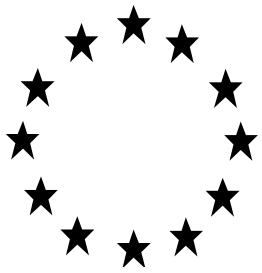
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



C(M)IT/MIT

Product-type 12
(Biocide for use as Slimicides)

April 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 12 (slimicides), 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 12 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 12.

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 12 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 27th of November 2012, 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 12, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 12 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 active substance is manufactured by two different companies: Thor and 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 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 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.

[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

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 missing however due to the rapid degradation of C(M)IT and MIT in soil, the confirmatory method is not required. Thor has not submitted methods for analysis of C(M)IT and MIT in soil and sediments and in food. A validated method for analysis of C(M)IT and MIT in food are required and should be provided before the product authorization stage. No method is necessary for soil due to the rapid degradation of C(M)IT and MIT.

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 toxicological consideration.

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's product: KathonTM WT

Dow's product 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 formulation 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'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). The product Acticide SPX is a dilution of the active substance as manufactured with water.

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 as it is a dilution of the technical active substance.

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

C(M)IT/MIT is a broad spectrum antimicrobial agent for preventing the growth of microorganisms (bacteria, fungi and algae) that may occur within papermill and (for Dow) oilfield injection systems. C(M)IT/MIT exhibits rapid inhibition of growth at low levels.

C(M)IT/MIT is highly effective and typically used at low use levels. The biocidal products are exclusively used by professionals or industrial users in PT12.

Typical use concentrations range claimed by Dow is respectively from 5 to 30 mg/L of C(M)IT/MIT in oilfield and from 1 to 15 mg/L in papermills. According to Thor, typical use concentrations range claimed is from 0.4 to 2 mg/L of C(M)IT/MIT in papermills. Concentrations of C(M)IT MIT for which an efficacy (microbicidal activity) is demonstrated, are presented in the following tables:

- ✓ For Dow Chemical

MG/PT	Field of use envisaged	Likely concentration at which C(M)IT/MIT (active substance, a.i.) will be used
PT12.01	The biocide is used in the wet end of paper mills to control the growth of target organisms in the circulating process water used in these systems.	Maintenance: 1 to 15 ppm total a.i.(in continuous)
PT12.02	Oilfield Injection Systems – The biocide is used to control the growth of target organisms in injection water lines and raw materials used in processing for enhanced oil recovery (drilling muds and fracture fluids).	Shock dose: 30 ppm total a.s. (contact time : 48h minimum)

- ✓ For Thor GmbH

MG/PT	Field of use envisaged	Likely concentration at which C(M)IT/MIT (active substance, a.i.) will be used
PT12.01	The biocide is used in paper mills to control the growth of target organisms in the circulating process water.	6.0 to 9.0 mg a.i/L by shock dosing up to 4 times delay per day separated to 6 hours

Based on studies submitted, the efficacy has been demonstrated only against the planktonic flora slimicide activity claimed by both (Dow & Thor) is not demonstrated.,

Additional data have to be submitted to prove the efficacy against sessile flora in order to validate the intended use "slimicide". Furthermore field studies have to be submitted at the authorization product stage to demonstrate the efficacy of the product in real conditions.

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 : bacteria, mould, yeast and algae. The different studies presented in doc III A and B list precisely these target organisms.

2.1.2.2 Resistance

C(M)IT/MIT has been used as a commercial antimicrobial agent since 1980. During this period of use, we have encountered situations where resistance to C(M)IT/MIT has occurred. In commercial use, C(M)IT/MIT is often used in combination or rotation with other biocides in various applications, which helps avoid the potential risk of developing resistance.
Although microbial resistance to C(M)IT/MIT has been reported, it is infrequently encountered relative to its widespread global use in numerous applications and it is easily remedied by increasing concentrations of the biocide, switching or alternating biocides, using combinations with other actives, or addition of surfactants or adjuvants (ex., EDTA) to enhance efficacy.

2.1.3 Classification

2.1.3.1 Current classification

- Active substance

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

- Active substance

Directive 67/548/EEC		
	C(M)IT/MIT 14%	C(M)IT/MIT 100 %
Class of danger	Xn: Harmful C: Corrosive Xi: Irritant N: Dangerous to the	T+: Very toxic C: Corrosive Xi: Irritant N: Dangerous for the environment

	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: Very toxic to aquatic organisms	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: Very toxic to aquatic organisms.
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 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	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**

	burns and eye damage** H 317: May cause an allergic skin reaction H335: 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 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.Cat 1A/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 harmonised 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 compartment 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

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

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 in 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

Rat tissues contain up to 4.72% of dosed radioactivity, four days after exposure. The highest amount of radioactivity is found in blood, particularly in red blood cells (up to 4.11%), followed by muscle and liver. Therefore, C(M)IT/MIT is not considered to have an accumulative potential in human.

- Metabolism

Following an oral administration of CMIT in solution with MIT, approximately twenty-nine radioactive components were observed in urine and faeces samples of rats 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 CMIT are both rapidly excreted. Urine and faeces are equal major routes of excretion for CMIT 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.

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 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.
The studies from Rohm and Haas and Thor result in a classification 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 Kathon 886F induced a 50% reduction in the respiratory rate in mice (RD50). C(M)IT/MIT should therefore be

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

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 Buehler 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 were also reported after exposure to C(M)IT/MIT but 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 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.
In the 90-day dermal study in rabbit submitted by Rohm & Haas, mortalities due to pulmonary complications appeared only in treated rabbits. It is difficult to appreciate the relevance of these effects; nevertheless, it seemed to be due to endemic respiratory disease, further aggraved by stress associated with dermal application of the corrosive tested substance. Furthermore, some histopathological finding in lung occurred variously in all groups, including control. These effects were not observed in a fully adequate study

in rat submitted by Thor. Thus, the deaths were not attributed to a direct systemic effect of C(M)IT/MIT.
Additionally, the Rohm & Haas study shows some methodological limitations: the tested substance was not analytically verified in the dosing solutions for concentration or stability and there were 6 animals/sex/group rather than the suggested 10/sex/group (OECD 411).
Therefore, considering the elements above, 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*.

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

MG/PT	Field of use envisaged	Likely concentration at which a.s. will be used
PT12	Papermill Slimicide – The biocide is used in the wet end of paper mills to control the growth of slime producing organisms in the circulating process water used in these systems.	6-9 ppm ai for Acticide SPX 1-15 ppm ai for Kathon WT

PT12	Mineral Slurries – The biocide is used to control the growth of slime producing organisms in mineral slurries. These mineral slurries are added to the wet end of paper mills and function as fillers in the paper.	This use was not evaluated since no dose was judged as efficient
PT12	Oilfield Injection Systems – The biocide is used to control the growth of slime producing organisms in pipes used for injection water in oilfield applications.	30 ppm ai for Kathon WT

C(M)IT/MIT is used as a slimicide (PT 12) and is specifically used in the sub-applications PT 12.01 (Slimicides for paper pulp) and PT 12.02 (Slimicides for mineral oil extraction for Kathon WT only).

2.2.1.3.1 Kathon WT (Dow's product)

C(M)IT/MIT based products like Kathon™ WT is used as slimicides for paper pulp, and mineral oil extractions . This biocidal product is 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. ingestion of paper).

PRIMARY EXPOSURE

- Production/formulation of the C(M)IT/MIT active substance and Kathon™ WT (14% a.s. typical concentration) biocidal product (Professional Users).
- Formulation of Kathon™ WT into biocidal concentrates used as slimicides in paper mills (Professional Users).
- Applications of biocidal product as a papermill slimicide (Professional Users).
- Applications of biocidal product in oilfield injection systems (Professional Users).

INDIRECT AND/OR SECONDARY EXPOSURE

- Indirect exposure from paper.
- Indirect exposure to residues via environmental compartments.

Main paths of human exposure

End-use application	Exposure path	Industrial use	Professional use	General public	Via the environment
Papermill slimicide	Inhalation	Yes	Yes	No	No*
	Dermal	Yes	Yes	No	No*
	Oral	No	No	No	No*
Oilfield injection systems	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), rapid biodegradation in the environment and lack of bioaccumulation potential of the active substance.

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).

Application of biocidal product as papermill slimicides PT12.01 (Professional users)

The active substance in Kathon™ WT (14% C(M)IT/MIT) is used in the wet-end of paper mills to control the growth of slime producing organisms in the circulating process water used in these systems. Professional exposure to C(M)IT/MIT from the in-use wet-end paper manufacturing process from the papermill slimicide added to these systems. The two levels of professional use include service companies who manage the addition of concentrate, and wet-end paper mill workers, making and drying paper.

The potential for exposure to biocidal products used in papermill applications may occur via inhalation and/or dermal contact.

There are three primary exposure task scenarios identified for the use of PT 12.01 products:

1. Mixing/Loading; manual dispensing, pouring, and changing out the concentrate reservoir for systems with automatic dosimeters,

The mixing/loading task has been defined in the TNsG (2002) as changing out the concentrate reservoir for systems with automatic dosimeters and manual administration (dispensing and pouring) of the biocidal product to the process water. In the automated process, the biocide is metered directly into the process water from a holding tank or other type of bulk container. The manual process involves a worker dispensing (tap or poured) a measured quantity of product into a container (e.g., jug) and manually pouring the product into the process water.
Manual pouring is considered as a worst case scenario compared to the automated transfer. The exposure will be assessed following this scenario.
The recommended efficient end-use concentration of C(M)IT/MIT (a.i.) in the process water has been determined as 1 to 15 ppm ai for Kathon WT. However, significant dilution occurs in the wet-end process due to circulation and mixing within the entire water circuit reducing the actual wet-end concentration. Regardless of the manner of treatment, the total active substance concentration of C(M)IT/MIT in the system should not exceed 15 ppm ai Kathon WT in the process water.

2. Post application (includes disposal); cleaning the dispensing pump for maintenance, equipment maintenance, shut down deep clean, process water sampling, and disposal of waste.

Water treatment service professionals clean (decontaminate) dosing pumps prior to conducting maintenance and/or repairs on these equipments. It is also assumed the service company workers will clean dispensing pumps during routine dosing system drum

change outs (professional judgment). These service companies visit 4 facilities per day (TNsG, 2002; PT 11.02) and it is estimated to take 5 minutes to clean each pump or 20 minutes to clean 4 pumps per day (professional judgment). For the purpose of this exposure assessment, cleaning 4 pumps per day represents 1 exposure event. For both the Tier 1 and Tier 2 assessments, total exposure duration of 20 minutes/day was used as the exposure time frame per event. The maximum concentration of C(M)IT/MIT for biocidal products used to dose these systems is 14%, and these concentration were used as worst-case assumptions for this exposure scenario.
Routine testing of the process water is conducted to monitor for microbial contamination. The TNsG (2002) for PT 12.01 (Slimicides for paper pulp) suggests that sampling for microbial counting and examination involve transient hand contact with process water; however, no guidance is provided for the duration and/or frequency of this task. For a similar task involving plant workers inspecting and testing diluted in-use fluid, as described in the TNsG (2002) for PT 11.02 (Preservatives used in recirculating cooling systems), a frequency of once per week and a duration of 2 minutes/sample is suggested. The duration for sampling process water of 10 minutes has been chosen (1 exposure event). The highest end-use concentration of C(M)IT/MIT recommended for shock dose treatments is 15 ppm ai. For both the Tier 1 and Tier 2 assessments, total exposure duration of 10 minutes/event was assumed.
During certain maintenance operations, workers can potentially be exposed to process water that has dried on equipment and the concentration of the biocidal product in the dried residues may be above the estimated circulating level (15 ppm ai). For equipment maintenance tasks, workers use gloves, waterproof work clothing, eye protection and respiratory equipment if necessary (TNsG, 2002). Duration and frequency guidance were not indicated in the TNsG for equipment maintenance, however it is anticipated that this task could occur 8 hours per day on a daily basis. For both the Tier 1 and Tier 2 assessments, total exposure duration of 480 minutes/event (8 hours/day) was assumed as worst-case with an exposure to 15 ppm ai.

Following exposure determinants were used:

- Concentration of active substance (% w/w) in product during mixing and loading and cleaning of the pumps: 14% w/w ;
- Concentration of active ingredient in process water used for assessment: 15 ppm ai ;

- Tasks and duration :
  - Manual mixing and loading : 5 min per facility with up to 4 facilities visited /day, every week ;
  - Cleaning of the pumps : 5 min with up to 4 events per day ;
  - Equipment maintenance: 8 hours, once a month ;
  - Process water sampling, 10 minutes, every week ;
- Percutaneous absorption rate: concentrated product (> 0.6%) 100%; diluted product (< 0.6%) 50%
- Inhalation absorption rate: 100%

Table 2.2-1: Exposure estimates for water treatment service worker/plant worker using biocidal products as slimicide in paper mill plant for Kathon WT

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Potential deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
	Loading Kathon WT in process water systems (water treatment service worker) – every week				
Tier 1 : Without PPE	5.48×10^{-3}	9.14×10^{-4}	140 000	4.71	4.71
Tier 2 : With gloves, RPE and impermeable coveralls	5.48×10^{-4}	9.14×10^{-4}	140 000	4.71×10^{-2}	4.82×10^{-2}
	Cleaning Kathon WT dispensing pumps (water treatment service worker) – daily				
Tier 1 : Without PPE	negligible	negligible	140 000	2.57	2.57
Tier 2 : With gloves and coated coveralls	negligible	negligible	140 000	3.46×10^{-1}	3.46×10^{-1}
Tier 2 + rinse: With gloves and coated coveralls	negligible	negligible	1 400	1.73×10^{-3}	1.73×10^{-3}
	Equipment maintenance – every month				
Tier 1 : Without PPE	negligible	negligible	15	3.30×10^{-3}	3.30×10^{-3}
	Process water sampling – every week				
Tier 1 : Without PPE	negligible	negligible	15	6.88×10^{-5}	6.88×10^{-5}
	Waste disposal (water treatment service worker) - daily				
Covered by above scenarios.					

Tier	*Inhalation exposure*		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Potential deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
	Combined = cleaning pumps + equipment maintenance + process water sampling - daily				
Tier 1 : Without PPE	negligible	negligible	Not relevant*	2.57	2.57
Tier 2 (pump cleaning) + Tier1 (maintenance and water sampling)	negligible	negligible	Not relevant*	3.97×10^{-1}	3.97×10^{-1}
Tier 2 (pump cleaning with rinsing) + Tier1 (maintenance and water sampling)	negligible	negligible	Not relevant*	5.22×10^{-2}	5.22×10^{-2}

* As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

Assumptions:

Biocidal product concentration: 14% C(M)IT/MIT
Concentration in process water: 15 ppm a.i;
Task duration and frequency (maximum for a water treatment service worker) : 4 facilities visited per day, with up to 1 loading (5 minutes) and 1 pump cleaning (5 minutes) per facility.
PPE: chemical-resistant gloves (10% penetration), coated coverall (20% penetration), impermeable coveralls (5% penetration)
Dermal absorption: concentrated product (> 0.6%) 100%; diluted product (< 0.6%) 50%

Application of biocidal product in oilfield injection systems PT12.02 (Professional users)

The biocidal product, Kathon™ WT (14% C(M)IT/MIT), is used in oilfield injection systems to control the growth of slime on the internal surfaces of pipework. This process is essentially a once through operation where treated water is injected into downhole oil formations to replace the oil that is pumped out, but concerning mud injection it is a recirculating system. Typical maintenance treatment concentrations for the injection water or mud which has been determined as efficient is 30 ppm ai C(M)IT/MIT.
Biocidal products employed in oilfield injection systems are used by professionals only (no non-professional users). Professional users may include specialty service companies, consultants, and water treatment specialist who may be involved in dosing the biocides at end-use locations. Oil drilling operations are located outdoors either inland or offshore. These workers have little or no direct contact with the treated injection water since it is

enclosed and the biocide is fed (dosed) inside the injection pipe but considering mud, the worker is exposed to mud aerosol during recycling process of the mud.

The potential for exposure to the biocidal product is essentially limited to dermal and inhalation exposure during the mixing/loading task (which is in fact the application task) and while conducting maintenance (post application) on the dispensing pumps.

The two primary exposure task scenarios identified for oilfield injection operations (PT12.02):

1. Mixing/Loading (application); manual dispensing, pouring, and changing out the bulk biocide container for systems with automatic dosimeters,
2. Post application; cleaning the dispensing pump for maintenance.

The tables below summarize the exposure levels and resulting risk ratios calculated for Kathon™WT.

Table 2.2-2: Summary of the exposure estimates for water treatment service worker/plant worker using biocidal products as slimicide in mineral oil extraction

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Potential deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
	Manual loading Kathon WT in process water systems – every week				
Tier 1 : Without PPE	5.42×10^{-3}	9.03×10^{-4}	140 000	2.99	2.99
Tier 2 : With gloves, RPE and impermeable coveralls*	5.42×10^{-3}	9.03×10^{-4}	0*	0*	9.03×10^{-4}
	Automated loading Kathon WT in process water systems – every week				
Tier 1 : Without PPE	negligible	negligible	140 000	2.15×10^{-2}	2.15×10^{-2}
Tier 2 : With gloves, RPE and impermeable coveralls*	Negligible	Negligible	140 000	2.15×10^{-3}	2.15×10^{-3}
	Cleaning Kathon WT dispensing pumps – daily				
Tier 1 : Without PPE	negligible	negligible	140 000	2.57	2.57
Tier 2 : With gloves and coated coveralls	negligible	negligible	140 000	3.46×10^{-1}	3.46×10^{-1}
Tier 2 + rinse: With gloves and coated coveralls	negligible	negligible	1 400	1.73×10^{-3}	1.73×10^{-3}
	Equipment maintenance – every month				
Tier 1 : Without PPE	negligible	negligible	30	6.60×10^{-3}	6.60×10^{-3}
	Process water sampling – every week				
Tier 1 : Without PPE	negligible	negligible	30	1.38×10^{-4}	1.38×10^{-4}

*In such conditions, it may be assumed that dermal exposure would occur only in accidental circumstances.

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Potential deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
	Combined = cleaning pumps + equipment maintenance + process water sampling - daily				
Tier 1 : Without PPE	negligible	negligible	Not relevant*	2.57	2.57
Tier 2 (pump cleaning) + Tier1 (maintenance and water sampling)	negligible	negligible	Not relevant*	3.53×10^{-1}	3.53×10^{-1}
Tier 2 (pump cleaning with rinsing) + Tier1 (maintenance and water sampling)	negligible	negligible	Not relevant*	8.47×10^{-3}	8.47×10^{-3}

*As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

Assumptions:

Biocidal product concentration: 14% C(M)IT/MIT
Concentration in process water: 30 ppm a.i;
PPE: chemical-resistant gloves (10% penetration), coated coverall (20% penetration), impermeable coveralls (5% penetration)
Dermal absorption: concentrated product (> 0.6%) 100%; diluted product (< 0.6%) 50%

SECONDARY EXPOSURE

A) INDIRECT EXPOSURE FOR USE OF C(M)IT/MIT AS A PAPERMILL SLIMICIDE

The critical endpoints for indirect exposure are as described above.

→ Professionals

The secondary exposure of professionals occurs when bystanders are exposed to the humidified air containing the biocidal product.

- **Inhalation exposure:**

Table 2.2-3 Summary of the inhalation exposure for secondary exposure of professionals by inhalation route

Inhalation exposure		
	External concentration (8-hrs TWA)	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day
Vapour phase		
Kathon WT (15 ppm ai)	6×10^{-4}	1.0×10^{-4}
Aerosol phase		
Kathon WT (15 ppm ai)	6.08×10^{-3}	1.01×10^{-3}
Total		
Kathon WT (15 ppm ai)	6.68×10^{-3}	1.11×10^{-3}

- **Dermal exposure :**

In theory, exposure to residual C(M)IT/MIT may be possible due to indirect or secondary exposure from paper. However, it is likely that due to its high water solubility, C(M)IT/MIT is not bound to paper but stays in the water phase, and that any trace residues present in wet paper will quickly degrade or evaporate during the drying process.

The local dermal exposure concentration is very difficult to assess since the C(M)IT/MIT is in the paper and it not possible to determine the remaining concentration of drying.

Exposure following such scenarios is not thought to be significant due to a number of factors including:

It has been determined that the remaining dose of C(M)IT/MIT in paper will be 25 mg ai/kg paper for Kathon WT.

A confidential study was submitted by Thor GmbH nevertheless this study has not been taken into account since it has not been possible to prove that this study has been performed with the intended dose rate. Then the quantity of C(M)IT/MIT has been calculated using a worst-case scenario of ESD (EC, 2003)[6].

Based on these exposure assumptions, the deposit concentration (considering that the subsequent deposits accumulate over the day) and systemic dermal exposure to C(M)IT/MIT from the scenario described above may be calculated as follows:

Systemic dose = 3.91×10^{-2} mg a.i. /kg bw /day

[6] EC. 2003. Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for slimicides (product type 12). European Commission DG ENV/RIVM, September 2003. http://ecb.jrc.ec.europa.eu/documents/Biocides/EMISSION_SCENARIO_DOCUMENTS/ESD_PER_PRODUCT_TYPE/PT_12/PT_12_Slimicides.pdf

- **Total Combined exposure:**

As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

When a worker is exposed during both primary and secondary exposure (including inhalation route for both vapor and aerosol phases and vapor phase only for dermal route) , a total combined exposure has been calculated.

Table 2.2-4 Total combined exposure for primary and secondary exposure

Total combined exposure				
	Units	**Tier 1**	**Tier 2**	**Tier 2 + rinse**
Total systemic dose for primary exposure	**mg/kg bw/day**	2.57	3.51×10^{-1}	6.01×10^{-3}
Total systemic dose for secondary exposure	**mg/kg bw/day**	4.02×10^{-2}	4.02×10^{-2}	4.02×10^{-2}
Total combined exposure	**mg/kg bw/day**	2.61	3.91×10^{-1}	4.62×10^{-2}

- **Dermal exposure to aerosol phase :**

Exposure to humidified air containing residual biocide represents also a secondary exposure for dermal contact with the aerosol phase of the air. Since it is very difficult to assess this exposure RMS choose to use a reverse scenario approach.

The Margin of Exposure for dermal exposure has been calculated by subtracting from the chronic systemic AEL of 0.09 mg ai/kg bw/d, the value of the total combined exposure of $4.38*10^{-2}$ mg/kg bw/d.

Table 2.2-5 Reverse scenario to determine the value of the dermal exposure which would lead to systemic effects

Margin of Exposure for dermal exposure	4.38 x 10-2	mg ai/kg bw/d
Exposure for one worker	5.25	mg ai/d
Exposure for product	3.50 x 105	mg
Equivalent in kg or L	0.35	kg

Then it appeared that 0.35 kg (or litre since the density of the product is almost 1) of the product would be necessary for a worker to generate systemic effects due to the dermal secondary exposure, this dermal exposure can be then considered very unrealistic.

➔ General public

In theory, exposure to residual C(M)IT/MIT may be possible due to indirect or secondary exposure from paper. However, it is likely that due to its high water solubility, C(M)IT/MIT is not bound to paper but stays in the water phase, and that any trace residues present in wet paper will quickly degrade or evaporate during the drying process. To address potential indirect exposure from paper, two worst-case scenarios are presented: ingestion of paper and food packaging.

Paper ingestion

Indirect or secondary oral exposure may be possible for an infant or child who intentionally ingests paper manufactured in a process that uses C(M)IT/MIT as a wet-end slimicide In order to determine which dose would not lead to systemic effects a reverse scenario was used :

Exposure estimates:

- Maximum in-use wet-end concentration of 25 mg ai/kg paper for Kathon WT were assumed in the finished paper product
- Oral absorption value: 100%
- Weight of an infant: 10 kg
- Weight of a child: 15 kg
- DJT : 0.02 mg ai/kg bw/d

The reverse worst-case exposure scenario is calculated as follows for Kathon WT:

Infant: 0.17 * 10 kg /(25 mg a.s./kg paper) /100% absorp. = **0.07 kg paper**[7]

Child: 0.17 * 15 kg /(25 mg a.s./kg paper) / 100% absorp. = **0.10 kg paper**

Then, it is considered as highly unrealistic that a unacceptable risk occured concerning paper ingestion by infants and children.

Migration from food packaging

In theory, oral indirect exposure to residues of C(M)IT/MIT may be possible. Indeed, residues of the actives substances and their degradation products could migrate from paper used in food packaging to food.

As a first tier approach, the worst-case oral exposure scenario of ESD (EC, 2003)[8] for adult has been performed in Doc IIB for each applicant for completeness purposes. Results of exposure scenario are presented below in **Table 2.2-6**.

Table 2.2-6: Exposure scenarios from paper used as packaging material

	C(M)IT/MIT use concentration in paperpulp	C(M)IT/MIT resulting concentration in dry paper	Concentration in food (mg as/kg food)	Exposure (mg/kg bw/day)
DOW	15 ppm ai	25 mg a.i./kg	0.15	2.5×10^{-3}

[7] This weight is equivalent to 14 sheets of paper (basis weight = 80g/m²)

[8] EC. 2003. Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for slimicides (product type 12). European Commission DG ENV/RIVM, September 2003. http://ecb.jrc.ec.europa.eu/documents/Biocides/EMISSION_SCENARIO_DOCUMENTS/ESD_PER_PRODUCT_TYPE/PT_12/PT_12_Slimicides.pdf

		paper		

Furthermore, a biocide intended to be used as a slimicide in process water for paper manufacturing may fall under the Food Contact Material Legislation. The maximum total amounts of C(M)IT/MIT in paper (25 and 15 µg/dm² respectively) do not exceed the maximum residual amount of C(M)IT/MIT in paper use as food contact material recently derived by EFSA to 25 µg/dm² (2010[9]).
During the paper making process, some degradation of C(M)IT/MIT may occur. Therefore, exposure could occur by contact of food to degradation products of the biocidal product in paper and orally incorporated by user. Thor identified the following degradation products: NMMA, acetic acid, formic acid, urea and ethylene glycol. As a worst case, assuming a complete degradation of CIT/MIT, degradation products could be found in paper in the same amount as parent compound.
As feed may also be packaged with paper, livestock exposures have been calculated using default scenario from the draft document from ARTfood[10] (previously DRAWG[11]) Guidance on Estimating Livestock Exposure to Biocidal Active Substances (see Document IIB). No exposure values calculated with the worst-case scenario (10% feed consumed wrapped) are above the trigger value of 0.004 mg a.i./kg bw/d. It can therefore be concluded that no significant residues of active substance could occur in food of animal origin.

B) INDIRECT EXPOSURE FOR USE OF C(M)IT/MIT AS SLIMICIDE IN OILFIELD INJECTION SYSTEM

After mud is pumped to the drill, it emerges from the well and it passes over a shale shaker, to remove debris and return to the mud pit. The workers who keep the shaker screens operational are exposed to substantial aerosols.

Inhalation exposure

There is no model for assessing such exposure in the TNsG 2007 and 2002. It has been decided to use the Advanced Reach Tool model for the inhalation exposure. This model is focused on inhalation exposure during industrial processes. It is a web based tool[12] recommended in the REACH guidance on information requirements and chemical safety assessment, chapter R14: Occupational exposure estimation[13].

[9] EFSA Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF); Scientific Opinion on the safety evaluation of the substance, 5-chloro-2-methyl-2H-isothiazol-3-one, mixture with 2-methyl-2H-isothiazol-3-one (3:1), CAS No. 55965-84-9, as a biocide for processing coatings and paper and boards. EFSA Journal 2010; 8(3): 1541. [12 pp.].
[10] Assessment of residue tranfer to food
[11] Dietary Risk Assessment Working Group
[12] http://www.advancedreachtool.com/
[13] http://guidance.echa.europa.eu/docs/guidance_document/information_requirements_r14_en.pdf

Table 2.2-7: Indoor mud aerosol exposure

	Tier 1	Tier 2
Inhalation exposure (mg a.i./m^3 TWA)	5.1×10^{-2}	5.1×10^{-3}
Inhalation exposure (mg a.i./kg bw/d)	8.5×10^{-3}	8.5×10^{-4}

Table 2.2-8: Outdoor mud aerosol exposure

	Tier 1
Inhalation exposure (mg a.i./m^3 TWA)	2.5×10^{-3}
Inhalation exposure (mg a.i./kg bw/d)	4.2×10^{-4}

Dermal exposure

Dermal exposure to mud aerosol containing residual biocide represents also a secondary. Since it is very difficult to assess this exposure RMS chooses to use a reverse scenario approach.

The Margin of Exposure for dermal exposure has been calculated by substracting from the chronic systemic AEL of 0.09 mg ai/kg bw/d, the value of the inhalation systemic exposure of $8.5*10^{-4}$ mg/kg bw/d.

Margin of Exposure for dermal exposure	**8.92×10^{-2}**	**mg ai/kg bw/d**
Exposure for one worker	10.7	mg ai/d
Exposure for product	**3.57×10^{5}**	**mg**
Equivalent in kg or L	0.357	kg

Then it appeared that 0.357 kg (or liter since the density of the product is almost 1) of the product would be necessary for a worker to generate systemic effects due to the dermal secondary exposure, this dermal exposure can be then considered very unrealistic.

According to TNsG worker preparing the mud and the one managing drilling and shale shaking are different so no combined exposure is proposed between secondary and primary exposure.

Indirect exposure to human via the environment

Indirect exposure to man via the environment is considered insignificant based upon the low production volume, rapid environmental degradation and lack of bioaccumulation potential of the active substance.

2.2.1.3.2 Acticide SPX (Thor's product)

C(M)IT/MIT based products like Acticide SPX is used as slimicides for paper pulp. This biocidal product is for professional/industrial use only and is not sold to non-professional users (consumers). However, indirect exposure to the general public is possible for certain end-use applications (e.g. ingestion of paper).

PRIMARY EXPOSURE

- Production/formulation of the C(M)IT/MIT active substance Acticide SPX (1.5%) (Professional Users).
- Formulation of Acticide SPX into biocidal concentrates used as slimicides in paper mills (Professional Users).
- Applications of biocidal product as a papermill slimicide (Professional Users).

INDIRECT AND/OR SECONDARY EXPOSURE

- Indirect exposure from paper.
- Indirect exposure to residues via environmental compartments.

Main paths of human exposure

End-use application	Exposure path	Industrial use	Professional use	General public	Via the environment
Papermill slimicide	Inhalation	Yes	Yes	No	No*
	Dermal	Yes	Yes	No	No*
	Oral	No	No	No	No*
Oilfield injection systems	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), rapid biodegradation in the environment and lack of bioaccumulation potential of the active substance.

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).

Application of biocidal product as papermill slimicides PT12.01 (Professional users)

The active substance Acticide SPX (1.5% C(M)IT/MIT) is used in the wet-end of paper mills to control the growth of slime producing organisms in the circulating process water used in these systems. Professional exposure to C(M)IT/MIT from the in-use wet-end paper manufacturing process from the papermill slimicide added to these systems. The two levels of professional use include service companies who manage the addition of concentrate, and wet-end paper mill workers, making and drying paper.

The potential for exposure to biocidal products used in papermill applications may occur via inhalation and/or dermal contact.

There are three primary exposure task scenarios identified for the use of PT 12.01 products:

1. Mixing/Loading; manual dispensing, pouring, and changing out the concentrate reservoir for systems with automatic dosimeters,

The mixing/loading task has been defined in the TNsG (2002) as changing out the concentrate reservoir for systems with automatic dosimeters and manual administration (dispensing and pouring) of the biocidal product to the process water. In the automated process, the biocide is metered directly into the process water from a holding tank or other type of bulk container. The manual process involves a worker dispensing (tap or poured) a measured quantity of product into a container (e.g., jug) and manually pouring the product into the process water.
Manual pouring is considered as a worst case scenario compared to the automated transfer. The exposure will be assessed following this scenario.
The recommended efficient end-use concentration of C(M)IT/MIT (a.i.) in the process water has been determined as 6 to 9 ppm a.i. for Acticide SPX. However, significant dilution occurs in the wet-end process due to circulation and mixing within the entire water circuit reducing the actual wet-end concentration. Regardless of the manner of treatment, the total active substance concentration of C(M)IT/MIT in the system should not exceed 9 ppm ai of Acticide SPX in the process water.

2. Application: process operation;

3. Post application (includes disposal); cleaning the dispensing pump for maintenance, equipment maintenance, shut down deep clean, process water sampling, and disposal of waste.

Water treatment service professionals clean (decontaminate) dosing pumps prior to conducting maintenance and/or repairs on these equipments. It is also assumed the service company workers will clean dispensing pumps during routine dosing system drum change outs (professional judgment). These service companies visit 4 facilities per day (TNsG, 2002; PT 11.02) and it is estimated to take 5 minutes to clean each pump or 20 minutes to clean 4 pumps per day (professional judgment). For the purpose of this exposure assessment, cleaning 4 pumps per day represents 1 exposure event. For both the Tier 1 and Tier 2 assessments, a total exposure duration of 20 minutes/day was used as the exposure time frame per event. The maximum concentration of C(M)IT/MIT for biocidal products used to dose these systems is 1.5% a.i. for Acticide SPX and this concentration was used as worst-case assumptions for this exposure scenario.
Routine testing of the process water is conducted to monitor for microbial contamination. The TNsG (2002) for PT 12.01 (Slimicides for paper pulp) suggests that sampling for microbial counting and examination involve transient hand contact with process water;

however, no guidance is provided for the duration and/or frequency of this task. For a similar task involving plant workers inspecting and testing diluted in-use fluid, as described in the TNsG (2002) for PT 11.02 (Preservatives used in recirculating cooling systems), a frequency of once per week and a duration of 2 minutes/sample is suggested. The duration for sampling process water of 10 minutes has been chosen (1 exposure event). The highest end-use concentration of C(M)IT/MIT recommended for shock dose treatments is ppm ai for Acticide SPX. For both the Tier 1 and Tier 2 assessments, total exposure duration of 10 minutes/event was assumed.
During certain maintenance operations, workers can potentially be exposed to process water that has dried on equipment and the concentration of the biocidal product in the dried residues may be above the estimated circulating level (9 pm a.i.). For equipment maintenance tasks, workers use gloves, waterproof work clothing, eye protection and respiratory equipment if necessary (TNsG, 2002). Duration and frequency guidance were not indicated in the TNsG for equipment maintenance, however it is anticipated that this task could occur 8 hours per day on a daily basis. For both the Tier 1 and Tier 2 assessments, total exposure duration of 480 minutes/event (8 hours/day) was assumed as worst-case with an exposure to 9 ppm a.i.

Following exposure determinants were used:

- Concentration of active substance (% w/w) in process water used by professionals during mixing and loading and cleaning of the pumps: 1.5% w/w.
- Concentration of active ingredient in process water used for assessment: 9 ppm ai.

- Tasks and duration :
  - Manual mixing and loading : 5 min per facility with up to 4 facilities visited /day, every week ;
  - Cleaning of the pumps : 5 min with up to 4 events per day ;
  - Equipment maintenance: 8 hours, once a month ;
  - Process water sampling, 10 minutes, every week ;
- Percutaneous absorption rate: Concentrated solution (> 0.6%) 100 % / Diluted solutions (< 0.6%) 50%%
- Inhalation absorption rate: 100%

Table 2.2-9 Summary of the exposure estimates for Acticide SPX used as slimicide in papermills

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame :	**Loading Acticide SPX in process water systems (water treatment service worker) – every week**				
Tier 1 : Without PPE	5.88×10^{-4}	9.79×10^{-5}	15 000	5.05×10^{-1}	5.05×10^{-1}
Tier 2 : With gloves impermeable coveralls	5.88×10^{-4}	9.79×10^{-5}	15 000	5.05×10^{-3}	5.05×10^{-3}
Task (public) – time frame :	**Cleaning Acticide SPX dispensing pumps (water treatment service worker) – daily**				
Tier 1 : Without PPE	negligible	negligible	15 000	2.75×10^{-1}	2.75×10^{-1}
Tier 2 : With gloves and *coated coverall*	negligible	negligible	15 000	3.71×10^{-2}	3.71×10^{-2}
Tier 2 + rinse: With gloves and *coated coverall*	negligible	negligible	150	1.86×10^{-4}	1.86×10^{-4}
Task (public) – time frame :	**Equipment maintenance – every month**				
Tier 1 : Without PPE	negligible	negligible	9	1.98×10^{-3}	1.98×10^{-3}
Task (public) – time frame :	**Process water sampling – every week**				
Tier 1 : Without PPE	negligible	negligible	9	4.13×10^{-5}	4.13×10^{-5}

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task (public) – time frame :	**Waste disposal (water treatment service worker) - daily**				
Covered by above scenarios.					
Task (public) – time frame :	**Combined = cleaning pumps + equipment maintenance + process water sampling - daily**				
Tier 1 : Without PPE	negligible	negligible	Not relevant	2.77×10^{-1}	2.77×10^{-1}
Tier 2 (pump cleaning) + Tier1 (maintenance and water sampling)	negligible	negligible	Not relevant	3.91×10^{-2}	3.91×10^{-2}
Tier 2 (pump cleaning with rinsing) + Tier1 (maintenance and water sampling)	negligible	negligible	Not relevant	2.21×10^{-3}	2.21×10^{-3}

Assumptions:

Biocidal product concentration: 1.5% C(M)IT/MIT

Concentration in process water: 9 ppm a.i;

Task duration and frequency (maximum for a water treatment service worker) : 4 facilities visited per day, with up to 1 loading (5 minutes) and 1 pump cleaning (5 minutes) per facility.

PPE: chemical-resistant gloves (10% penetration), impermeable coveralls (5% penetration)

Dermal absorption: *Concentrated solution (> 0.6%) 100 % / Diluted solutions (< 0.6%) 50%%*

SECONDARY EXPOSURE

A) INDIRECT EXPOSURE FOR USE OF C(M)IT/MIT AS A PAPERMILL SLIMICIDE

The critical endpoints for indirect exposure are as described above.

➔ Professionals

The secondary exposure of professionals occurs when bystanders are exposed the humidified air containing the biocidal product.

- **Inhalation exposure:**

Table 2.2-10 Summary of the inhalation exposure for secondary exposure of professionals by inhalation route

Inhalation exposure		
	External concentration (8-hrs TWA)	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day
Vapour phase		
Acticide SPX (9 ppm ai)	3.6×10^{-4}	6×10^{-5}
Aerosol phase		
Acticide SPX (9 ppm ai)	3.65×10^{-3}	6.08×10^{-4}
Total		
Acticide SPX (9 ppm ai)	4.01×10^{-3}	6.68×10^{-4}

- **Dermal exposure :**

In theory, exposure to residual C(M)IT/MIT may be possible due to indirect or secondary exposure from paper. However, it is likely that due to its high water solubility, C(M)IT/MIT is not bound to paper but stays in the water phase, and that any trace residues present in wet paper will quickly degrade or evaporate during the drying process.
The local dermal exposure concentration is very difficult to assess since the C(M)IT/MIT is in the paper and it not possible to determine the remaining concentration of drying.
Exposure following such scenarios is not thought to be significant due to a number of factors including:
It has been determined that the remaining dose of C(M)IT/MIT in paper will be 15 mg ai/kg paper for Acticide SPX.
A confidential study was submitted by Thor GmbH nevertheless this study has not been taken into account since As it has not been possible to prove that this study has been performed with the intended dose rate. Then the quantity of C(M)IT/MIT has been calculated using a worst-case scenario of ESD (EC, 2003)[3]
Based on these exposure assumptions, the deposit concentration (considering that the subsequent deposits accumulate over the day) and systemic dermal exposure to C(M)IT/MIT from the scenario described above may be calculated as follows:

Systemic dose = 2.35 x 10^{-2} mg a.i. /kg bw /day

- **Total Combined exposure:**

As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

When a worker is exposed during both primary and secondary exposure (including inhalation route for both vapor and aerosol phases and vapor phase only for dermal route) , a total combined exposure has been calculated.

Table 2.2-11: Total combined exposure for primary and secondary exposure

Total combined exposure				
		Tier 1	**Tier 2**	**Tier 2 +rinse**
Total systemic dose for primary exposure	mg/kg bw/day	2.77 x 10^{-1}	3.91 x 10^{-2}	2.21 x 10^{-3}
Total systemic dose for secondary exposure	mg/kg bw/day	2.42 x 10^{-2}	2.42 x 10^{-2}	2.42 x 10^{-2}
Total combined exposure	mg/kg bw/day	2.77 x 10^{-1}	3.91 x 10^{-2}	2.64 x 10^{-2}

- **Dermal exposure to aerosol phase :**

Exposure to humidified air containing residual biocide represents also a secondary exposure for dermal contact with the aerosol phase of the air. Since it is very difficult to assess this exposure RMS choose to use a reverse scenario approach.

Table 2.2-12: Reverse scenario to determine the value of the dermal exposure which would lead to systemic effects

The Margin of Exposure for dermal exposure has been calculated by subtracting from the chronic systemic AEL of 0.09 mg ai/kg bw/d, the value of the total combined exposure of 2.64 x 10^{-2} mg/kg bw/d.

Margin of Exposure for dermal exposure	6.36 x 10^{-2}	mg ai/kg bw/d
Exposure for one worker	7.63	mg ai/d
Exposure for product	8.48 x 10^{5}	mg

Equivalent in l	0.848	l

Then it appeared that 0.848L of the product would be necessary for a worker to generate systemic effects due to the dermal secondary exposure, this dermal exposure can be then considered as very unrealistic.

➔ General public

In theory, exposure to residual C(M)IT/MIT may be possible due to indirect or secondary exposure from paper. However, it is likely that due to its high water solubility, C(M)IT/MIT is not bound to paper but stays in the water phase, and that any trace residues present in wet paper will quickly degrade or evaporate during the drying process. To address potential indirect exposure from paper, two worst-case scenarios are presented: ingestion of paper and food packaging.

Paper ingestion

Indirect or secondary oral exposure may be possible for an infant or child who intentionally ingests paper manufactured in a process that uses C(M)IT/MIT as a wet-end slimicide In order to determine which dose would not lead to systemic effects a reverse scenario was used :

Exposure estimates:

- Maximum in-use wet-end concentration of 15 mg ai/kg paper for Acticide SPX was assumed in the finished paper product
- Oral absorption value: 50%
- Weight of an infant: 10 kg
- Weight of a child: 15 kg
- ARfD: 0.02 mg ai/kg bw/d
-

The reverse worst-case exposure scenario is calculated as follows:
Infant: 0.02 * 10 kg /(15 mg a.i./kg paper) = **0.013 kg paper**

Child: 0.02 * 15 kg /(15 mg a.i./kg paper) = **0.02 kg paper**

Then, it is considered highly unrealistic that an unacceptable risk occurred concerning paper ingestion by infants and children.

Migration from food packaging

In theory, oral indirect exposure to residues of C(M)IT/MIT may be possible. Indeed, residues of the actives substances and their degradation products could migrate from paper used in food packaging to food. The main requirements for the use as "food contact material" is established in REGULATION (EC) No 1935/2004 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 27 October 2004 on materials and articles intended to come into contact with food and repealing Directives 80/590/EEC and 89/109/EEC. The principle underlying this Regulation is that any material or article intended to come into contact directly or indirectly with food must be sufficiently inert to preclude substances from being transferred to food in quantities large enough to endanger human health or to bring about an unacceptable change in the composition of the food or a deterioration in its organoleptic properties. The regulation shall apply for the intended use of both products in the paper and cardboard industry.

As a first tier approach, the worst-case oral exposure scenario of ESD (EC, 2003)[14] for adult has been performed in Doc IIB for each applicant for completeness purposes. Results of exposure scenario are presented below in Table 2.2-13.

Table 2.2-13: Exposure scenarios from paper used as packaging materia

	C(M)IT/MIT use concentration in paperpulp	C(M)IT/MIT resulting concentration in dry paper	Concentration in food (mg as/kg food)	Exposure (mg/kg bw/day)
THOR	6-9 ppm ai	15 mg a.i./kg paper	0.090	1.5×10^{-3}

Furthermore, a biocide intended to be used as a slimicide in process water for paper manufacturing may fall under the Food Contact Material Legislation. The maximum total amounts of C(M)IT/MIT in paper (25 and 15 µg/dm² respectively) do not exceed the maximum residual amount of C(M)IT/MIT in paper use as food contact material recently derived by EFSA to 25 µg/dm² (2010[15]).
During the paper making process, some degradation of C(M)IT/MIT may occur. Therefore, exposure could occur by contact of food to degradation products of the biocidal product in paper and orally incorporated by user. Thor identified the following degradation products: NMMA, acetic acid, formic acid, urea and ethylene glycol. As a worst case, assuming a complete degradation of CIT/MIT, degradation products could be found in paper in the same amount as parent compound.
As feed may also be packaged with paper, livestock exposures have been calculated using default scenario from the DRAWG[16] Guidance on Estimating Livestock Exposure to Biocidal Active Substances (see Document IIB). No exposure values calculated with the worst-case scenario (10% feed consumed wrapped) are above the trigger value of 0.004 mg a.i./kg bw/d. It can therefore be concluded that no significant residues of active substance could occur in food of animal origin.

Indirect exposure to human via the environment

Indirect exposure to man via the environment is considered insignificant based upon the low production volume, rapid environmental degradation and lack of bioaccumulation potential of the active substance.

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.

[14] EC. 2003. Supplement to the methodology for risk evaluation of biocides. Harmonisation of Environmental Emission Scenarios for slimicides (product type 12). European Commission DG ENV/RIVM, September 2003. http://ecb.jrc.ec.europa.eu/documents/Biocides/EMISSION_SCENARIO_DOCUMENTS/ESD_PER_PRODUCT_TYPE/PT_12/PT_12_Slimicides.pdf
[15] EFSA Scientific Opinion of the Panel on food contact materials, enzymes, flavourings and processing aids (CEF); Scientific Opinion on the safety evaluation of the substance, 5-chloro-2-methyl-2H-isothiazol-3-one, mixture with 2-methyl-2H-isothiazol-3-one (3:1), CAS No. 55965-84-9, as a biocide for processing coatings and paper and boards. EFSA Journal 2010; 8(3): 1541. [12 pp.].
[16] Dietary Risk Assessment Working Group

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 Level (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) = 0.11 mg ai/kg bw/d
- Long-term AEL= (17.2/100) = 0.09 mg ai/kg bw/d

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

A) Application in papermills

Table 2.2-14: Exposure estimates for water treatment service worker/plant worker using biocidal products as slimicide in paper mill plant for Kathon WT

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame :	**Loading Kathon WT in process water systems (water treatment service worker) – every week**				
Tier 1 : Without PPE	5.48×10^{-3}	9.14×10^{-4}	140 000	3.65	3.65
Tier 2 : With gloves, RPE and impermeable coveralls	5.48×10^{-4}	9.14×10^{-4}	140 000	3.65×10^{-2}	3.74×10^{-2}
Task (public) – time frame :	**Cleaning Kathon WT dispensing pumps (water treatment service worker) – daily**				
Tier 1 : Without PPE	negligible	negligible	140 000	1.99	1.99
Tier 2 : With gloves and impermeable coveralls	negligible	negligible	140 000	0.164	0.164
Tier 2 + rinse: With gloves and impermeable coveralls	negligible	negligible	1 400	1.64×10^{-3}	1.64×10^{-3}
Task (public) – time frame :	**Equipment maintenance – every month**				
Tier 1 : Without PPE	4.95×10^{-6}	8.25×10^{-7}	15	5.12×10^{-3}	5.12×10^{-3}
Task (public) – time frame :	**Process water sampling – every week**				
Tier 1 : Without PPE	1.03×10^{-7}	1.72×10^{-8}	15	1.07×10^{-4}	1.07×10^{-4}
Task (public) – time frame :	**Waste disposal (water treatment service worker) - daily**				
Covered by above scenarios.					

Tier	*Inhalation exposure*		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task (public) – time frame :	**Combined = loading + cleaning pumps + equipment maintenance + process water sampling - daily**				
Tier 1 : Without PPE	5.49×10^{-3}	9.15×10^{-4}	Not relevant*	5.65	5.65
Tier 2 : With gloves and impermeable coveralls	5.49×10^{-3}	$9.15x\ 10^{-4}$	Not relevant*	2.02×10^{-1}	2.02×10^{-1}
Tier 2 + rinse: With gloves and impermeable coveralls	5.49×10^{-3}	$9.15x\ 10^{-4}$	Not relevant*	3.90×10^{-2}	3.99×10^{-2}

Table 2.2-15: Summary of the exposure estimates for combined exposure to Kathon WT

* As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

- Quantitative risk assessment for systemic effects

Table 2.2-16: Summary of risk assessment for professionals when loading water systems and post-application tasks for Kathon WT

	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
	Loading Kathon WT in process water systems (water treatment service worker) - daily					
Tier 1 : Without PPE	4.71	8.6	100	**1.9**	0.09	**5 233**
Tier 2: With gloves, RPE and impermeable coveralls	4.82×10^{-2}	8.6	100	179	0.09	53.5
	Cleaning Kathon WT dispensing pumps (water treatment service worker) – daily					
Tier 1: Without PPE	2.57	8.6	100	**3.4**	0.09	**2 856**
Tier 2: With gloves and impermeable coveralls	3.46×10^{-1}	8.6	100	**25**	0.09	**384**
Tier 2 + rinse: With gloves and impermeable coveralls	1.73×10^{-3}	8.6	100	4 971	0.09	1.9
	Equipment maintenance – every month					
Tier 1: Without PPE	3.30×10^{-3}	8.6	100	2 606	0.09	3.7
	Process water sampling – every week					
Tier 1: Without PPE	6.88×10^{-5}	8.6	100	13×10^{4}	0.09	0.08
	Waste disposal - daily					
	Covered by above scenarios.					
	Combined = cleaning pumps + equipment maintenance + water monitoring - daily					
Tier 1 : Without PPE	2.57	8.6	100	**3.4**	0.09	**2 856**
Tier 2: With gloves and impermeable coveralls	3.97×10^{-1}	8.6	100	**22**	0.09	**441**
Tier 2 + rinse: With gloves and impermeable coveralls	5.22×10^{-2}	8.6	100	165	0.09	58

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

The risk characterisation for systemic exposure during the loading is not acceptable in Tier 1, but the risk became acceptable when PPE and RPE are worn with a MOE (179) higher than the MOE_{ref} (100) and a %AEL (53.5%) below 100%.
The risk for the cleaning scenario (cleaning of the dispensing pumps) is considered acceptable, in Tier 2 only, i.e with wearing PPE and a rinse step.
The risk during equipment maintenance and process water monitoring is acceptable in Tier 1 (MOE > MOE_{ref} and %AEL<100%).
Concerning the combined exposure the risk is considered acceptable in Tier 2 since MOE (165) is higher than the MOE_{ref} (100) and the %AEL (58%) is below 100% provided that a rinse is performed before cleaning.

- Quantitative risk assessment for local effects
  - By inhalation

Table 2.2-17: Summary of risk assessment as repeated inhalation exposure for professionals using Kathon WT

	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 :	**Loading Kathon WT in process water system (water treatment service worker) - daily**					
Tier 1 : Without PPE	5.48×10^{-3}	0.34	16	62	0.02	27.4
Task– time frame :	**Cleaning pump**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Equipment maintenance**					
Tier 1 : Without PPE	Negligible	0.34	16	6.87×10^4	0.02	Negligible
Task– time frame :	**Process water monitoring**					
Tier 1 : Without PPE	Negligible	0.34	16	3.30×10^6	0.02	Negligible
Task – time frame :	**Combined = loading + cleaning pumps (water treatment service worker) - daily**					
Tier 1 : Without PPE	Negligible	0.34	16	61.9	0.02	Negligible

The risk characterisation for inhalation exposure during the loading only leads to risks that are acceptable, with a MOE higher than the MOE_{ref}. As well, the $\%AEC_{inhalation}$ is below 100% indicating that risks are considered as acceptable. For the other different tasks, inhalation exposure is considered negligible.

- Qualitative risk assessment for local effects
  - By dermal contact

Table 2.2-18 Summary of repeated dermal exposure values for professionals using Kathon™ WT

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task – time frame :	**Loading Kathon ™ WT in process water system (water treatment service worker) – every week**	
Tier 1 : Without PPE	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 : Rinse prior the cleaning	1 400	15
Task – time frame :	**Equipment maintenance – every month**	
Tier 1 : Without PPE	15	15
Task (public) – time frame :	**Process water sampling – every week**	
Tier 1 : Without PPE	15	15
Task (public) – time frame :	**Waste disposal (water treatment service worker) - daily**	
	Covered by above scenarios.	

As the threshold value is expressed as ppm, 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 equal or above the concentration that would lead to sensitization (15 ppm a.i.).

However, 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.

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) Application in oilfield injection system

Table 2.2-19 Summary of the exposure estimates for water treatment service worker/plant worker using biocidal products as slimicide in mineral oil extraction

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	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 Kathon WT in injection systems – every week**				
Tier 1 : Without PPE	5.42 x 10^{-3}	9.03 x 10^{-4}	140 000	2.32	2.32
Tier 2 : With gloves, RPE and impermeable coveralls	5.42 x 10^{-3}	9.03 x 10^{-4}	0	0	9.03 x 10^{-4}
Task – time frame :	**Automated loading Kathon WT in injection systems – every week**				
Tier 1 : Without PPE	negligible	negligible	140 000	8.32 x 10^{-3}	8.32 x 10^{-3}
Tier 2 : With gloves, RPE and impermeable coveralls	Negligible	Negligible	140 000	8.32 x 10^{-4}	8.32 x 10^{-4}
Task (public) – time frame :	**Cleaning Kathon WT dispensing pumps – daily**				
Tier 1 : Without PPE	negligible	negligible	140 000	1.99	1.99
Tier 2 : With gloves and impermeable coveralls	negligible	negligible	140 000	0.164	0.164
Tier 2 + rinse: With gloves and impermeable coveralls	negligible	negligible	1 400	1.64 x 10^{-3}	1.64 x 10^{-3}
Task (public) – time frame :	**Equipment maintenance – every month**				
Tier 1 : Without PPE	9.90 x 10^{-6}	1.65 x 10^{-6}	30	1.022 x 10^{-2}	1.02 x 10^{-2}
Task (public) – time frame :	**Process fluid sampling – every week**				

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Tier 1 : Without PPE	2.06×10^{-7}	3.44×10^{-8}	30	2.13×10^{-4}	2.13×10^{-4}

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task (public) – time frame :	**Combined = loading + cleaning pumps + equipment maintenance + process fluid sampling - daily**				
Tier 1 : Without PPE	5.43×10^{-3}	9.05×10^{-4}	Not relevant*	4.32	4.32
Tier 2 : With gloves and impermeable coveralls	5.43×10^{-3}	9.05×10^{-4}	Not relevant*	1.67×10^{-1}	1.67×10^{-1}
Tier 2 + rinse: With gloves and impermeable coveralls	5.43×10^{-3}	9.05×10^{-4}	Not relevant*	4.14×10^{-3}	4.14×10^{-3}

*As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

- Quantitative risk assessment for systemic effects

Table 2.2-20 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
	Manual loading Kathon WT in process water systems - daily					
Tier 1 : Without PPE	2.99	8.6	100	**2.9**	0.09	**3 322**
Tier 2: With gloves and impermeable coveralls	9.03×10^{-4}	8.6	100	1×10^{4}	0.09	1
Task– time frame :	**Automated loading Kathon WT in process water systems - daily**					
Tier 1 : Without PPE	2.15×10^{-2}	8.6	100	400	0.09	23.9
Tier 2: With gloves, RPE and impermeable coveralls	2.15×10^{-3}	8.6	100	4 000	0.09	2.4
Task – time frame:	**Cleaning dispensing pumps (water treatment service worker) – daily**					
Tier 1: Without PPE	2.57	8.6	100	**3.4**	0.09	**2 856**
Tier 2: With gloves and coated coveralls	3.46×10^{-1}	8.6	100	**25**	0.09	**384**
Tier 2 + rinse: With gloves and coated coveralls	1.73×10^{-3}	8.6	100	5×10^{3}	0.09	1.9
Task – time frame:	**Equipement maintenance – every month**					
Tier 1: Without PPE	6.60×10^{-3}	8.6	100	1 303	0.09	7.3
Task – time frame:	**Process water sampling – every week**					
Tier 1: Without PPE	1.38×10^{-4}	8.6	100	0.6×10^{5}	0.09	0.15
Task – time frame :	**Combined = cleaning pumps + equipment maintenance + water monitoring - daily**					
Tier 1 : Without PPE	2.57	8.6	100	**3.4**	0.09	**2 856**
Tier 2 (pump cleaning) + Tier1 (maintenance and water sampling)	3.53×10^{-1}	17.2	100	**24.5**	0.09	**392**

	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
Tier 2 (pump cleaning with rinsing) + Tier1 (maintenance and water sampling)	8.47×10^{-3}	17.2	100	1 015	0.09	9.4

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

The risk characterization for systemic exposure during the loading is acceptable in Tier 2 only for the manual loading and in Tier 1 for the automated loading with a MOE (400) higher than the MOE_{ref} (100) and a %AEL (23.9%) below 100%.

The risk for the cleaning scenario (cleaning of the dispensing pumps) is considered acceptable, in Tier 2 only, i.e with wearing of PPE.

The risk during equipment maintenance and process water monitoring is acceptable in Tier 1 (MOE > MOE_{ref} and %AEL < 100%).

Concerning the combined exposure the risk is considered as acceptable in Tier 2 (pump cleaning with rinsing) + Tier 1 (maintenance and water sampling) since MOE (1015) is higher than the MOE_{ref} (100) and the %AEL (9.4%) is below 100%.

- Quantitative risk assessment for local effects
  - By inhalation

Table 2.2-21: Summary of risk assessment as repeated inhalation exposure for professionals when loading in water systems and post-application tasks

	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)	$\%AEC_{inhalation}$
	Manual loading in process water system - daily					
Tier 1 : Without PPE	5.42×10^{-3}	0.34	16	62.7	0.02	27.1
Task– time frame :	**Automated loading in process water system - daily**					
Tier 1 : Without PPE	negligible	0.34	16	∞	0.02	Negligible
	Cleaning pump					
Tier 1 : Without PPE	negligible	0.34	16	∞	0.02	Negligible
	Equipment maintenance					
Tier 1 : Without PPE	negligible	0.34	16	3.43×10^4	0.02	Negligible
	Process water monitoring					
Tier 1 : Without PPE	negligible	0.34	16	1.65×10^6	0.02	Negligible
	Combined = cleaning pumps (water treatment service worker) - daily					
Tier 1 : Without PPE	negligible	0.34	16	62.6	0.02	Negligible

The risk characterisation for inhalation exposure during the loading leads to risks that are considered acceptable, with a MOE higher than the MOE_{ref}. As well, the $\%AEC_{inhalation}$ is below 100%. For the other tasks, the exposure is considered negligible.

- Qualitative risk assessment forl local effects
  - By dermal conatct

As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure is not suitable.

Table 2.2-22: Summary of repeated dermal exposure values for professionals when loading chilled-water systems and cleaning dispensing pumps

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task – time frame :	**Loading Kathon™WT in process water system (water treatment service worker) – every week**	
Tier 1 : Without PPE	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 : Rinse prior the cleaning	1 400	15
Task – time frame :	**Equipment maintenance – every month**	
Tier 1 : Without PPE	30	15
Task (public) – time frame :	**Process water sampling – every week**	
Tier 1 : Without PPE	30	15
Task (public) – time frame :	**Waste disposal (water treatment service worker) - daily**	
	Covered by above scenarios.	

As the threshold value is expressed as ppm, 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 equal or above the concentration that would lead to sensitisation (15 ppm a.i.).

However, 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 accidental and manageable as such.

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.

SECONDARY EXPOSURE

A) Exposure of professionals to humidified air in papermills

- Quantitative risk assessment for systemic effects

Table 2.2-23:

	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
Secondary exposure for inhalation route						
Tier 1 : Without PPE	1.11×10^{-3}	8.6	100	0.8×10^{4}	0.09	1.2
Secondary exposure for dermal route						
Tier 1 : without PPE	3.91×10^{-2}	8.6	100	220	0.09	43
Total combined exposure for professionals (primary + secondary exposure)**						
Tier 1: Without PPE	2.61	8.6	100	**3.3**	0.09	**2 900**
Tier 2:	3.91×10^{-1}	8.6	100	**22**	0.09	**434**
Tier 2 + rinse:	4.62×10^{-2}	8.6	100	186	0.09	51.3

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

**As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

The risk for secondary exposure for professionals is considered acceptable for the systemic effects. Concerning the total combined exposure for a professional the risk is acceptable in Tier 2 provided that a rinse is performed before cleaning, meaning that professionals need to wear gloves and coated coveralls during the cleaning phase and that a rinse is performed before the pumps to be clean.

- Quantitative risk assessment for local effects
  - By inhalation

Table 2.2-24: Summary of the risk characterisation for local effect by inhalation for secondary exposure to workers for Kathon™ WT

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref}	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Total secondary exposure for Kathon WT						
Tier 1 : Without PPE	6.68×10^{-3}	0.34	16	50.9	0.02	7.4

The risk is considered acceptable for local effects via an inhalation exposure as a secondary exposure for professionals.

- Qualitative risk assessment for local effects
  - By dermal contact

Dermal exposure to humidified air containing residual biocide can occur for professionals.

The concentration of C(M)IT/MIT used for this exposure scenario is equal to the concentration that would lead to sensitisation (15 ppm a.i.) and wearing of PPE is not considered for secondary exposure.

In order to take into account the sensitizing properties of the C(M)IT/MIT, the product concentration of use in papermills must be reduced below the threshold value of 15 ppm a.i.

B) Indirect ingestion of C(M)IT/MIT residues from paper used as food contact material

The risk characterization for indirect ingestion of C(M)IT/MIT residues from paper used as food contact material is presented below in **Table 2.2-25.**

Table 2.2-25: Risk characterization of secondary exposure scenario (adult-oral) for residues of C(M)IT/MIT from paper

Adult (oral)	**DOW**
Exposure (mg/kg bw/day)	2.5×10^{-3}
NOAEC chronic **NOAEL acute**	0.4 2
ADI (mg/kg bw/d) **ARfD (mg/kg bw/d)**	0.004 0.02
MOE chronic **MOE acute**	160 800
%ADI **% ARfD**	62.5 12.5

Regarding oral exposure from residues from food packaging, MOE is higher than 100 and exposure represents not more than 62.5 % of the ADI and 12.5 % of the ARfD. No

unacceptable risk is associated with indirect exposure to C(M)IT/MIT from food paper packaging.
As consumers are not only exposed to C(M)IT/MIT but also to their degradation product, data on minor degradation products 'identification, quantitative distribution and genotoxic potential) should be provided. These data were provided by Thor but not by Dow who only reported the major degradation product NMMA. The ADI of C(M)IT/MIT (0.004 mg/kg) is lower than toxicological reference values of its degradation products (see Document IIC). As these degradation products could not be found in paper at levels higher than C(M)IT/MIT itself which is more toxic, no unacceptable risk is associated with indirect exposure to degradation products of CIT/MIT in paper.

Conclusion:
Regarding oral exposure from residues on paper used as food contact material, MOE is greater than 100 and exposure represents no more than 62.5 % of the ADI and 12.5 % of the ARfD, even considering the theoretical worst case scenario. No unacceptable risk is associated with indirect exposure to C(M)IT/MIT following use in paper pulp as slimicide.

C) Exposure to aerosols from oilfield injection system

- Quantitative risk characterization for systemic effects

Table 2.2-26 Summary of the risk characterisation for systemic effects for secondary exposure to workers

	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
Indoor mud aerosol exposure						
Tier 1 : Without PPE	8.5×10^{-3}	8.6	100	1012	0.09	9.4
Outdoor mud aerosol exposure						
Tier 1 : without PPE	4.2×10^{-4}	8.6	100	2.1×10^{4}	0.09	0.5

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

The risk for secondary exposure for professionals is considered acceptable for the systemic effects.

- Quantitative risk characterization for local effects
  - By inhalation

Table 2.2-27 Summary of the risk characterisation for local effects by inhalation route for secondary exposure to workers

	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 :	**Indoor mud aerosol exposure**					
Tier 1 : Without PPE	5.1×10^{-2}	0.34	16	**6.7**	0.02	**255**
Tier 2 : with RPE	5.1×10^{-3}	0.34	16	67	0.02	25.5
Task – time frame :	**Outdoor mud aerosol exposure**					
Tier 1 : without PPE	2.5×10^{-3}	0.34	16	136	0.02	12.5

The risk is considered acceptable for local effects via an inhalation exposure as a secondary exposure for professionals in Tier 2 only for exposure to local effects of indoor mud aerosol and in Tier 1 for outdoor mud aerosol.

- Qualitative risk assessment for local effects
  - By dermal route

Table 2.2-28: Summary of the risk characterisation for local effects by dermal route for secondary exposure to workers

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task – time frame :	**Indoor mud aerosol exposure**	
Tier 1 : Without PPE	30	15
Task – time frame :	**Indoor mud aerosol exposure**	
Tier 1 : Without PPE	30	15

Dermal exposure to mud aerosol containing residual biocide can occur for professionals.

The concentration of C(M)IT/MIT used for this exposure scenario is above to the concentration that would lead to sensitisation (15 ppm a.i.) and wearing of PPE is not considered for secondary exposure.

In order to take into account the sensitizing properties of the C(M)IT/MIT, the product concentration of use in oilfield injection must be reduced below the threshold value of 15 ppm a.i.

2.2.1.5 Risk characterisation for Acticide SPX (Thor's product)

PRIMARY EXPOSURE

A) Application in papermills

Table 2.2-29: Summary of the exposure estimates for Acticide SPX used as slimicide in papermills

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task – time frame :	**Loading Acticide SPX in process water systems (water treatment service worker) – every week**				
Tier 1 : Without PPE	5.88×10^{-4}	9.79×10^{-5}	15 000	3.91×10^{-1}	3.91×10^{-1}
Tier 2 : With gloves and impermeable coveralls	5.88×10^{-4}	9.79×10^{-5}	15 000	3.91×10^{-3}	4.01×10^{-3}
Task (public) – time frame :	**Cleaning Acticide SPX dispensing pumps (water treatment service worker) – daily**				
Tier 1 : Without PPE	negligible	negligible	15 000	2.13×10^{-1}	2.13×10^{-1}
Tier 2 : With gloves and impermeable coveralls	negligible	negligible	15 000	1.76×10^{-2}	1.76×10^{-2}
Tier 2 + rinse: With gloves and impermeable coveralls	negligible	negligible	150	1.76×10^{-4}	1.76×10^{-4}
Task (public) – time frame :	**Equipment maintenance – every month**				
Tier 1 : Without PPE	2.97×10^{-6}	4.95×10^{-7}	9	3.07×10^{-3}	3.07×10^{-3}
Task (public) – time frame :	**Process water sampling – every week**				
Tier 1 : Without PPE	6.19×10^{-8}	1.03×10^{-8}	9	6.39×10^{-5}	6.39×10^{-5}
Task (public) – time frame :	**Waste disposal (water treatment service worker) - daily**				
Covered by above scenarios.					

Table 2.2-30: Summary of the combined exposure estimates for Acticide SPX used as slimicide in papermills

Tier	Inhalation exposure		Dermal exposure		Total exposure
PPE	External concentration (8-hrs TWA)	Systemic dose	Deposit on skin (hands)	Systemic dose	Systemic dose
	mg a.i. /m^3 air	mg a.i. / kg bw /day	ppm a.i.	mg a.i. / kg bw /day	mg a.i. / kg bw /day
Task (public) – time frame :	**Combined = loading + cleaning pumps + equipment maintenance + process water sampling - daily**				
Tier 1 : Without PPE	5.91×10^{-4}	9.84×10^{-5}	Not relevant*	6.08×10^{-1}	6.08×10^{-1}
Tier 2 :With gloves and impermeable coveralls	5.91×10^{-4}	9.84×10^{-5}	Not relevant*	2.20×10^{-2}	2.21×10^{-2}
Tier 2 + rinse: With gloves and impermeable coveralls	5.91×10^{-4}	9.84×10^{-5}	Not relevant*	4.57×10^{-3}	4.67×10^{-3}

* As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.

- Quantitative risk assessment for systemic effects

Table 2.2-31: Summary of risk assessment for professionals during loading in 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 :	**Loading Acticide SPX in process water systems (water treatment service worker) - daily**					
Tier 1 : Without PPE	5.05×10^{-1}	8.6	100	**17**	0.09	**561**
Tier 2: With gloves, RPE and impermeable coveralls	5.05×10^{-3}	8.6	100	1 703	0.09	5.6
Task – time frame:	**Cleaning Acticide SPX dispensing pumps (water treatment service worker) – daily**					
Tier 1: Without PPE	2.75×10^{-1}	8.6	100	**32**	0.09	**306**
Tier 2: With gloves and coated coverall	3.71×10^{-2}	8.6	100	232	0.09	41
Tier 2 + rinse: With gloves and coated coverall	1.86×10^{-4}	8.6	100	4.6×10^{4}	0.09	0.21
Task – time frame:	**Equipement maintenance – every month**					
Tier 1: Without PPE	1.98×10^{-3}	8.6	100	4 344	0.09	2.2
Task – time frame:	**Process water sampling – every week**					
Tier 1: Without PPE	4.13×10^{-5}	8.6	100	2.1×10^{5}	0.09	0.05
Task – time frame:	**Waste disposal - daily**					
Covered by above scenarios.						
Task – time frame :	**Combined = cleaning pumps + equipment maintenance + water monitoring - daily**					
Tier 1 : Without PPE	2.77×10^{-1}	8.6	100	**31**	0.09	**308**
Tier 2 (pump cleaning) + Tier1 (maintenance and water sampling)	3.91×10^{-2}	8.6	100	220	0.09	43
Tier 2 (pump cleaning with rinsing) + Tier1 (maintenance and water sampling)	2.21×10^{-3}	8.6	100	3 892	0.09	2.5

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

The risk characterisation for systemic exposure during the loading is is not acceptable in Tier 1, but is the risk became acceptable when PPE are worn with a MOE (1703) higher than the MOE_{ref} (100) and a %AEL (5.6%) below 100%.
The risk for the cleaning scenario (cleaning of the dispensing pumps) is considered acceptable, in Tier 2 only.
The risk during equipment maintenance and process water monitoring is acceptable in Tier 1 (MOE > MOE_{ref} and %AEL<100%).
Concerning the combined exposure the risk is considered as acceptable in Tier 2 (pump cleaning with rinsing) + Tier1 (maintenance and water sampling) since MOE (3 892) is higher than the MOE_{ref} (100) and the %AEL (2.5) is lower than 100.

- Quantitative risk assessment for local effects

  - By inhalation

Table 2.2-32: Summary of risk assessment as repeated inhalation exposure for professionals when loading in process water systems and for post-application tasks

	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 :	**Loading Acticide SPX in process water system (water treatment service worker) - daily**					
Tier 1 : Without PPE	5.88×10^{-4}	0.34	16	578	0.02	2.9
Task– time frame :	**Cleaning pump**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task– time frame :	**Equipment maintenance**					
Tier 1 : Without PPE	Negligible	0.34	16	114 478	0.02	Negligible
Task– time frame :	**Process water monitoring**					
Tier 1 : Without PPE	Negligible	0.34	16	5.49×10^6	0.02	Negligible
Task – time frame :	**Combined = cleaning pumps (water treatment service worker) - daily**					
Tier 1 : Without PPE	Negligible	0.34	16	575	0.02	Negligible

The risk characterisation for inhalation exposure during the loading is acceptable, with a MOE higher than the MOE_{ref}. As well, the $\%AEC_{inhalaion}$ is below 100. For the other scenarios, the exposure is considered negligible.

- Qualitative risk assessment for local effects

- By dermal contact

Table 2.2-33: Summary of risk assessment as repeated dermal exposure for professionals when loading chilled-water systems and cleaning dispensing pumps

	Concentration of active ingredient on skin (ppm a.i.)	Threshold value (ppm a.i.)
Task – time frame :	**Loading Acticide SPX in process water system (water treatment service worker) – every week**	
Tier 1 : Without PPE	15 000	15
Task – time frame :	**Cleaning Acticide SPX dispensing pumps (water treatment service worker) - daily**	
Tier 1 : Without PPE	15 000	15
Tier 2 : Rinse prior the cleaning	150	15
Task – time frame :	**Equipment maintenance – every month**	
Tier 1 : Without PPE	9	15
Task (public) – time frame :	**Process water sampling – every week**	
Tier 1 : Without PPE	9	15
Task (public) – time frame :	**Waste disposal (water treatment service worker) - daily**	
	Covered by above scenarios.	

As the threshold value is expressed as ppm, 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 the exposure scenarios of post application (equipment maintenance and process water sampling) are below the concentration that would lead to sensitisation (15 ppm a.i.), no unacceptable risk is therefore identified.

Concerning the loading of the biocidal product and the cleaning of the dispensing pumps, 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.). However, 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.

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.

SECONDARY EXPOSURE

A) Professional exposure to humidified air in papermills

- Quantitative risk assessment for systemic effects

Table 2.2-34:

	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
Secondary exposure for inhalation route						
Tier 1 : Without PPE	6.68×10^{-4}	8.6	100	1.3×10^{4}	0.09	0.7
Secondary exposure for dermal route						
Tier 1 : without PPE	7.84×10^{-2}	8.6	100	110	0.09	87
Total combined exposure for professionals (primary + secondary exposure)* *						
Tier 1: Without PPE	8.61×10^{-1}	8.6	100	**10**	0.09	**957**
Tier 2:	1.23×10^{-1}	8.6	100	70	0.09	**137**
Tier 2 + rinse:	8.64×10^{-2}	8.6	100	100	0.09	96

* NOAEL corrected by the oral absorption factor of 50%.
** As for local dermal effect it is the concentration of the C(M)IT/MIT during the event of contact that is relevant, combined exposure have only been assessed for systemic exposure.
The risk for secondary exposure for professionals is considered as acceptable for the systemic effects. Concerning the total combined exposure for a professional the risk is acceptable in Tier 2, considering that a rinsing step is performed before cleaning and meaning that professionals need to wearPPE during the cleaning phase.

- Quantative risk assessment for local effects
  - By inhalation

Table 2.2-35: Summary of the risk characterisation for local effects by inhalation for secondary exposure to workers for Acticide SPX

	Inhalation exposure (mg a.i. /m^3 air)	Relevant NOAEC (mg a.i. /m^3 air)	MOE_{ref}	MOE	$AEC_{inhalation}$ (mg a.i./m^3 air)	$\%AEC_{inhalation}$
Total secondary exposure for Acticide SPX						
Tier 1 : Without PPE	4.01×10^{-3}	0.34	16	84.8	0.02	20.1

The risk is considered as acceptable for local effects via an inhalation exposure as a secondary exposure for professionals.

- Qualitative risk assessment for local effects
  - By dermal contact

Dermal exposure to humidified air containing residual biocide can occur for professionals. The concentration of C(M)IT/MIT used for this exposure scenario (9 ppm a.i.) is below the concentration that would lead to sensitisation (15 ppm a.i.) . The risk is therefore considered as acceptable.

B) Indirect ingestion of C(M)IT/MIT residues from paper used as food contact material

The risk characterization for indirect ingestion of C(M)IT/MIT residues from paper used as food contact material is presented below in **Table 2.2-36**.

Table 2.2-36: Risk characterization of secondary exposure scenario (adult-oral) for residues of C(M)IT/MIT from paper

Adult (oral)	**THOR**
Exposure (mg/kg bw/day)	1.5×10^{-3}
NOAEC chronic **NOAEL acute**	0.4 2
ADI (mg/kg bw/d) **ARfD (mg/kg bw/d)**	0.004 0.02
MOE chronic **MOE acute**	2.7×10^{2} 1.3×10^{3}
%ADI **% ARfD**	37.5 7.5

Regarding oral exposure from residues from food packaging, MOE is higher than 100 and exposure represents not more than 37.5 % of the ADI and 7.5 % of the ARfD. No unacceptable risk is associated with indirect exposure to C(M)IT/MIT from food paper packaging.
As consumers are not only exposed to C(M)IT/MIT but also to their degradation product, data on minor degradation products 'identification, quantitative distribution and genotoxic potential) should be provided. These data were provided by Thor but not by Dow who only reported the major degradation product NMMA. The ADI of C(M)IT/MIT (0.004 mg/kg) is

lower than toxicological reference values of its degradation products (see Document IIC). As these degradation products could not be found in paper at levels higher than C(M)IT/MIT itself which is more toxic, no unacceptable risk is associated with indirect exposure to degradation products of C(M)IT/MIT in paper.

Conclusion:
Regarding oral exposure from residues on paper used as food contact material, MOE is greater than 100 and exposure represents no more than 37.5 % of the ADI and 7.5 % of the ARfD, even considering the theoretical worst case scenario. No unacceptable risk is associated with indirect exposure to C(M)IT/MIT following use in paper pulp as slimicide.

OVERALL CONCLUSION OF THE RISK CHARACTERIZATION FOR HUMAN HEALTH

No unacceptable risks related to possible systemic effects are identified whatever the scenario considered.
Regarding local effects, the handling of undiluted solution of C(M)IT/MIT (at 14% for Kathon WT or 1.5% for Acticide SPX) induces an unacceptable risk for local effects in case of repeated contact with skin. However, as the product is classified and labeled as corrosive (only for Kathon^{TM}WT) and sensitizing, it has to be handled with sufficient risk mitigation measures, including collective systems (e.g. automated dosing systems) additionally to PPE, in order to prevent any spillage on skin. In such conditions, considering furthermore that the intended users are skilled operators, it may be assumed that dermal exposure would occur only in accidental circumstances.

Therefore, the RMS considers that biocidal products containing up to 14% C(M)IT/MIT can be used as slimicides in papermills or oilfield injection systems provided that appropriate risk mitigation measures are applied during the loading of the product and the cleaning of the dispensing pumps. Possible measures (non exhaustive list) are:

- The containers of the products are designed to prevent spillages during pouring,
- Automated systems preventing contacts with the product are used,
- Procedures are implemented to prevent contacts and spillages,
- Chemical-resistant coveralls, gloves, shoes and face-mask are worn,
- 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.

Unlike dermal exposure, no unacceptable risk was identified for the respiratory tract, whatever the scenario considered.

For use of C(M)IT/MIT as slimicide in papermills, secondary exposures can occur through dermal and inhalation exposure of professionals. No wearing of PPE is considered for professional secondary exposure. **Thus, in order to take into account the sensitizing properties of C(M)MIT/MIT the product concentration of use in papermill must be reduced below the threshold value of 15 ppm a.i.** Concerning the general public, exposure can occur if infants or children ingested treated paper, or if food wrapped in treated paper is ingested. No unacceptable risk was identified for these scenarios.

For oilfield injection application (Kathon WT only), secondary exposure can occur through dermal and inhalation exposure of professionals. No unacceptable risk was identified for these scenarios.

In conclusion, the use of C(M)IT/MIT as PT12 can be considered as safe for human health on the basis of the available data, provided adequate risk mitigation measures are implemented in order to avoid any dermal primary exposure and considering a concentration of use below the threshold value of 15 ppm a.i. in papermills.

Table 2.2-37: Primary Exposure – Use of the concentrated product Kathon™WT (14% a.i) as slimicide in papermill and for mineral oil extraction

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
Loading product in process water system (Mixing and Loading)										
High	Skin Corr 1B (H314) Skin Sens 1A (H317)	-	12	Professional users	Manual dispensing, pouring, and changing out the concentrate reservoir for systems with automatic dosimeters (product with 14% a.i)	Skin	Once per week or 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	Acceptable: + Minimization of manual phases; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

									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 (Post application)										
High	Skin Corr 1B (H314) Skin Sens 1A (H317)	-	12	Professional users	Cleaning the dispensing pump for maintenance	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	Acceptable: + Minimization of manual phases; + Professionals using PPE; + Rinse step with water before

									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 inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	cleaning; + Professionals following instructions for use; + Good standard of personal hygiene.

Table 2.2-38: Primary Exposure - Use of concentrated product ACTICIDE SPX (1.5% a.i) as slimicide in papermill

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
Loading product in process water system (Mixing and Loading)										
High	Skin Sens 1A (H317)	-	12	Professional users	Manual loading of the biocidal product (containing 1.5% w/w C(M)IT/MIT) to the reservoir for system	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 diversity of types.	Acceptable: Minimization of manual phases; Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.

									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 (Post application)										
High	Skin Sens 1A (H317)	-	12	Professional users	Cleaning the dispensing pump for maintenance	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	Acceptable: Minimization of manual phases; Professionals using PPE; Rinse step with water before

									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 inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	cleaning; Professionals following instructions for use; Good standard of personal hygiene.

Table 2.2-39: Primary Exposure – Use of diluted product as slimicides in papermill (15 ppm for Kathon™WT and 9 ppm for ACTICIDE SPX) and for mineral oil extraction (30 ppm for Kathon™WT only)

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
Equipment maintenance and Process water sampling (Post application)										
High	Skin Sens 1A (H317)	-	12	Professional users	Equipment maintenance, equipment maintenance, shut down deep clean, process water sampling, and disposal of waste	Skin	Once a month	<u>Maintenance:</u> direct contact with residues <u>Process water monitoring:</u> accidental contact with spills	**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 (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:	Acceptable: Low frequency; Minimization of manual phases; Professionals using PPE; Professionals following instructions for use; Good standard of personal hygiene.

									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).	

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 ready 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 higher 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. However, 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 Kd_{oc}. 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 expected 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 document IIA of 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 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. The NOEC obtained (0.91 mg a.i./L) divided by an assessment factor of 10 lead to a PNEC$_{\text{m croorganisms}}$ 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 Chemical with Lumbriculus variegates 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 weight sediment. A safety factor of 10 is applied, resulting in a **PNEC$_{\text{sediment}}$** of 0.027 mg a.i./kg$_{\text{dry sediment}}$ corresponding to **0.0058 mg a.i./kg$_{\text{wet sediment}}$**.

2.2.2.2.2 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.

2.2.2.3 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 **$PNEC_{soil, initial}$** 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 a.i./$kg_{wet\ soil}$** from EC_{50} of 18 mg a.i./$kg_{dry\ soil}$ issued from a plant tests and an assessment factor of 1000 (Cf. Document IIA of MIT dossier).

2.2.2.4 Summary of PNEC values

Table 2.2-40 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
$PNEC_{soil,\ in\ tial}$	0.009	0.0417	mg a.i./kg_{wwt}
$PNEC_{soil,\ TWA}$	0.0004	-	mg a.i./kg_{wwt}

2.2.2.5 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.

2.2.2.6 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.

2.2.2.6.1 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.

2.2.2.6.2 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.

2.2.2.6.3 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.

2.2.2.7 Environmental exposure

The risk characterisation has been carried out for the representative products from the two applicants: Kathon™ WT (Dow Chemical) 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 common intended use for Kathon™ WT and for Acticide® SPX is application to control the growth of slime producing organisms in the circulating process water used in the wet-end of paper mills. In the Dow Chemical dossier, another field of use is intended to control the growth of slime producing organisms in injection water lines and raw materials used in processing for oil recovery.

The use phase of Kathon™ WT and Acticide® SPX as slimicides in paper mill and in the oilfield injection systems (only for Kathon™ WT) has been evaluated via exposure analysis based on the specific EUBEES Emission Scenario Document for PT12[17]. Moreover and to cover the various oil exploration processes, in particular reservoir injections, the draft document proposed by NL and discussed at the first WG in 2014, "*Environmental risk assessment of biocides applied in the offshore oil exploration industry*", was used.

Paper Mill Slimicides

Concerning the sub-application "**slimicides in paper production processes**", two different scenarios are considered.

[17] Harmonization of Environmental Emission Scenarios for biocides: PT 12 – Slimicides, European Commission DG ENV/RIVM. September 2003

- The "realistic worst case" where no connection to a pulp mill is assumed and water from the paper mill is subjected to settling and mechanical/chemical treatment in the paper mill and then discharged to surface water.
- The "typical case" where a connection to a pulp mill is assumed which means that a dilution factor is introduced into the model and wastewater after settling is discharged to an industrial STP and then discharged to surface water.

According to the applicants, Kathon™ WT is added to the wet-end paper-making process like routine maintenance dosage at a concentration of 1 to 5 ppm in the system (i.e. 1 to 5 g $_{a.i.}.m^{-3}$). A shock dose of 15 ppm (i.e. 15 g $_{a.i.}.m^{-3}$) would only be employed when fouling is evident. Acticide® SPX is added to the wet-end paper-making process with a continuous dosing at concentrations of 0.4 to 2 ppm (i.e. 0.4 to 2 g $_{a.i.}.m^{-3}$). The same range of concentrations is claimed for a shock dosing.
Additionally, in the Dow Chemical dossier, the efficacy of the active substance has been demonstrated for a concentration of 1 to 15 ppm (i.e. 1 to 15 g $_{a.i.}.m^{-3}$) for a continuous dosing. In the Thor dossier, the efficacy of the active substance has been demonstrated for a concentration of 6 to 9 ppm (i.e. 6 to 9 g $_{a.i.}.m^{-3}$) for a shock dosing only (4 times per day, 6 hours between each dose).
Moreover as C(M)IT/MIT is stable to hydrolysis at all pH, no degradation is taken into account in paper production processes; consequently for the exposure assessment purposes it is considered that shock dosing leads to the same environmental concentrations as continuous dosing.

Therefore, based on the conclusions of the efficacy assessment and the dose rates claimed by the two applicants, only continuous dosage is taken into account for the risk assessment at the concentrations of 2 to 15 g $_{a.i.}.m^{-3}$. To determine the predicted environmental exposure concentrations in water, air, soil and groundwater compartment, if relevant, equations from the TGD were used.

In the realistic worst case scenario, the aquatic compartment is the primary and the only relevant compartment of exposure. In the typical case scenario, the industrial STP is the primary compartment of exposure. Secondary compartments considered for the risk assessment in the typical case scenario are surface water, soil and groundwater.

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 (freshwater and marine) sediment risk assessment is needed.

Only for the "Typical case scenario" and for soil and groundwater, a tiered approach has been considered.

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 or after settling and mechanical/chemical treatment. The only compound considered at the outlet of the STP or the paper mill was MIT. The fraction of MIT emission directed to water by STP was considered as 0.122. Consequently the risk assessment has been carried out considering a ratio PEC_{MIT} / $PNEC_{MIT}$.

A **Tier I** approach is carried out considering the fraction of MIT emission directed to sludge by STP defined in the simulation study for MIT (F_{stp} sludge = 6.6% of the total radioactivity). A **Tier II** approach**,** considering the STP half-life value of 0.04 days derived of the STP simulation study on MIT and in coherence with the MIT dossier, a fraction of MIT emission directed to sludge by the STP of 7.18E-04 was considered. 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.

To calculate the PECs in surface water, finally and according the WG II 2014, the dilution factors for freshwater recipients were 5, 10, 200 or 1000. According to the TGD and the WG II 2014, the dilution factors of 5 and 10 were used after municipal STP. The dilution factors of 5, 10, 200 or 1000 were used after industrial STP (typical case scenario) or in case of direct releases to surface water (realistic worst case).

Oil well slimicides

Concerning the sub-application "**slimicides in oil drilling processes**" (intended use for Dow Chemical only), marine water is the primary and the only relevant compartment of exposure. According to the applicant, Kathon™ WT is used at the dose rates of 1 to 5 ppm (i.e. 1 to 5 g $_{a.i.}.m^{-3}$) in the mud to reflect a continuous treatment and a continuous release. A shock dose of 15 ppm (i.e. 15 g $_{a.i.}.m^{-3}$) would only be employed when fouling is evident. Additionally, in the Dow Chemical dossier, the efficacy of the active substance has been demonstrated only for a shock treatment at a concentration of 30 ppm (i.e. 30 g $_{a.i.}.m^{-3}$) (contact time of 48 h minimum) in injection water lines and raw materials used in processing for enhanced oil recovery. Therefore, exposure and risk assessments have been carried out to reflect continuous application with concentrations of 1 g $_{a.i.}.m^{-3}$ and 5 g $_{a.i.}.m^{-3}$ and to reflect shock application with a concentration of 15 g $_{a.i.}.m^{-3}$.

2.2.2.8 Risk characterization for the environment

To carry out a quantitative assessment of a potential risk for the environment when Kathon™ WT is used as slimicide in paper production processes and in oil drilling processes, and when ACTICIDE® SPX is used as slimicide in paper production processes, the PEC values are compared to the respective PNEC values for the different compartments, resulting in the following PEC/PNEC ratios.

Paper Mill Slimicides

The Tables below summarized the PEC/PNEC ratios considering the different approaches for the two products, ACTICIDE® SPX and Kathon™ WT.

Table 2.2-41: Summary of PEC/PNEC values for ACTICIDE® SPX use for the relevant compartments – paper production processes

ACTICIDE® SPX	PEC_{MIT} / $PNEC_{MIT}$ ratio		
	2 $g.m^{-3}$	6 $g.m^{-3}$	9 $g.m^{-3}$
TIER I			
Realistic worst case scenario			
Surface water			
DILUTION 5	**18.95**	**56.92**	**85.38**
DILUTION 10	**9.49**	**28.46**	**42.56**

ACTICIDE® SPX	PEC_{MIT} / $PNEC_{MIT}$ ratio		
	2 g.m^{-3}	**6 g.m^{-3}**	**9 g.m^{-3}**
DILUTION 200	0.47	**1.42**	**2.13**
DILUTION 1000	0.09	0.28	0.43
Typical case scenario			
Sewage treatment plant	0.06	0.19	0.29
Surface water			
DILUTION 5	0.76	**2.29**	**3.44**
DILUTION 10	0.38	**1.15**	**1.72**
DILUTION 200	0.02	0.06	0.09
DILUTION 1000	0.004	0.01	0.02
Agricultural Soil	**2.00**	**6.02**	**9.02**
Groundwater	**> 0.1 µg/L**	**> 0.1 µg/L**	**> 0.1 µg/L**
TIER II			
Typical case scenario			
Agricultural Soil	0.02	0.07	0.10
Groundwater	< 0.1 µg/L	< 0.1 µg/L	< 0.1 µg/L

Table 2.2-42: Summary of PEC/PNEC values for Kathon™ WT use for the relevant compartments – paper production processes

Kathon™ WT	PEC_{MIT} / $PNEC_{MIT}$ ratio		
	1 g.m^{-3}	**5 g.m^{-3}**	**15 g.m^{-3}**
TIER I			
Realistic worst case scenario			
Surface water			
DILUTION 5	**9.49**	**47.44**	**142.05**
DILUTION 10	**4.74**	**24.15**	**71.03**
DILUTION 200	0.24	**1.18**	**3.56**
DILUTION 1000	0.05	0.24	0.71
Typical case scenario			
Sewage treatment plant	0.03	0.16	0.49
Surface water			
DILUTION 5	0.38	**1.91**	**5.74**

Kathon™ WT	PEC_{MIT} / $PNEC_{MIT}$ ratio		
	1 g.m^{-3}	**5 g.m^{-3}**	**15 g.m^{-3}**
DILUTION 10	0.19	0.96	**2.87**
DILUTION 200	0.01	0.05	0.14
DILUTION 1000	0.002	0.01	0.03
Agricultural Soil	**1.00**	**5.01**	**15.04**
Groundwater	**> 0.1 µg/L**	**> 0.1 µg/L**	**> 0.1 µg/L**
TIER II			
Typical case scenario			
Agricultural Soil	0.01	0.05	0.16
Groundwater	< 0.1 µg/L	< 0.1 µg/L	**> 0.1 µg/L**

Oil well slimicides

The Table below summarized the PEC/PNEC ratios product, Kathon™ WT used as slimicide in oil drilling process.

Table 2.2-43: PEC/PNEC values for Kathon™ WT use for the relevant compartments – oil drilling processes

Kathon™ WT	$PEC_{C(M)IT/MIT}$ / $PNEC_{C(M)IT/MIT}$ ratio		
	CHARM/EUSES		**MAMPEC MODEL**
	Continuous discharge	Batchwise discharge	Oil storage in gravity + Reservoir injection
	Dose of 1 g a.i.m^{-3}		
Marine water	0.01	NR	**105.10**
	Dose of 5 g a.i.m^{-3}		
	0.05	NR	**119.39**
	Dose of 15 g a.i.m^{-3}		
	0.01	**117.35**	NR

NR = not relevant

2.2.2.8.1 Aquatic compartment

Paper mill slimicides

Estimated risks from use of Kathon™ WT or ACTICIDE® SPX as slimicides in paper mill at the intended application rates (from 1 to 15 $g.m^{-3}$) are considered as acceptable for the freshwater aquatic organisms with a dilution factor value greater than the standard default value of 10, proposed in the TGD. Therefore, it must be ensured at the authorisation stage that the river dilution factor value is sufficient to consider the risk acceptable in taking account the information below:

- In the case of a paper production processes with no connection to a pulp mill, a settling phase and a mechanical/chemical treatment in the paper mill, the minimal river dilution must be:

DOSE RATE	MINIMAL RIVER DILUTION*
1 - 2 ppm	100
5 – 6 ppm	285
9 – 15 ppm	710

*Minimal river dilution values obtained by reverse calculation method

- In the case of a paper production processes with a connection to a pulp mill and where wastewaters after settling are discharged to an industrial STP, the minimal river dilution must be:

DOSE RATE	MINIMAL RIVER DILUTION*
1 - 6 ppm	12
9 – 15 ppm	30

*Minimal river dilution values obtained by reverse calculation method

Oil well slimicides

Estimated risks from use of Kathon™ WT as slimicides in oil drilling processes are considered as acceptable for the marine aquatic organisms for a continuous treatment and a continuous discharge at concentrations of 1 $g.m^{-3}$ and 5 $g.m^{-3}$. On the other hand, the risk is not deemed acceptable at the shock dose of 15 $g.m^{-3}$. At last, the risk is unacceptable whatever the dose for the additional scenario from emission for oil storage tanks and reservoir injection. Consequently for the concentration of 30 ppm total a.i. (in shock dose - contact time of 48 h minimum) validated by the efficacy data, the risk for marine water compartment is considered as unacceptable.

2.2.2.8.2 Sewage treatment plant

Paper mill slimicides

A risk assessment for the sewage treatment plant is relevant only for the typical case scenario, considering that paper mill release is directed to the STP.

Estimated risks from the use of Kathon™ 886F or ACTICIDE® SPX as slimicide in paper production processes connected to a STP are considered as acceptable at the intended application rates (from 1 to 15 $g.m^{-3}$) for the organisms involved in the biological processes of the sewage treatment works.

Oil well slimicides

Marine water is considered as the only relevant compartment of exposure for oil drilling processes. Therefore STP compartment is not relevant for this sub-application.

2.2.2.8.3 Atmosphere

Paper mill slimicides

The proposed use of C(M)IT/MIT biocidal products as slimicide in paper production processes is predicted to result in no or low concentrations in air. Any presence in air could only be via treatment in STPs. However, considering the STP simulation results based on C(M)IT, no emission of this compound in the different environmental compartments was foreseen (C(M)IT was considered to be totally degraded in the STP). Concerning the MIT substance (and in harmonization with MIT dossier) the calculated fractional loss to air in EUSES is effectively 0% (see MIT dossier). In this case the concentration in air will be negligible. Consequently further analysis and risk assessment is not warranted.

Oil well slimicides

Marine water is considered as the only relevant compartment of exposure for oil drilling processes. Therefore the atmosphere is not relevant for this sub-application.

2.2.2.8.4 Terrestrial compartment

Paper mill slimicides

A risk assessment for the terrestrial compartment is relevant only for the typical case scenario, considering that paper mill release is directed to the STP.

In Tier II approach, estimated risks from use of Kathon™ WT or ACTICIDE® SPX as slimicides in paper mill connected to a STP are considered as acceptable at concentrations of 1 $g.m^{-3}$ to 15 $g.m^{-3}$.

Oil well slimicides

Marine water is considered as the only relevant compartment of exposure for oil drilling processes. Therefore the terrestrial compartment is not relevant for this sub-application.

2.2.2.8.5 Groundwater

Paper mill slimicides

A risk assessment for groundwater is relevant only for the typical case scenario, considering that paper mill release is directed to the STP.

In Tier 2 approach, the concentration in porewater (surrogate for groundwater) is below 0.1 µg/L set up for directive 98/83/EC only for a use of Kathon™ 886F or ACTICIDE® SPX

as slimicides in paper mill connected to a STP at concentrations of 1 $g.m^{-3}$ to 9 $g.m^{-3}$. The risk for groundwater is still unacceptable at concentration of 15 $g.m^{-3}$.

Oil well slimicides

Marine water is considered as the only relevant compartment of exposure for oil drilling processes. Therefore the groundwater compartment is not relevant for this sub-application.

2.2.2.9 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 modelling 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

For Human health, since the product is sensitizing, the concentration in papermills and in oilfield injection systems should not exceed the value of 15 ppm ai., in order to avoid any effects.

SCENARIO		Human primary exposure		Human secondary exposure		STP	Aquatic compartment[1]	Terrestrial compartment	Groundwater	Air	Secondary poisoning
		Professional	Non professional	Worker	General public						
APPLICATION in papermills											
Continuous dose:	**Kathon WT** (Dow Chemical) **1 mg ai L^{-1}**	Not assessed	Not assessed	Not assessed	Not assessed	Acceptable	Acceptable[2]	Acceptable	Acceptable	NR	NR
	Acticide SPX (Thor GmbH) **2 mg ai L^{-1}**	Not assessed	Not assessed	Not assessed	Not assessed	Acceptable	Acceptable[2]	Acceptable	Acceptable	NR	NR
	Kathon WT (Dow Chemical) **5 mg ai L^{-1}**	Not assessed	Not assessed	Not assessed	Not assessed	Acceptable	Acceptable[2]	Acceptable	Acceptable	NR	NR
	Acticide SPX (Thor GmbH) **6 mg ai L^{-1}**	Not assessed	Not assessed	Not assessed	Not assessed	Acceptable	Acceptable[2]	Acceptable	Acceptable	NR	NR
	Acticide SPX (Thor GmbH) **9 mg ai L^{-1}**	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable[2]	Acceptable	Acceptable	NR	NR

SCENARIO		Human primary exposure		Human secondary exposure		STP	Aquatic compartment[1]	Terrestrial compartment	Groundwater	Air	Secondary poisoning
		Professional	Non professional	Worker	General public						
	Kathon WT (Dow Chemical) **< 15 mg ai L^{-1}**	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable	Acceptable[2]	Acceptable	**Not acceptable**	NR	NR
APPLICATION oilfield injection systems											
Continuous dose:	**Kathon WT** (Dow Chemical) **1 mg ai/L**	Not assessed	Not assessed	Not assessed	Not assessed	NR	**Not Acceptable**	NR	NR	NR	NR
	Kathon WT (Dow Chemical) **5 mg ai/L**	Not assessed	Not assessed	Not assessed	Not assessed	NR	**Not Acceptable**	NR	NR	NR	NR
Batchwise dose	**Kathon WT** (Dow Chemical) **< 15 mg ai/L**	Acceptable*	Acceptable	Acceptable	Acceptable	NR	**Not acceptable**	NR	NR	NR	NR
Overall conclusions:											

NR: Not relevant

[1] Freshwater for an application in paper mill and marine water for an application in oilfield injection system

[2] In the case of a paper production processes with no connection to a pulp mill, a settling phase and a mechanical/chemical treatment in the paper mill, the minimal river dilution must be: 1-2 ppm: DIL > 100; 6 ppm: DIL > 285; 9-15 ppm: DIL > 710 // In the case of a paper production processes with a connection to a pulp mill and where wastewaters after settling are discharged to an industrial STP, the minimal river dilution must be: 1-6 ppm: DIL > 12; 9-15 ppm: DIL > 30.

*: Considering the wear of PPE and use restricted to trained professionals

2.2.5 Data requirement for the representative product

- For off-shore installations, unacceptable risks were shown for the environment. Applicants for product authorization intending for such kind of use should therefore prove that risks can be reduced to an acceptable level.

- 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.

- The intended use "slimicide" has to be proved at product authorisation stage. Furthermore, field studies have to be submitted to demonstrate the efficacy of the product in real conditions with no unacceptable risks to the human health and the environment.

2.3 OVERALL CONCLUSIONS

The outcome of the assessment for C(M)IT/MIT in product-type 12 is specified in the BPC opinion following discussions at the 10th meeting of the Biocidal Products Committee (BPC). The BPC opinion is available from the ECHA website.

Appendix I: Listing of endpoints

Listing of end points to be included in the document Overall Summary and Assessment - Doc. I [18]

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.

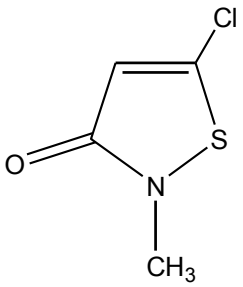
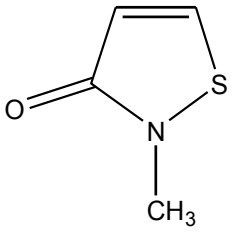
Chapter 1: Identity, Physical and Chemical Properties, Details of Uses, Further Information, and Proposed Classification and Labelling

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%

[18] Other end points will be relevant in particular cases - decisions as to the additional end points to be included can only be made on a case by case basis.

	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	C(M)IT: (T)

> 290 nm state ε at wavelength)

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 **<u>Thor :</u>** 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	<u>C(M)IT and MIT</u>: Not highly flammable (T) <u>C(M)IT/MIT (3:1)</u>: purified: not highly flammable (DOW) 14% in water: not flammable (DOW) 14% in water: not flammable (T)
Explosive properties	<u>C(M)IT and MIT</u>: do not have explosive properties (T) <u>C(M)IT/MIT (3:1)</u>: 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 (H335: 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.Cat 1A/H317: May cause an allergic skin reaction C ≥ 0.0015% This specific concentration limit is considered 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 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) No confirmatory submitted. No confirmatory method is needed due to the rapid degradation of C(M)IT and MIT in soil. T: No method submitted. No method is needed due to the rapid degradation of C(M)IT and MIT in soil
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. Must be provided.
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. Must be provided.

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	Following oral administration,	All the C(M)IT/MIT is

excretion:	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.	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 brackets)	2.36 mg/L (corr. to 0.33 mg a.i./L)	**1.23 mg/L (corr. to 0.171 mg a.i./L)**
Skin irritation (rabbit) C(M)IT/MIT 14% (and	Irritant	**Corrosive**

C(M)IT/MIT 100%)		
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, 2 years**	**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 NOEL = 157 mg/kg bw/d (corr. to 22 mg a.i./kg bw/ day) **Rat, 2 years (Letter of**

	-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.))**	**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/m³ (corr. to 0.34 mg a.i./m³ based on irritation to the respiratory tract)**	**Rat, 90 days (Letter of access)** **NOAEC = 2.4 mg/m³ (corr. to 0.34 mg a.i./m³ 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, point 6.6)	Genotoxic *in vitro* (Ames, mammalian cell gene mutation test) Not a genotoxic *in vivo* (*in vivo* unscheduled DNA synthesis, *in*	Genotoxic *in vitro* (Ames, mammalian chromosome aberration test, mammalian cell gene mutation test) Not a genotoxic *in vivo* (*in vivo*

	vivo chromosome aberration assay)	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	Rat, 2 years, oral drinking water **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 Mice, 30-months study **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	Rat, 2 years, oral drinking water (Letter of access) **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 mg/kg bw/d (corr. to 8 mg a.i./kg bw/day) based on no systemic effects = NOAEL developmental NOAEC maternal = 14 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 mg/kg bw/d (corr. to 8 mg a.i./kg bw/day) based on no systemic effects = NOAEL developmental NOAEC maternal = 14 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)

ADI (if residues in food or feed)	n.a		
AEL (Acceptable Exposure Level (C(M)IT/MIT 3:1)	NO(A)EL	Study	Safety factor
Acute, mid-term AEL= 0.22 mg ai/kg bw/d	22 mg ai/kg bw/d	90-day	100
Long-term AEL= 0,17 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
Acute AEC_{oral}			
Mid-term AEC_{oral}			
Long-term AEC_{oral}			
Dermal route:	Specific concentration limit for sensitising effect: 15 ppm		
Acute AEC_{dermal}			
Mid-term AEC_{dermal}			
Long-term AEC_{dermal}			
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 days at 30°C (66.7 days at 12°C)
	MIT, pH 5, 7, and 9 : stable	
	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	Tested as ACTICIDE® 14 CIT: elimination >96% MIT: elimination >80%

	22°C MIT, $DT_{50\ (dissipat\ on)}$ = 0.03-0.04 day at 22°C $DT_{50\ (mineralisation)}$ = 1.69 days at 22°C	Tested on MIT only MIT: $DT_{50\ (dissipat\ on)}$ = 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	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):

	12 °C DT_{50} = 8.7 for threshold and 20.0 for PEC calculation (10 µg/L) − 29.6 days (100 µg/L) at 9 °C	DT_{50} = 3.9 days at 15°C DT_{50} = 5.0 days at 12°C DT_{50} = 6.3 days at 9°C
	<u>Estuarine water</u> **<u>CMIT</u> DT_{50} = 5.82 days at 12°C** **<u>MIT</u> DT_{50} = 2.63 days at 12°C** **<u>C(M)IT/MIT</u>: DT_{50} = 5.82 days at 12°C (endpoint for the risk assessment)**	
	<u>Marine water</u> **<u>CMIT</u> DT_{50} = 41.7 days at 9 °C** **<u>MIT</u> DT_{50} = 29.7 days at 9 °C** **<u>C(M)IT/MIT</u>: DT_{50} = 41.7 days at 9 °C (endpoint for the risk assessment if necessary)**	
Distribution in water sediment systems	<u>CMIT</u>, 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 <u>MIT</u>, 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	<u>CIT</u>: 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 <u>MIT</u>: 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
	<u>Aerobic Freshwater/sediment</u> **<u>CMIT</u> DT_{50} whole system = 2.22 days at 12°C (geometric mean)** **<u>MIT</u> DT_{50} whole system = 2.21 days at 12°C (geometric mean)**	
Distribution in water sediment systems (metabolites)	<u>Aerobic, CMIT</u> Not relevant <u>Aerobic, MIT</u> <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%	<u>Aerobic, CMIT</u> 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).

	in the Cedar Hill water: sediment system, (3.3% at day 30).	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 days 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} = 0.27day 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, 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.	Not applicable (all compounds <10% of the applied activity)
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	MIT Ka_{oc} << 5.6

pH dependence (yes / no) (if yes type of dependence)	Ka_{oc} (sludge) = 54.1-152.7 Ka_{oc} (soil and sediment) = 6.4-10 Kd_{oc} (soil and sediment) not determined 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)	
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)	
	Acute-96 hr Flow through	(nominal concentration)	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. to0.71 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 35.3µg/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 3.82.1 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 = 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) LC_{50} inhalation : 2.36 mg./L air	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 a.i./kg bw)

	(rat) (eq. to 0.33 mg a.i./L) Skin irritation : Irritant (rabbit) Eye irritation : Corrosive (rabbit) Skin sensitization : Sensitising	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
	Not available

Acute toxicity to	

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	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)
		Red Clover :	9.29 mg /kg dry soil (eq. to 1.30 mg ai/kg)
		- Nominal :	
		EC_{50}, emergence	2.93 mg /kg dry soil (eq. to 0.41 mg ai/kg)
		EC_{50}, survival	9.11 mg /kg dry soil (eq. to 1.27 mg ai/kg)
		EC_{50}, shoot weight	2.73 mg /kg dry soil (eq. to 0.38 mg ai/kg)
		NOEC, emergence	0.82 mg /kg dry soil (eq. to 0.11 mg ai/kg)
		NOEC, survival	
		NOEC, shoot weight	
		- Twa:	
		EC_{50}, emergence	
		EC_{50}, survival	
		EC_{50}, shoot weight	
		NOEC, emergence	
		NOEC, survival	230.71 mg /kg dry soil (eq. to 32.3 mg ai/kg)
		NOEC, shoot weight	85 mg /kg dry soil (eq. to 11.9 mg ai/kg)
		Rice :	
		- Nominal :	48.36 mg /kg dry soil (eq. to 6.77 mg ai/kg)
		EC_{50}, emergence	64.3 mg /kg dry soil eq. to 9.0 mg ai/kg)
		EC_{50}, survival	19.3 mg /kg dry soil (eq. to 2.7 mg ai/kg)
		EC_{50}, shoot weight	19.3 mg /kg dry soil (eq. to 2.7 mg ai/kg)
		NOEC, emergence	
		NOEC, survival	
		NOEC, shoot weight	
		- Twa:	
		EC_{50}, emergence	9.80 mg /kg dry soil (eq. to 1.37 mg ai/kg)
		EC_{50}, survival	3.61 mg /kg dry soil (eq. to 0.51 mg ai/kg)
		EC_{50}, shoot weight	2.05 mg /kg dry soil (eq. to 0.29 mg ai/kg)
		NOEC, emergence	2.73 mg /kg dry soil eq. to 0.38 mg ai/kg)
		NOEC, survival	0.82 mg /kg dry soil (eq. to 0.11 mg ai/kg)
		NOEC, shoot weight	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 (Dow)

Object and/or situation	Member State or Country	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 ai/L min max	water L/m^2 min max	g as/m^2 min max	

Preservation of papermaking systems mineral oil extraction systems.	EU	C(M)IT/MIT containing biocidal products Kathon™WT	A wide variety of microorganisms (bacteria, algae in fungi), over a broad range of environmental conditions that occur within PT12 applications. In these systems, the most common organisms to be controlled are bacteria and fungi.	Kathon™WT: aqueous concentrate	14% (Kathon™ WT). This product may also be diluted to obtain 1.5% aqueous formulations.	Dose directly into manufactured product manually by pouring or by pumping using metered addition with adequate mixing.	The dosing frequency will depend on the turnover rate of the material being preserved, the degree of contamination and the extent of control desired. Repeat as needed to maintain control.	N/A	<u>Continous application</u> 1 - 15 ppm total a.i. <u>Shock dose</u> 30 ppm total a.i. (contact time 48 hours)	N/A	N/A	C(M)IT/MIT biocidal products are not typically diluted prior to use.

Summary of intended uses (Thor)

Object and/or situation (a)	Member State or Country	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 a.i/L min max	water L/m^2 min max	g as/m^2 min max
PT 12: Preservation of papermaking systems	F	ACTICIDE ®MV	Bacteria and fungi.	solution	1.5 % CIT/MIT	Automatic dosing device	Shock dosing up to 4 per day	Shock: 6 hours	Shock dosing 6 - 9 mg a.i./L	NA	NA

Appendix III: 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)[19]	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
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

[19] 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).

A3/04	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:	Eisensch mied, 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 Alexande r	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, Alexande r	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)[20]	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
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

[20] 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.

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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 2007. Non-GLP, Unpublished	Yes	Thor GmbH
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,	2007c	The solubility in water and	Yes	Thor

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	R., Verhaar, H.		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		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. 20071144.01, November 29, 2007 GLP, Unpublished	Yes	Thor GmbH
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	Yes	Thor GmbH

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			no. RS/01/023, 19-03-2002 GLP, Unpublished		
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-Flammability (solids) A.10, Siemens AG, Report No. 20071145.02, November 29, 2007 GLP, Unpublished	Yes	Thor 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

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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-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)*	Yes	Thor GmbH
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
A4.2(b)-02	Riemann, A./ anonymous		Translation from German to English of study A4.2-02: Quantitative determination of isothiazolinones (MIT and CIT) in room air and emission test chamber atmosphere using thermodesorption (2007) Non-GLP/ published	No	Thor GmbH
A5-01	Gillatt, J.	2007	ACTICIDE®14: Evaluation of	Yes	Thor

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			Microbiological Efficacy for Product Type 13 (Definition in Annex V of 98/8/EC), report no. 23163, 05-06-2007 Non-GLP/unpublished		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.
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

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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. Huntingdon Life Sciences Ltd., 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
A6.1.5-01	[redacted]	2000	Acute Skin Sensitization Study of Test Item Acticide 14 in Guinea Pigs by [redacted] Method TRC Ltd., 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,	Yes	Thor GmbH

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			Report No.: 1154/62-1007, GLP, Unpublished		
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. Fd. Chem.Toxic., Vol.24, 1, pp43-49 Published	No	-
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),		

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			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 Dog. [redacted], Study No.: 1154/57-1050 GLP, Unpublished	Yes	Thor GmbH
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	Yes	Thor

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			dose range-finding study in the rat + replaced pages [redacted], Study No.: 1127-1154-001 GLP, Unpublished		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
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	Yes	Thor

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			of Treated Mice. [redacted], Study No.: 1154/63, Report No.: 1154/63-1052, 13-03-97 GLP, Unpublished		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
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,	Yes	Thor GmbH (Rohm and

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	[redacted]		Study No.: 91R-074 (letter of access included) GLP, Unpublished		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)
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

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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
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

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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
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

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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
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

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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
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

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
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
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 T.R. [redacted] Inc. 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

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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
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

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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					
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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B 2.2-01 (confidential)	Anonymous	2007	Sales 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
B5-01	Schoester, M.	2003	ACTICDE 14 en ACTICIDE MV 14 Bergbauhygienische prüfung und Beurtelung gemäss der Bergverordnung zum gesundheitlichten Schutz der Beschäftigten. Hygiene-Institut des Ruhrgebiets. GLP not applicable, Unpublished	Yes	Thor GmbH
B5.3-02 (English)	Wensing, M.	2004	Measurment of 2-methyl-4-isothiazolin-3-one (MIT) emitted from water-based paints Fraunhofer, Braunsweig, Germany GLP not applicable, Unpublished	Yes	Thor GmbH
B5.3-02 (German)	Wensing, M.	2004	Untersuchung von 2-methyl-4-isothiazolin-3-one (MIT) als Emission von waserlöslichen Dispersionsfarben. Fraunhofer, Braunsweig, Germany GLP not applicable, 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 (PT12)	Grabbe R	2008g	ACTICIDE®MV: Examination of microbiological efficacy for Product Type 12, THOR Technical Service Report No. 27009, Report No. 27997/6, 31-07-2008, 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
B6.6-01 (confidential)	Hemmerling H	2007	Measurement of the concentration of airpollutants in the workplace within the framework of prevention based on SGB VII (German Social Security Code), BG Chemie 1140010072204, non-GLP, unpublished	Yes	Thor GmbH
B6.6-02 (confidential)	Hemmerling H	2007	Measurement of the concentration of airpollutants in the workplace within the framework of prevention based on SGB VII (German Social Security Code), BG Chemie 1140127062204, non-GLP, unpublished	Yes	Thor GmbH
B6.6-03 (confidential)	Hemmerling H	2007	Measurement of the concentration of airpollutants in the workplace within the framework of prevention based on SGB VII (German Social Security Code), BG Chemie 1140118072204, non-GLP, unpublished	Yes	Thor GmbH
B6.7-01 II-B	Rueb B	2001	Monitoring Study in a Paper Factory. Thor GmbH, Report no. 0013-BR-S, 09-03-2001 GLP not applicable / unpublished	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