2006	Aerobic Transformation of RH-573 in Soil. Performed at Rohm and Haas Technical Center, Spring House, PA, USA, Technical Report N°. GLP-2006-012, (December 12, 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.2.3.1/01:	Reynolds, J.L.	1996	Aged Leaching of 14C-RH-651 in Four Soils. XenoBiotic Laboratories, Inc., Plainsboro, New Jersey, USA, XBL Report N°. RPT00171, Rohm and Haas Technical Report N° 34-95-91 (July, 18, 1996), Unpublished.	Y(ii)	Rohm and Haas

A7.3.1/01:	Guo, I.	2003	Calculation of Tropospheric Phototransformation of Isothiazolone Compounds; Rohm and Haas Company, Rohm and Haas Technical Report N° TR-03-001 (May 15, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.1a/01:	[redacted]	1990a	Acute flow-through toxicity of Kathon™ 886 biocide to the rainbow trout, Oncorhynchus mykiss, [redacted] Study Nº 9003-RH, Rohm and Haas Report Nº 89RC-0343 (November 28, 1990), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.1a/02:	[redacted]	1990b	Acute flow-through toxicity of Kathon™ 886 biocide to the bluegill sunfish, Lepomis macrochirus, [redacted] Study N° 9002-RH, Rohm and Haas Report N° 89RC-0342 (November 29, 1990), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.1b/01:	[redacted]	1980	Acute toxicity of Kathon™ WT to sheepshead minnows (Cyprinodon variegatus), [redacted] Report N° BP-80-3-53, Rohm and Haas Report N° 80RC-0020 (March 1980), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.1c/01:	[redacted]	2002a	Acute toxicity of N-methyl malonamic acid to the rainbow trout, Oncorhynchus mykiss, determined under static test conditions (metabolite), [redacted] Project ID 47178, Rohm and Haas Report N° 01RC-300 (September 30, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.1c/02:	[redacted]	2002a	Acute toxicity of N-methyl acetamide to the rainbow trout, Oncorhynchus mykiss, determined under static test conditions (metabolite), [redacted] Study No 47185, Rohm and Haas Report N° 01RC-303 (August 5, 2002), Unpublished.	Y(ii)	Rohm and Haas

A7.4.1.1c/03:	[redacted]	2002b	Acute toxicity of malonamic acid to the rainbow trout, Oncorhynchus mykiss, determined under static test conditions. (metabolite), [redacted] Study No 47182, Rohm and Haas Report No 01RC-306 (September 13, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.2.a/01:	Ward T.J. and Boeri R.L.	1990	Acute flow-through toxicity of Kathon™ 886 biocide to the Daphnid, Daphnia magna, EnviroSystems Study N° 9001-RH, Rohm and Haas Report N° 89RC-0345 (November 29, 1990), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.2.b/01:	Palmer S.J., Kendall T.Z. and Krueger H.O.	2002	Kathon™ 886F biocide: a 96-hour flow-through acute toxicity test with the saltwater mysid (Americamysis bahia), Wildlife International Project Nº 129A-186, Rohm and Haas Report Nº 02RC-0026 (October 9, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.2.b/02:	Weideborg M.	1995a	Toxicity test results with Abra alba for the chemical Kathon™ OM; Aquateam – Norwegian Water Technology Centre Report N° 93-029, Rohm and Haas Report N° 93RC-1013A (February 14, 1995), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.2.b/03:	Weideborg M.	1995b	Toxicity test results with Acartia tonsa for the chemical Kathon™ OM; Aquateam – Norwegian Water Technology Centre Report N° 93-028, Rohm and Haas Report N° 93RC-1011A (February 14, 1995), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.2.c/01:	Madsen T.	2002c	Acute toxicity of N-methyl malonamic acid to the water flea, Daphnia magna, determined under static test conditions (metabolite), ABC Laboratories Study No 47177, Rohm and Haas Report No 01RC-301 (August 13, 2002), Unpublished.	Y(ii)	Rohm and Haas

A7.4.1.2.c/02:	Rhodes J.E.	2002b	Acute toxicity of N-methyl acetamide to the water flea, Daphnia magna, determined under static test conditions. (metabolite), ABC Laboratories Study No 47184, Rohm and Haas Report No 01RC-304 (August 5, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.2.c/03:	Madsen T.	2002d	Acute toxicity of malonamic acid to the water flea, Daphnia magna, determined under static test conditions (metabolite), ABC Laboratories Study No 47181, Rohm and Haas Report No 01RC-307 (September 10, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.3.a/01:	Boeri R.L, Kowalski P.L. and Ward T.J.	1995a	Acute Toxicity of Kathon™ WT 14 % to the freshwater alga, Selenastrum capricornutum, TR Wilbury Study N° 658-RH, Rohm and Haas Report N° 95RC-0061 (August 2, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.3.b/01:	Boeri R.L., Kowalski P.L. and Ward T.J.	1995b	Acute toxicity of Kathon WT 14 % to the marine alge, Skeletonema costatum; TR Wilbury Study N° 659-RH, Rohm and Haas Report N° 95RC-0062 (August 21, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.3.b/03	Palmer S.J., Cartee T.L., Kendall T.Z. and Krueger H.O.	2009	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1: A 96-hour toxicity test with the marine diatom (Skeletonema costatum), Wildlife International Project No 129A-226, Rohm and Haas Report No 09RC-009 (July 29, 2009), GLP, Unpublished	Y(i)	Rohm and Haas
A7.4.1.3.c/01:	Madsen T.	2002e	Toxicity of N-methyl malonamic acid to the unicellular green alga, Selenastrum capricornutum, (metabolite), ABC Laboratories Study No 47179, Rohm and Haas Report No 01RC-302 (September 9, 2002), Unpublished.	Y(ii)	Rohm and Haas

A7.4.1.3.c/02:	Rhodes J.E.	2002c	Toxicity of N-methyl acetamide to the unicellular green alga, Selenastrum capricornutum, (metabolite), ABC Laboratories Study No 47186, Rohm and Haas Report No 01RC-305 (September 5, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.3.c/03:	Madsen T.	2002f	Toxicity of malonamic acid to the unicellular green alga, Selenastrum capricornutum, (metabolite), ABC Laboratories Study No 47183, Rohm and Haas Report No 01RC-308 (September 20, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.4/01:	Ward T.J., Kowalski P.L. and Boeri, R.L.	1995	Activated sludge respiration inhibition test with Kathon ™ WT 14 %; TR Wilbury Laboratories Study N° 665-RH, Rohm and Haas Report N° 95RC-0063 (June 27, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.1.a/01:	[redacted]	1991a	Acute flow-through toxicity of Kathon™ 886 biocide to the rainbow trout, Oncorhynchus mykiss – 14 day prolonged test, [redacted] Study N° 9006-RH, Rohm and Haas Report N° 89RC-0348 (June 19, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.2.a/01:	[redacted]	1991b	Early life stage toxicity of Kathon™ 886 biocide to the fathead minnow, Pimephales promelas; [redacted] Study N° 9004-RH, Rohm and Haas Report N° 89RC-0347 (June 21, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.3.1.a/01:	[redacted]	1996	RH-651 Bioconcentration and Elimination of 14C-Residues by Bluegill Sunfish (In-Life), [redacted] Unpublished [redacted] Study N°42387, 6 August 1996, Rohm and Haas Technical Report N° 34-96-40, Unpublished.	Y(ii)	Rohm and Haas

A7.4.3.4.a/01:	Ward T.J. and Boeri R.L.	1991c	Chronic toxicity of Kathon™ 886 biocide to the daphnid, Daphnia magna, EnviroSystems Study N° 9005-RH, Rohm and Haas Report N° 89RC-0346 (June 17, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.5.1a/01	Aufderheide J.	2006	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1 (supplied as Kathon™ 886F): chronic toxicity in whole sediment to the freshwater midge, Chironomus riparius; ABC Laboratories Study N° 49248, Rohm and Haas Report N° 04RC-080 (February 15, 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.4.3.5.1a/02	Thomas S.T., Krueger H.O., Kendall T.Z., and Nixon W.B.	2007	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1: A sediment-water Lumbriculus toxicity test using spiked sediment, Wildlife International Ltd Project N° 129A-211A, Rohm and Haas Report N° 06RC-216 (December 3, 2007), GLP, Unpublished.	Y(ii)	Rohm and Haas
A7.4.3.5.1a/03	Thomas S.T., Krueger H.O., Kendall T.Z., and Nixon W.B.	2008	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1: A prolonged sediment toxicity test with Hyalella azteca toxicity test using spiked sediment, Wildlife International Ltd Project N° 129A-212B, Rohm and Haas Report N° 06RC-217 (February 29, 2008), GLP, Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.1/01:	Schaefer E.C. and Flaggs R.S.	2003a	Kathon™ 886F biocide: soil microorganisms: carbon transformation test. Wildlife International Project N° 129E-108, Rohm and Haas Report N° 02RC-0210, (November 3, 2003), Unpublished.	Y(ii)	Rohm and Haas

A7.5.1.1/02:	Schaefer E.C. and Flaggs R.S.	2003 b	Kathon™ 886F biocide: soil microorganisms: nitrogen transformation test. Wildlife International Project N° 129E-109, Rohm and Haas Report N° 02RC-0028, (October 31, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.2/01:	Armstrong K. and White D.	2000	Kathon™ 886F determination of acute toxicity (LC50) to the earthworms, Inveresk Research Project N°: 396112, Inveresk Report N° 18165, Rohm and Haas Report N°: 99RC-0210 (February 28, 2000), Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.3/01:	Porch, J.R., Martin, K.H., Krueger, H.O.	2003 a	Kathon™ 886F biocide: a toxicity test to determine the effects of the test substance on seedling emergence and growth of three species of plants, Wildlife International Project N°: 129-179, Rohm and Haas Report N°: 02RC-0027A (January 9, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.3/02:	Porch, J.R., Martin, K.H., Krueger, H.O.	2003 b	Kathon™ 886F biocide: a toxicity test to determine the effects of the test substance on vegetative vigour of three species of plants, Wildlife International, Ltd., Project N° 129-180, Rohm and Haas Report N° 02RC-0027 (January 20, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.5.3.1.1/01:	[redacted]	1990 a	Kathon™ 886 biocide: 21-day acute oral LD50 study in bobwhite quail. [redacted] Project ID: BLAL 90 QD 148, Rohm and Haas Report No 89RC-0339 (August 14, 1990), Unpublished.	Y(ii)	Rohm and Haas
A7.5.3.1.2/01:	[redacted]	1990 b	Kathon™886 biocide: 8-day acute dietary LC50 study in Mallard ducklings. [redacted] Project ID: BLAL 90 DC 145. Rohm and Haas Report No 89RC-0341 (October 18, 1990), Unpublished.	Y(ii)	Rohm and Haas

A7.5.3.1.2/02:	[redacted]	1990c	Kathon™ 886 biocide: 8-day acute dietary LC50 study in bobwhite quail. [redacted] Project ID: BLAL 90 QC 148. Rohm and Haas Report No 89RC-0340 (October 18, 1990), Unpublished.	Y(ii)	Rohm and Haas

B03/01: covering section IIIB 3.7	M. L. Bates	2005	Kathon™ 886 MW Biocide: Two Year Ambient Temperature Storage Stability, Covance Laboratories Ltd., Harrogate, UK. Technical Report N°: 0616/034-D2149. Rohm and Haas Compagny, Report N°: 24P-2002-037 (December, 2005), GLP-2005-038, Unpublished.	Y(ii)	Rohm and Haas
B03/02: covering sections IIIB 3.3, 3.5, 3.6, 3.7 (Low temp), 3.8	M. L. Bates	2003	Kathon™ 886 MW Biocide: Evaluation of Chemical and Technical Properties (Active Ingredient, Content, pH, Acidity, Relative Density, Foaming, Persistence, Low Temperature Stability, Oxidising Properties), Covance Laboratories Ltd., Harrogate, UK. Technical Report N° : 616/33-D2149. Rohm and Haas Compagny, Report N°: 24P-2002-037 (19 November 2003), GLP-2003-015, Unpublished.	Y(ii)	Rohm and Haas
B03/03: covering section IIIB 3.7	M. L. Bates	2004	Kathon™ 886 MW Biocide: Evaluation of the stability to light. Covance Laboratories Ltd., Harrogate, UK.Technical Report N°: 0616/38-D2149. Rohm and Haas Compagny, Report N°: 24P-2004-046 (December 2004), GLP-2004-046, Unpublished.	Y(ii)	Rohm and Haas
B03/04: covering section IIIB 3.9	T. Ghosh	1997	A Summary of our Knowledge on the Conditions and Mechanism of Isothiazolone Degradation. Rohm and Haas Biocides Research Technical Report. TR-97-28, Dr. Tirthankar Ghosh, July 10, 1997.	Y(i)	Rohm and Haas
B03/05: (**cross reference to Doc IIIA ref**	R. B. Petigara	2001	Biocides Product Directives Common Core Data Set for Active (Chemical). Substances, Parts 2 and 3: Identity, and Physical and	Y(ii)	Rohm and Haas

A3/01) covering section IIIB 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.10			Chemical Properties of Kathon™ 886F Biocide. Rohm and Haas Company, Research Laboratories, Spring House, USA. Technical Report N°.: TR-01-058 (December 2001).		
B4.1.a/01 (A4.1.b/01)	Doshi, Deepak,	2001	"CIS Dept. Test method #89-03-03, Reverse phase HPLC analysis of Kathon™ Formulations for active ingredients" March 5, 2001, Unpublished.	Y(ii)	Rohm and Haas
B4.1.a/02 (A4.1.b/02)	Doshi, Deepak	2001	"GLP report on validation of CIS test method #89-03-03 (Draft) for the analysis of Kathon™ formulations for active ingredients under protocol # GLP 24P-2000-026" Rohm and Haas Report # GLP-2001-006, February 15, 2001, Unpublished.	Y(ii)	Rohm and Haas
B4.1.a/03 (A4.1.b/03)	Doshi, Deepak	2003	"Round robin study for the analysis of active ingredients in Kathon™ formulations in support of European Biocidal Product Directives", Rohm and Haas Report # GLP-2002-072, April 1, 2003, Unpublished.	Y(ii)	Rohm and Haas
B4.1.a/04 (A4.1.b/04)	Eisenschmied, Mark A	2006	"GLP LC-MS peak identity verification of AI in Kathon™ CG and Kathon™ 886F as detected by CIS TM 89-03-03", CAs Technical document # TD2006-182. July 19, 2006, Unpublished.	Y(ii)	Rohm and Haas
B5.10/01	Diehl MA	2006a	The Antimicrobial Activity of Chloromethylisothiazolinone + Methylisothiazolinone (CMIT/MIT): Frame Formulation Minimum Inhibitory Concentration (MIC) Studies versus Bacteria and Fungi; TR-06-001; (January 10, 2006) Not GLP, Unpublished	Y(ii)	Rohm and Haas
B5.10/02	Diehl MA	2006b	The Speed of Kill (SOK) and Multiple Challenge Efficacy Test with Chloromethylisothiazolinone + Methylisothiazolinone (CMIT/MIT) in an In-Can Model Preservative Sytem. Rohm and Haas Company, Technical Report Nº BPD-06-017 (May 23, 2006) Not GLP, unpublished.	Y(ii)	Rohm and Haas
B5.10/03	Thery F. and Lens C.	2007	Evaluation of basic bactericidal and fungicidal activities of CMIT/MIT active substance.	Y(ii)	Rohm and Haas

			Keybio laboratory – France. Study 46340701. Study was conducted in accordance with GLP Procedure 98-1312 Decree (12/31/1998), Unpublished.		
B5.10/04	Walker J.T.	1999	Determination of the bactericidal activity against *Legionella pneumophila*. Centre for Advanced Microbiology and Research (CAMR), 1999, Report N° 98Q/029 (January 5, 1999), not GLP, Unpublished.	Y(ii)	Rohm and Haas
B5.10/05:	Williams, T.M.	2008	Efficacy of KATHON™ WT biocide versus mixed cultures of bacteria, fungi, and algae in simulated industrial process waters. Rohm and Haas Company, Technical Report Nº BPD-08-008 (April 10, 2008), Not GLP, Unpublished.	Y(ii)	Rohm and Haas
B5.10/06:	Williams, T.M.	2008	Efficacy of KATHON WT biocide versus the sulfate-reducing bacterium Desulfovibrio desulfuricans. Rohm and Haas Company, Technical Report Nº BPD-08-006 (April 7, 2008), Not GLP, Unpublished.	Y(ii)	Rohm and Haas
B5.10/07:	Askew, P.D.	2007	Kathon™ LXE – Efficacy as a preservative in Product Type 11 of the EU Biocidal Product Directive. Preservation of Timber Treatment Solutions. Industrial Microbiological Services Ltd. (IMSL) Technical Report Nº IMSL2005/05/002/01.8A, (September 25, 2007). Not GLP, unpublished.	Y(ii)	Rohm and Haas
B6.1.1/01 (cross ref A6.1.1/01)	[redacted]	1993	Kathon™ 886 all-magnesium formulation: acute oral toxicity study in male rats, Rohm and Haas Company, Rohm and Haas Report N° 77R-038A, July 23, 1993.	Y(i)	Rohm and Haas
B6.1.2/01 (cross ref A6.1.2/01)	[redacted]	1993b	Kathon™ 886 all-magnesium formulation: acute dermal toxicity study in male rabbits, Rohm and Haas Company, Rohm and Haas Report N° 76R-056A, July 23, 1993.	Y(i)	Rohm and Haas

B6.1.3/01 (cross ref A6.1.3.a/01)	[redacted]	1991	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 91R-018, July 10, 1991.	Y(i)	Rohm and Haas
B6.1.3/02 (cross ref A6.1.3.a/02)	[redacted]	1991	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018A, August 12, 1991.	Y(i)	Rohm and Haas
B6.1.3/03 (cross ref A6.1.3.a/03)	[redacted]	1992	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018B, June 9, 1992.	Y(i)	Rohm and Haas
B6.1.3/04 (cross ref A6.1.3.b/01)	Papagiannis C.N.	1993	Kathon™ 886F biocide: evaluation of the upper airway irritation potential (RD_{50}), International Research and Development Corporation Project ID: 285-047, Rohm and Haas Report N° 91RC-047, April 23, 1993.	Y(i)	Rohm and Haas
B6.2/01 (cross ref A6.1.4.a/01)	[redacted]	1986	Kathon™ 886 – 13.9 %: determination of the acute dermal irritation or corrosion in male rabbits, [redacted] Protocol N° BT0102, Rohm and Haas Report N° 86RC-1005, November 26, 1986.	Y(ii)	Rohm and Haas
B6.2/02 (cross ref A6.1.4.a/02)	Parsons, RD	1980	Kathon™ 886MW: DOT skin corrosivity test, Rohm and Haas Company, Rohm and Haas Report N° 80R-1, January 9, 1980.	Y(ii)	Rohm and Haas
B6.2/03 (cross ref A6.1.4.a/03)	[redacted]	1985	Kathon™ 886 1.5 % Biocide: skin irritation study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 84R-244A, B, C, D, January 16, 1985.	Y(i)	Rohm and Haas
B6.2/04 (cross ref A6.1.4.b/01)	Longacre, S.L.	1995	Kathon™ 886 Biocide: revised acute toxicity reports, Rohm and Haas Company, Rohm and Haas Report N° 76-56B, March 20, 1995.	Y(i)	Rohm and Haas

B6.3/01 (Cross ref A6.1.5/01)	House R.V.	2000a	Murine local lymph node assay with Chloromethylisothiazolinone and Methylisothiazolinone, Covance Laboratories Study ID: 6228-145, Rohm and Haas Report N° 00RC-148A, November 7, 2000.	Y(ii)	Rohm and Haas
B6.3/02 (Cross ref A6.1.5/02)	[redacted]	2001	Chloromethylisothiazolinone/Methylisothiazolinone 3:1 - Open epicutaneous test in guinea pigs, [redacted] Project ID N 31H0367/002132, US Ref N° 01RC-1030, July 12, 2001.	Y(ii)	Rohm and Haas
B6.3/03 (cross ref A6.1.5/03)	House R.V.	2000b	Murine local lymph node assay to evaluate Chloromethylisothiazolinone/Methylisothiazolinone, Covance Laboratories Study ID: 6228-146, Rohm and Haas Report N° 00RC-148B, November 7, 2000.	Y(ii)	Rohm and Haas
B6.3/04 (Cross ref A6.1.5/04)	[redacted]	2000	Chloromethylisothiazolinone and Methylisothiazolinone 3:1: Dermal sensitization study in guinea pigs Maximization test, Rohm and Haas Company Report N° 00R-140, September 28, 2000.	Y(i)	Rohm and Haas
B6.3/05 (cross ref A6.1.5/05)	Hazelton G.A.	1991	In-house development of local lymph node assay – status report, Rohm and Haas Company, Rohm and Haas Report N° 91R-1130, October 10, 1991.	Y(ii)	Rohm and Haas
B6.3/06 (cross ref A6.1.5/06)	[redacted]	1982	Kathon™ 886: a study of the concentration-dependent delayed contact hypersensitivity in guinea pigs, Rohm and Haas Company, Rohm and Haas Report N° 81R-66, August 24, 1982.	Y(i)	Rohm and Haas

B6.4/01 (cross ref A6.2.a/04)	[redacted]	2003	2-Methyl-4-isothiazolin-3-one: In vitro percutaneous absorption through rat skin, Rohm and Haas Company, Rohm and Haas Company Report No. 00R-066, August 22, 2003.	Y(ii)	Rohm and Haas
B6.4/02 (cross ref A6.2.a/05)	Ward R.J.	2005	2-Methyl-4-isothiazolin-3-one (MIT): in vitro absorption from water and three formulations through human epidermis, Central Toxicology Laboratory Study No: JV1839, Rohm and Haas Report N° 04RC-066 (August 16, 2005), Unpublished.	Y(ii)	Rohm and Haas
B6.4/03 (cross ref A6.2.b/04)	Ward RJ	2005a	5-Chloro-2-methyl-4-isothiazolin-3-one (CMIT) and 2-Methyl-4-isothiazolin-3-one (MIT) in a 3:1 w/v mixture: in vitro absorption of CMIT from aqueous solutions through human epidermis, Central Toxicology Laboratory Study N°: JV1858, Rohm and Haas Report N°: 04RC-067, August 16, 2005.	Y(ii)	Rohm and Haas
B6.4/04 (cross ref A6.2.b/05)	Ward RJ	2005b	5-Chloro-2-methyl-4-isothiazolin-3-one (CMIT)/2-Methyl-4-isothiazolin-3-one (MIT): in vitro absorption of CMIT from an aqueous solution and three formulations through human epidermis, Central Toxicology Laboratory Study N°: JV1870, Rohm and Haas Report N°: 05RC-055, October 20, 2005.	Y(ii)	Rohm and Haas
B6.6.1/01	Shade, W.D. and Jayjock M.A.	1994	Kathon™ 886 Biocide and Skane® M-8 Microbicide: Inhalation Risk Assessment for Offgassing from Interior Latex Paint, Rohm and Haas Company Report N° 94R-002 (November 23, 1994), Unpublished.	Y(ii)	Rohm and Haas

Reference list sorted by section: Thor

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
A2.10-01	-	-	ISO certificate English	No	-
A2.10-02	-	-	ISO certificate German	No	-
A2.10-03	-	2007	THOR information on PPE and safe use of biocides	No	-
A3.1.1-01	Werle, H.	1999a	Determination of the melting point of 5-Chloro-2-methyl-4-isothiazoline-3-one (CIT) according to OECD Guideline No. 102. BioChem, report no. 99 50 40 063 B, 30-03-2003 GLP, Unpublished	Yes	Thor GmbH
A3.1.1-02	Werle, H.	1999b	Determination of the melting point of 2-methyl-4-isothiazoline-3-one (MIT) according to OECD Guideline No. 102. BioChem, report no. 99 50 40 063 A, 29-03-2003 GLP, Unpublished	Yes	Thor GmbH
A3.1.2-01	Werle, H.	1992b	First amendment boiling point Aticid 14, BioChem report no. 92 50 40 216 C, 28-10-1992 GLP, Unpublished	Yes	Thor GmbH
A3.1.2-02	Tognucci, A	2002a	Determination of the boiling point/boiling range of 5-chloro-2-methyl-3(2H)-isothiazolone, RCC Ltd, report no. RCC study no. 840976 GLP, Unpublished	Yes	Thor GmbH
A3.1.2-03	Tognucci, A	2002b	Determination of the boiling point/boiling range of 2-methyl-3(2H)-isothiazolone, RCC Ltd, report no. RCC study no. 840972, 24-04-2002 GLP, Unpublished	Yes	Thor GmbH
A3.1.3-01	Werle, H.	1992a	Report-Density-Acticide 14 BioChem GmbH, report no. 92 50 40 216 D, 10-12-2002 GLP, unpublished report	Yes	Thor GmbH
A3.1.3-02	Tognucci, A	2002c	Determination of the relative density of 6-chloro-2-methyl-3(2H)-isothiazolone, 12-03-	Yes	Thor GmbH

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
			2002. RCC Ltd, report no. RCC study no. 840977 GLP, Unpublished		
A3.1.3-03	Tognucci, A	2002d	Determination of the relative density of 2-methyl-3(2H)-isothiazolone, 16-10-2002. RCC Ltd, report no. RCC study no. 840873 GLP, Unpublished	Yes	Thor GmbH
A3.1.4-01	Lander, H.J.	2007a	Determination of some physico-chemical properties of Acticide 14. TNO, report number. 031.11950/01.04_1 24-4-2007 GLP/unpublished	Yes	Thor GmbH
A3.2-01	Werle, H.	1994	Report- Vapour Pressure Curve Acticide 14, BioChem GmbH, report no. 94 50 40 834 A, 31-08-2002 GLP, Unpublished report	Yes	Thor GmbH
A3.2-02	Badt-Tognucci, A	2007	Determination of the vapour pressure of 5-chloro-2-methyl-4-isothiazolin-3-one (CIT) RCC Ltd., RCC Study no. A90077, 25-05-2007. GLP, Unpublished	Yes	Thor GmbH
A3.2-03	Weissenfeld, M.	2006	Determination of the vapour pressure of 2-methyl-2H-isothiazol-3-one (MIT), RCC Ltd, report no. RCC study no. A42917, 15-12-2006 GLP, Unpublished	Yes	Thor GmbH
A3.3/A8-01	Anonymous		MSDS ACTICIDE 14. Thor GmbH GLP not applicable / unpublished report	No	Thor GmbH
A3.4-02	Herling, H.	2007	Spectral Service SSLO3207, June 2007. GLP, Unpublished	Yes	Thor GmbH
A3.4-03	Kirsch, F.	2007a	MIT-Standard and CIT-Standard- UV-Vis absorption Spectra (Spectrophotometric method), Thor GmbH, report no. AP-No. 15870A, November	Yes	Thor GmbH

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
			2007. Non-GLP, Unpublished		
A3.4-04	Kirsch, F.	2007b	MIT/CIT Standard- IR transmission Spectra, Thor GmbH, report no. AP-No. 15870B, November 2007. Non-GLP, Unpublished	Yes	Thor GmbH
A3.5-01	Tognucci, A	2002e	Determination of the water solubility of 5-chloro-2-methyl-3(2H)-isothiazolone including effect of pH and temperature. RCC report no. 840978, August 28, 2002 GLP, unpublished	Yes	Thor GmbH
A3.5-04	Werle, H.	1999d	Determination of the water solubility of 2-Methyl-4-isothiazoline-3-one (MIT) following OECD Guideline No. 105, BioChem GmbH, report no. 99 50 40 063 C, 30-03-1999 GLP, Unpublished	Yes	Thor GmbH
A3.5-05	Hanstveit, R., Verhaar, H.	2007c	The solubility in water and organic solvents of the mixture of active substances CIT and MIT (CIT/MIT, 3:1) in ACTICIDE®14. ENVIRON, report no. 77THBPD-20070110, 25-June-2007 Non-GLP, Unpublished	Yes	Thor GmbH
A3.7-01	Werle, H.	1997c	Solubility in n-Heptane and Xylene, 5-Chloro-2-methyl-4-isothiazoline-3-one (CIT), BioChem Report no. 96 50 40 436 B, 13-01-1997 GLP, Unpublished	Yes	Thor GmbH
A3.7-02	Werle, H.	1997d	Solubility in n-Heptane and Xylene, 2-Methyl-4-isothiazoline-3-one (MIT), BioChem Report no. 96 50 40 436 A, 10-01-1997 GLP, Unpublished	Yes	Thor GmbH
A3.7-03	Wielpütz, T.	2007a	CIT, Batch No.:LM2001-Solubility in acetonitrille (following A.6 and OECD 105), Siemens AG, Report No.	Yes	Thor GmbH

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
			20071144.01, November 29, 2007 GLP, Unpublished		
A3.7-04	Wielpütz, T.	2007b	MIT, Batch No.:LM2000-Solubility in acetonitrille (following A.6 and OECD 105), Siemens AG, Report No. 20071145.01, November 29, 2007 GLP, Unpublished	Yes	Thor GmbH
A3.9-01	Bates, M.L..	1993	Determination of the physico-chemical properties of ACTICIDE 14 according to EEC requirements Hazleton Europe, report no. 1154/9A-1014, 25-10-1993 GLP, Unpublished	Yes	Thor GmbH
A3.9-02	Seal, K.J.	2002	Determination of the Partition Coefficient (n-octanol/water) of the active ingredients of ACTICIDE® RS at a range of temperatures and pHs. Thor Specialties (UK) Limited, Study no. RS/01/023, 19-03-2002 GLP, Unpublished	Yes	Thor GmbH
A3.10-01	Rüb, B	1993	Determination of stability of ACTICIDE 14, Thor Chemie, report no. 9301-BR-4, 19-04-1993 GLP, Unpublished	Yes	Thor GmbH
A3.10-02	Anonymous	2007	Scheme for autocatalytic degradation non-stabilized isothiazolones.	N	Thor GmbH
A3.11-01	Schied, G.	2003	Expert statement on physical-chemical properties of ACTICIDE® 14, Thor GmbH, 27-10-2003 GLP not applicable, Unpublished	Yes	Thor GmbH
A3.11-02	Wielpütz, T.	2007c	CIT, Batch No.:LM2001-Flammability (solids) A.10, Siemens AG, Report No. 20071144.02, November 29, 2007 GLP, Unpublished	Yes	Thor GmbH
A3.11-03	Wielpütz, T.	2007d	MIT, Batch No.:LM2000-	Yes	Thor

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
			Flammability (solids) A.10, Siemens AG, Report No. 20071145.02, November 29, 2007 GLP, Unpublished		GmbH
A3.12-01 (see A3.1.4-01)	Lander, H.J.	2007a	Determination of some physico -chemical properties of Acticide 14. TNO, report number. 031.11950/01.04_1 24-4-2007 GLP, Unpublished	Yes	Thor GmbH
A3.13-01 (see A3.1.4-01)	Lander, H.J.	2007a	Determination of some physico-chemical properties of Acticide 14. TNO, report number. 031.11950/01.04_1 24-4-2007 GLP, Unpublished	Yes	Thor GmbH
A3.14-01	Werle, H.	1993	Viscosity Acticid 14 BioChem GmbH, Report no. 92 50 40 216 B, 21-01-1993 GLP, Unpublished report	Yes	Thor GmbH
A3.15-01	Hanstveit, R.	2007b	Explosive and oxidizing properties of the active substances CIT and MIT of ACTICIDE 14 (CIT/MIT 3:1) ENVIRON, Report no. 77TH-BPD-20070069 Non-GLP, Unpublished	Yes	Thor GmbH
A3.16-01 (see A3.15-01)	Hanstveit, R.	2007b	Explosive and oxidizing properties of the active substances CIT and MIT of ACTICIDE 14 (CIT/MIT 3:1) ENVIRON, Report no. 77TH-BPD-20070069 Non-GLP, Unpublished	Yes	Thor GmbH
A3.17-02	Thor	2007a	Suitable materials for the storage of biocides for in-can preserving, Summary of Thor experience, October 2007, Non-GLP, Published	No	Thor GmbH
A4.2(c)-01	Wolf, S.	2004	Development and validation of the residue analytical method for 2-methyl-4-isothiazolin-3-	Yes	Thor GmbH

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
			one (MIT) and 5-chloro-2-methyl-4-isothiazolin-3-one (CIT) in surface water RCC Ltd; Study no. 851805; March 31, 2004 *(GLP, unpublished)*		
A4.2(c)-02	Verhaar, H.	2007a	EXPERT STATEMENT: Analytical method for ACTICIDE® 14 (CIT/MIT 3:1) in groundwater ENVIRON, report no. TH-BPD-20070104, 05-07-2007 Non-GLP/unpublished And: A4.2(c)-01	No	Thor GmbH
A5-02	Grabbe R.	2008a	Evaluation of Minimum inhibitory Concentrations (MIC)for ACTICIDE 14 against Moulds, Yeasts and Bacteria Thor, report no. 26990, 12.09.2008. Non-GLP/unpublished	Yes	Thor GmbH
A5-03	Paulus, W.	2005a	Directory of Microbicides for the protection of materials, Microbiocide data - chapter 2-relationship between chemical structure and activity or mode of action of microbicides, Springer 2005: 9-23 Non-GLP/publishedDirectory of	No	n.a.
A5-04	Paulus W	2005b	Directory of Microbicides for the protection of materials, Microbiocide data – chapter 15: Heterocyclic N,S compounds, Springer 2005: 5657-671 Non-GLP/published	No	n.a.
A5-05	Williams, Terry M	2006	The Mechanism of Action of Isothiazolone Biocides, CORROSION NACExpo 2006 61st Annual Conference & Exposition; San Diego, CA; USA; 12-16 Mar. 2006. Non-GLP/published	No	n.a.
A 5.7	Pickardt T	2006	BfR-Background paper considering the potential of resistance in the efficacy and risk evaluation of biocidal compounds, TIMGEN-item14b,	No	n.a.

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
			Version March 01, 2006		
A 5.7	Rees R	2006	Technical Bulletin: Biocide Resistance, Edition 2 - April 24, 2006	No	Thor GmbH
A 5.7	Roden K	1999	Technical Bulletin: Biocide Resistance, TBIA/01/99	No	Thor GmbH
A6.1.1-01	[redacted]	1994	Test to Evaluate the Acute Toxicity following a single oral administration (LD50), in the Rat of Acticide 14 [redacted] report No. 53293, GLP, Unpublished	Yes	Thor GmbH
A6.1.1-02	[redacted]	1998	Akute orale Toxizität von ACTICIDE 14 (L) an der Ratte [redacted] report No. 009 TOX 97 GLP, Unpublished	Yes	Thor GmbH
A6.1.2-01	[redacted]	1994b	Test to Evaluate the Acute Toxicity following a single cutaneous application (Limit Test) in the Rat of Acticide 14, [redacted] report No. 53193 GLP, Unpublished	Yes	Thor GmbH
A6.1.3-01	[redacted]	1997	ACTICIDE 14: Acute Inhalation Toxicity in Rats, 4-Hour Exposure. [redacted] Study No. THR 48/971458 GLP, Unpublished	Yes	Thor GmbH
A6.1.3-02	Jackson GC	1994	ACTICIDE 14: Acute Inhalation System. Huntingdon Life Sciences Ltd., Study No. THR 31/942439 GLP, Unpublished	Yes	Thor GmbH
A6.1.4-01	[redacted]	1994	Test to Evaluate Acute Primary Cutaneous Irritation and Corrosivity in the Rabbit of ACTICIDE 14, [redacted] report No. 53093. GLP, Unpublished	Yes	Thor GmbH

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
A6.1.5-01	[redacted]	2000	Acute Skin Sensitization Study of Test Item Acticide 14 in Guinea Pigs [redacted], Study No. 99/430-104T GLP, Unpublished	Yes	Thor GmbH
A6.1.5-02	[redacted]	2002	ACTICIDE 14 – Local Lymph Node Assay (LLNA) in mice (identification of contact allergens). [redacted] Study No. 843741 GLP, Unpublished	Yes	Thor GmbH
A6.2-01	[redacted]	1998	(^{14}C)-CIT and (^{14}C)-MIT: Absorption, distribution, metabolism and excretion following oral administration to the rat, [redacted] Study No.: 1154/62, Report No.: 1154/62-1007, GLP, Unpublished	Yes	Thor GmbH
A6.2-02	[redacted]	2000	(^{14}C)-CIT and (^{14}C)-MIT: Characterisation of metabolites following oral administration to the rat, [redacted], Study No.: 1154/70, 19-12-00 GLP, Unpublished	Yes	Thor GmbH
A6.2-03	[redacted]	1982	^{14}C-kathon 886 disposition after percutaneous application to male rats. Rohm and Haas Company, Report no. 82R-21 (letter of access included) GLP, Unpublished	Yes	Thor GmbH (Rohm and Haas)
A6.2-04	[redacted]	1986	Absorption and disposition of ^{14}C-labelled Kathon® biocide, a mixture of 5-chloro-2-methyl-4-isothiazolin-3-one, following intravenous or dermal administration to male Sprague-Dawley rats. [redacted] Vol.24, 1, pp43-49 Published	No	-

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
A6.2-05 (See A7.1.2-02)	Krzeminski	1975a	Fate of Microbicidal 3-isothiazolone Compounds in the Environment: Products of Degradation. J.Agric. Food Chem.,Vol 3, 6(1975) 1068-1075.	No	na
A6.2-06 (See A7.1.2-03)	Krzeminski	1975b	Fate of Microbicidal 3-isothiazolone Compounds in the Environment: Modes and rates of dissipation J.Agric. Food Chem.,Vol 3, 6(1975) 1060-1068.	No	na
A6.2-07	CIR	1992	Final report on the Safety assessment of Methylisothiazolinone and Methylchloroisothiazolinone. *Journal of the American college of toxicology*, Vol. 11, 1(1992), pp 75-128 Published		
A6.2-08	Jayjock, M.A.	1996	Formulation Effect on the Dermal Bioavailability of Isothiazolone Biocide Fd. Chem. Toxic. Vol 34(3), 1996	No	-
A6.2-09	Søderlund, E.	1992	Kathon. IN: Healt effects of selected chemicals – volume 2. Nord 1993, 29.	No	-
A6.4.1-01	[redacted]	1982a	Kathon 886 Three month rat drinking water study and one generation reproduction study. Rohm and Haas Company, Study No.: 81P-398 (letter of access included) GLP, Unpublished	Yes	Thor GmbH (Rohm and Haas)
A6.4.1-02	[redacted]	1998a	Acticide 14: 13 Week Oral (Dietary Administration) Toxicity Study in the Dog, [redacted], Study No.: 1154/58, 01-02-98 GLP, Unpublished	Yes	Thor GmbH
A6.4.1-03	[redacted]	1998b	Acticide 14: Pilot (dietary administration) study in the	Yes	Thor GmbH

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			Dog. [redacted], Study No.: 1154/57-1050 GLP, Unpublished		
A6.4.1-04	[redacted]	1994	ACTICIDE 14: 14-day oral (gavage) dose range-finding study in the female rat + amendment [redacted], Study No.: 1147-1154-004 GLP, Unpublished	Yes	Thor GmbH
A6.4.2-01	[redacted]	1994	Acticide 14: 90 Day Dermal Subchronic Toxicity Study to the Rat, [redacted] Report no: 1127-1154-002, 13-06-94 GLP, Unpublished	Yes	Thor GmbH
A6.4.2-02	[redacted]	1994a	ACTICIDE 14: 14-day dermal dose range-finding study in the rat + replaced pages [redacted], Study No.: 1127-1154-001 GLP, Unpublished	Yes	Thor GmbH
A6.5-01 (See A6.7-01)	[redacted]	1994b	Kathion Biocide: 24-month drinking water chronic/oncogenic study in rats. Rohm and Haas Company, Study No.: 91R-074 (letter of access included) GLP, Unpublished	Yes	Thor GmbH (Rohm and Haas)
A6.6.1-01	Clare CB	1994	Study to Determine the Ability of Acticide 14 to Induce Mutation in Five Histidine-Requiring Straints of Salmonella Typhimurium, Hazleton Europe Study no: 1154/10R, 29-06-94 GLP, Unpublished	Yes	Thor GmbH
A6.6.1-02	Poth, A.	1992	Salmonella typhimurium: Reverse mutation assay with ACTICIDE 14. CCR Study no: 269201 GLP, Unpublished	Yes	Thor GmbH

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A6.6.2-01	Marshall R	1994	Study to Evaluate the Chromosome Damaging Potential of Acticide 14 by its Effects on Cultured Human Peripheral Blood Lymphocytes using an in Vitro Cytogenetics Assay, Hazleton Europe Study no: 1154/11, GLP, Unpublished	Yes	Thor GmbH
A6.6.3-01	[redacted]	1994	Study to Determine the Ability of Acticide 14 to Induce Mutations at the Thymidine Kinase (tk) Locus in Mouse Lymphoma L5178Y Cells using a Fluctuation Assay, [redacted] Study no: 1154/15, GLP, Unpublished	Yes	Thor GmbH
A6.6.4-01	[redacted]	1997	Acticide 14: Induction of Micronuclei in the Bone Marrow of Treated Mice. [redacted], Study No.: 1154/63, Report No.: 1154/63-1052, 13-03-97 GLP, Unpublished	Yes	Thor GmbH
A6.6.4-02	[redacted]	1994	Study to Evaluate the Potential of ACTICIDE 14 to Induce Micronuclei in the Polychromatic Erythrocytes of CD-1 Mice, [redacted] Study no: 1154/23, 29-06-94 GLP, Unpublished	Yes	Thor GmbH
A6.6.5-01	[redacted]	1994	Study to Evaluate the Potential of ACTICIDE 14 to Induce Unscheduled DNA Synthesis in Rat Liver Using an In Vivo/In Vitro Procedure, [redacted] Study no: 1154/, 30-06-94 GLP, Unpublished	Yes	Thor GmbH

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A6.7-01	[redacted]	1994	Kathion Biocide: 24-month drinking water chronic/oncogenic study in rats. Rohm and Haas Company, Study No.: 91R-074 (letter of access included) GLP, Unpublished	Yes	Thor GmbH (Rohm and Haas)
A6.8.1-01	[redacted]	1994	ACTICIDE 14 - Oral (Gavage) Teratogenicity Study in the Rat, [redacted], Report no: 1178-1154-003, 26-05-94 GLP, Unpublished	Yes	Thor GmbH
A6.8.1-02	[redacted]	2002	Prenatal Development Toxicity Study of ACTICIDE 14 in Rabbits, [redacted] Study No.: 3494, 15-05-2002 GLP, Unpublished	Yes	Thor GmbH
A6.8.1-03	[redacted]	1992	Kathon Biocide: oral (gavage) developmental toxicity study in rabbits. Rohm and Haas Company, Study No.: 91R-074 (letter of access included) GLP, Unpublished	Yes	Thor GmbH (Rohm and Haas)
A6.8.2-01	[redacted]	1998	Two generation Oral (Gavage) Reproduction Toxicity Study in the Rat (One Litter Per Generation) [redacted] Study No.: 1154-067, Report No: 1413-1154-06, 13-11-98 GLP, Unpublished	Yes	Thor GmbH
A6.8.2-02 See A6.4.1-03	[redacted]	1982	Kathon 886 Three month rat drinking water study and one generation reproduction study. Rohm and Haas Company, Study No.: 81P-398 (letter of access included) GLP, Unpublished	Yes	Thor GmbH (Rohm and Haas)

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A6.12-01	Kapahnke, W.	2007	Medical data for CIT/MIT Thor GmbH GLP not applicable, Unpublished	Yes	Thor GmbH
A6.14-01	San RHC, VanDyke MR	2005	n-Methyl Malonamic Acid: Bacterial Reverse Mutation (Ames) Assay, BioReliance AB13CE.503.BTL, (R&H 05RC045), 09.09.2005, GLP/unpublished report	Yes	Thor GmbH (Rohm and Haas)
A6.14-02	Chapdelaine JM	2003	n-Methyl Malonamic Assay: Local Lymph Node Assay, Calvert Laboratories 0787XR07.001(R&H 02RC049), 08.08.2003, GLP/unpublished report	Yes	Thor GmbH (Rohm and Haas)
A7.1.1.1.1-01	Geffke, T	2002a	Acticide 14- Hydrolysis as a function of pH Dr. U.Noack-Laboratorium Report No: CPH80192 GLP, Unpublished	Yes	Thor GmbH
A7.1.1.1.1-02	Lucas, T.	1996a	(14C)-ACTICIDE 14: Hydrolytic stability Corning Hazleton GmbH Report No.: 1225-1154-043. GLP, Unpublished	Yes	Thor GmbH
A7.1.1.1.2-01	Purser, D.	1998	(14C)-Acticide 14: Photodegradation in Sterile, Aqueous Solution Covance, Report no. CHE 1154/60-D2142 GLP/Unpublished report	Yes	Thor GmbH
A7.1.1.1.2-02	Hamwijk, C.	2007a	Structural elucidation of degradation products from the photodegradation of 5-chloro-2-methyl-2H-isothiazol-3-one (CIT, CAS # 26172-55-4) TNO Quality of Life Report no. V6280/02 GLP/Unpublished report	Yes	Thor GmbH

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A7.1.1.1.2-03	Hamwijk, C.	2007b	Structural elucidation of degradation products from the photodegradation of 2-methyl-2H-isothiazol-3-one (MIT, applied as aqueous formulation ACTICIDE® M 20) TNO Quality of Life Report no. V6264/04 GLP/Unpublished report	Yes	Thor GmbH
A7.1.1.1.2-04	Hamwijk, C.	2007c	Structural elucidation of degradation products from the photodegradation of 2-methyl-2H-isothiazol-3-one (MIT, applied as aqueous formulation ACTICIDE® M 20) and 5-chlor-2-methyl-2H-isothiazol-3-one (CIT, CAS# 26172-55-4) TNO Quality of Life Report no. V7137 GLP/Unpublished report	Yes	Thor GmbH
A7.1.1.2.1-01	Noack M.	2002a	Acticide 14: Ready Biodegradability Closed Bottle Test. Dr. U. Noack-Laboratorium, Project No. 001025TS, Study No. AFW80191, 20 January 2002. GLP/ unpublished report	Yes	Thor GmbH
A.7.1.1.2.3-01	Hamwijk,C. and H. Oldersma	2005	Determination of the biodegradability of ACTICIDE® 14 in natural seawater by a Closed Bottle method (OECD Guideline No. 306), TNO Quality of Life, Report V6411/03, 16 November 2005 GLP/ unpublished report	Yes	Thor GmbH

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A 7.1.2-01	Scientific Committee on Cosmetic Products and Non-Food Products intended for Consumers	2003	Opinion concerning update of Entry no. 39 of Annex VI to Directive 76/768/EEC on cosmetic products: mixture of 5-Chloro-2-methyl-isothiazolin-3(2H)-one and 2 methylisothiazolin-3(2H)-one SSCNFP/0670/03, final COLIPA no. P56, 24-25 June 2003	No	na
A 7.1.2-02	Krzeminski, S.F.	1975a	Fate of Microbicidal 3-isothiazolone Compounds in the Environment: Products of Degradation. J.Agric. Food Chem.,Vol 3, 6(1975) 1068-1075.	No	na
A 7.1.2-03	Krzeminski, S.F.	1975b	Fate of Microbicidal 3-isothiazolone Compounds in the Environment: Modes and rates of dissipation J.Agric. Food Chem.,Vol 3, 6(1975) 1060-1068.	No	na
A 7.1.2.1.1-01	Fiebig, S.	2002	Acticide 14: Simulation Test-Aerobic Sewage Treatment Dr. U. Noack-Laboratorium, Project No. 001025TS, Study No. ACU80191, 29-01-2002 GLP/ unpublished report	Yes	Thor GmbH
A 7.1.2.1.1-02	Hanstveit, R.	2007a	Activated sludge die away biodegradation test with [14C]-Methyl-2H-isothiazol-3-one (MIT, CAS# 2682-20-4), TNO, V6264/05, draft, 2 February 2007 GLP/ unpublished report	Yes	Thor GmbH
A7.1.2.2.1-01	Hamwijk, C. and R.K.H. Cremers,	2007d	The determination of the degradation of 5-chloro-2-methyl-4-isothiazol-3-one (CIT, CAS # 26172-55-4) in seawater (OECD guideline 309), TNO Quality of Life, report nr. V6280/03, July 2007 GLP/ unpublished report	Yes	Thor GmbH

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A 7.1.2.2.1-02	Hamwijk, C. and R.K.H. Cremers	2007	The determination of the degradation of 2- Methyl-2H-isothiazol-3-one (MIT, CAS # 2682-20-4) in seawater (OECD guideline 309), TNO Quality of Life, report nr. V6264/02, 13 March 2007 GLP/ unpublished report	Yes	Thor GmbH
A 7.1.2.2.2-01	Noorloos, B. van	2007a	Aerobic degradation of 14C-CIT (5-chloro-2-methyl-[4,5-14C]-isothiazol-3-one) in two water/sediment systems, NOTOX B.V., Project no. 416508, October 2007 GLP/unpublished report	Yes	Thor GmbH
A7.1.2.2.2-02	Noorloos, B. van	2007b	Aerobic degradation of 14C-MIT (5-chloro-2-methyl-[4,5-14C]-isothiazol-3-one) in two water/sediment systems, NOTOX B.V., Project no. 416497, October GLP/unpublished report	Yes	Thor GmbH
A7.1.2.2.2-03	Lucas, T.	1996b	(14C)-ACTICIDE 14: degradation and retention in one water-sediment system, CORNING Hazleton GmbH, study no. 1154-042. GLP/unpublished report	Yes	Thor GmbH
A7.1.3-01	Geffke, Th	2002b	Acticide 14 – Estimation of the Adsorption Coefficient Koc on Soil and Sewage Sludge using High Performance Liquid Chromatography (HPLC), Dr Noack laboratorium, study no. CAH80192 GLP/ unpublished	Yes	Thor GmbH
A 7.1.3-02	Hamwijk, C.	2007e	Expert statement: Adsorption of 2-methyl-2H-isothiazol-3-one (MIT) to soil and sediment, TNO Quality of Life, report no. 6264/06, July 2007. Non GLP/ unpublished	Yes	Thor GmbH

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A7.2.1-01	Oldersma, H. and F.G.C. Salmon	2007a	Study for the determination of the degradation of 5-chloro-2-methyl-2H-isothiazol-3-one (CIT, CAS# 26172-55-4) in soil (OECD 307), TNO Quality of Life, report nr. V6280/01, July 2007 GLP/unpublished report	Yes	Thor GmbH
A7.2.1-02	Oldersma, H. and F.G.C. Salmon	2007b	Study for the determination of the degradation of 2-Methyl-2H-isothiazol-3-one (MIT, CAS # 2682-20-4) in soil (OECD 307)., TNO Quality of Life, report nr. V6264/03, September 2007 GLP/unpublished report	Yes	Thor GmbH
A7.2.3.1-01	Salmon, F.G.C and Cremers, R.K.H	2007	A study on the adsorption of [14C]-5-chloro-2-methyl-2H-isothiazol-3-one in five soil types and two sediment types (OECD 106) using sterilized soil and sediment., TNO, V6280/04, September 2007 GLP/unpublished report	Yes	Thor GmbH
A7.3.1-01	Hanstveit R.	2006b	Determination of the photolysis in air of 5-chloro-2-methyl-4-isothiazolin-3-one (CIT) and 2-methyl-2H-isothiazol-3-one (MIT) by Atkinson calculation (SETAC Europe (1995) Guideline). TNO Quality of Life, Report no. V6411/01, September 2006 GLP/ unpublished report	Yes	Thor GmbH
A7.4.1.1-01	Wyness, L.E.	1994a	Acticide 14: Acute toxicity to Oncorhynchus mykiss. Hazleton Europe; Report no. 1154/8R-1018 GLP/ unpublished report	Yes	Thor GmbH

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A7.4.1.1-02	Wyness, L.E.	1994b	Acticide 14: Acute toxicity to Lepomis macrochirus. Hazleton Europe; Report no. 1154/14R-1018 GLP/ unpublished report	Yes	Thor GmbH
A7.4.1.1-03	[redacted]	1998	Flow-through acute toxicity of Acticide 14 to the Sheepshead minnow Cyprinodon variegatus [redacted] Study no. 1405-TO. GLP/ unpublished report	Yes	Thor
A7.4.1.2-01	Mattock, S.D.	1996	Acticide PT: Acute immobilisation and reproduction test with Daphnia magna CORNING Hazleton (Europe); Report no. 1154/56 GLP/ Unpublished report	Yes	Thor
A7.4.1.2-02	Boeri, R.L. Magazu, J.P. and Ward, T.J	1998b	Flow-through acute toxicity of Acticide 14 to the Mysid, Mysidopsis bahia. T.R. wilbury Laboratories, Inc. study no. 1406-TO. GLP/ Unpublished report	Yes	Thor GmbH
A7.4.1.2-03	Boeri, L.B., Magazu, J.P. and Ward, T.J.;	1998c	Flow-through mollusc shell deposition test with Acticide 14 T.R. Wilbury Laboratories, Inc.; Study no. 1407-TO; April 13, 1998 GLP/unpublished	Yes	Thor GmbH
A7.4.1.3-01	Wyness, L.E.	1994e	Acticide 14: Effect on the growth and reproduction of non-target aquatic plants. Hazleton Europe, report no. 1154/6-1018 GLP/ unpublished report	Yes	Thor
A7.4.1.3-02 (see A7.4.13-01)	Wyness, L.E.	1994c	Acticide 14: Effect on the growth and reproduction of non-target aquatic plants. Hazleton Europe, report no. 1154/6-1018 GLP/ unpublished report	Yes	Thor GmbH

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A7.4.1.3-05	Scheerbaum, D.	2008	ACTICIDE® 14: Alga, Growth Inhibition Test with Pseudokirchneriella subcapitata, 96 h, Dr.U.Noack-Laboratorien; Report no. SPO120891; 08.08.2008, GLP, unpublished	Yes	Thor GmbH
A7.4.1.4-01	Noack, M.	2002c	ACTICIDE ® 14. Respiration test with activated sludge. Dr. U.Noack-Laboratorium Report No: BBR86592 GLP, Unpublished report	Yes	Thor GmbH
A7.4.2	Verhaar, H.J.M.	2007b	Bioconcentration behaviour of ACTICIDE® 14 (CIT/MIT 3:1), statement. ENVIRON Netherlands, report no. 77T-BPD2007105, July 2007 Expert statement, non GLP, unpublished	Yes	Thor GmbH
A7.4.3.2-01	[redacted]	1999b	Acticide 14: Fish (Rainbow trout), juvenile growth test, 28 d (semi-static). [redacted] Study no. FWR61772; GLP/ unpublished report	Yes	Thor GmbH
A7.4.3.4-01 (see A7.4.1.2-01)	Mattock, S.D.	1996	Acticide PT: Acute immobilisation and reproduction test with Daphnia magna. CORNING Hazleton (Europe) ; report no. 1154/56 GLP/ Unpublished report	Yes	Thor GmbH
A7.4.3.5.1-01	Scheerbaum, M.	1999	ACTICIDE 14: Effects on the development of Chironomus riparius in a water-sediment system. Dr. U. Noack-Laboratorium, Study no. IZS61773, 08-07-1999 GLP/unpublished	Yes	Thor GmbH
A 7.4.3.5.2-01 = A 7.4.1.3-02					

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A7.5.1.1-01	Hamwijk, C. and H. Oldersma	2006b	An assessment of the effects of ACTICIDE® 14 (an aqueous 14% formulation of CIT/MIT 3:1) on the nitrogen transformation and carbon mineralization activity of soil micro-organisms. (OECD 216 and 217 Guidelines), TNO Quality of Life, report nr. V6411/02, 27 February, 2006 GLP/unpublished	Yes	Thor GmbH
A7.5.1.2-01	Noack, M.	2001	Acticide 14: Earthworm (Eisenia fetida), Acute toxicity test in artificial soil, Dr. U. Noack-Laboratorium, Study no. RRA80191. GLP/ unpublished report	Yes	Thor GmbH
A 7.5.1.3-01	Wyness, L.E.	1994f	Acticide 14: Terrestrial Plants, Growth Test Hazleton Europe, report no. 1154/22-1018, 01-09-1994 GLP/ unpublished report	Yes	Thor GmbH

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B2.2-01	Anonymous	2007	Sale specification Acticide SPX	Yes	Thor GmbH
B3.7-01	Rüb, B.	1993	Determination of stability of Acticide 14 Thor Chemie GmBH, Germany. Report no. 9301-BR-4 Not GLP, Unpublished	Yes	Thor GmbH
B3.10-01	Lander, H.J.	2007	Determination of some physico-chemical properties of Acticide SPX. TNO, Rijswijk, NL, Report No.: PROTOCOL 031.11950/01.04_2 GLP, Unpublished	Yes	Thor GmbH

B3.10-02	Rueb, B.	2001	Viscosity of ACTICIDE SPX THOR, Speyer, Report No. 0101B-BR-63/18 GLP, Unpublished	Yes	Thor GmbH
B5.10	Grabbe R	2008	ACTICIDE®MV: Examination of microbiological efficacy for Product Type 11, THOR Technical Service Report No. 27009, Report No. 27009/5, 31-07-2008 non-GLP, unpublished	Yes	Thor GmbH
B5.10-01 (PT11)	Grabbe R.	2008f	ACTICIDE®MV: Examination of Microbiological Efficacy for Product Type 11 (Definition in Annex V of 98/8/EC), report no. 27009/5, 11-08-2008 Non-GLP/unpublished	Yes	Thor GmbH
B6.2-01 & -02	Dickhaus, S, Heisler, E.	1985	Prüfung der substance ACTICID SPX auf primäre hautreizwirkungen beim kaninchen Pharmatox, Report No. - GLP, Unpublished + certified translation into English.	Yes	Thor GmbH
B8-01	Anonymous	2005	MSDS ACTICIDE SPX Thor GmbH GLP not applicable, Unpublished	No	Thor GmbH
B8-02	Anonymous	2005	PDS ACTICIDE SPX Thor GmbH GLP not applicable, Unpublished	No	Thor GmbH
II-B (PT11)	Thor GmbH	2008	Questionnaire to end-users of CIT/MIT biocidal products in liquid cooling systems (PT 11.02) (Quest CIT_MIT_SPX PT11_02 recirc EndUse ThorRev3.pdf)	Yes	Thor GmbH