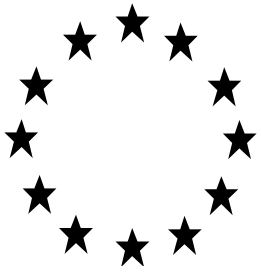
Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products

Evaluation of active substances

Assessment Report



C(M)IT/MIT

Product-type 2
(Biocide for use as disinfectants and algaecides not intended for direct application to humans or animals)

April 2015

France

Table of contents

1 STATEMENT OF SUBJECT MATTER AND PURPOSE 3
1.1 Principle of evaluation and procedure followed 3
1.2 Purpose of the assessment 4
2 OVERALL SUMMARY AND CONCLUSIONS 5
2.1 PresentAtion of the active substance 5
2.1.1 Identity, Physico-Chemical properties & Methods of Analysis 5
2.1.1.1 Active substance 5
2.1.1.2 Biocidal products 6
2.1.2 Intended uses and efficacy 6
2.1.2.1 Field of use / Function / Mode of action 6
2.1.2.2 Objects to be protected, Target organisms 6
2.1.2.3 Resistance 7
2.1.3 Classification and Labelling 7
2.1.3.1 Current classification 7
2.1.4 Proposed classification 8
2.2 Summary of the risk assessment 10
2.2.1 Human health Risk Assessment 10
2.2.1.1 Hazard identification 10
2.2.1.2 Effects assessment 10
2.2.1.3 Exposure assessment 15
2.2.1.4 Risk characterisation 24
2.2.2 Environment risk assessment 37
2.2.2.1 Fate and distribution in the environment 37
2.2.2.2 Effects assessement on environmental organisms (active substance) 39
2.2.2.3 Summary of PNEC values 41
2.2.2.4 Environmental effect assessment (product) 41
2.2.2.5 PBT Assessment and endocrine properties 41
2.2.2.6 Environmental exposure assessment 42
2.2.2.7 Risk characterisation 43
2.2.2.8 Non compartment specific effects relevant to the food chain (secondary poisoning) 45
2.2.3 Assessment of endocrine disruptor properties 45
2.2.4 Overall conclusions 46
2.2.5 Data requirement for the representative product 46
2.3 Overall conclusions 46
Appendix I: Listing of endpoints 47
Appendix II: List of intended uses 82
Appendix III: List of studies 83

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 2 (disinfectants and algaecides not intended for direct application to humans or animals), 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 2 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") in product-type 2.

C(M)IT/MIT was also notified as an existing active substance by another applicant, Thor, in other product-types. Data submitted by the applicant for PT 2 i.e. Dow, and data presented by Thor in other product types dossiers were collected to compile a single dossier on the hazard assessment of the active substance for all notified product types. Therefore, there will be references to the data submitted by Thor in this report, even if Thor is not a applicant for product type 2.

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 2 was the 31st of July 2007, in accordance with Article 9 paragraph 2 of Regulation (EC) N° 1451/2007.

On 12th of July 2007, 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 5th of February 2008.

[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.

On 19th of October 2011, 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 2, and should it be approved, to facilitate the authorisation of individual biocidal products in product-type 2 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 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 appendix to doc IIA for details of accepted sources and calculation.

The notified active substance is manufactured by two different companies: Thor and Dow. Only Dow is applicant for product type 2, here assessed in this dossier.

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

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

Validated methods for analysis of C(M)IT, MIT, additives and impurities in the active substance as manufactured have been provided. However some validation data are missing to fully validate the analytical methods: complete validation data for one impurity in one source and for another impurity in another source.

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

[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

due to the rapid degradation of C(M)IT and MIT in soil, the confirmatory method is not required.

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 full CAR, it is also referred to the active ingredient C(M)IT/MIT (a.i) 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: Kathon™ 886F

Dow' product contains between 12.21 and 15.78% w/w of C(M)IT/MIT (3:1) in water. Kathon™ 886F 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.

2.1.2 Intended uses and efficacy

2.1.2.1 Field of use / Function / Mode of action

2.1.2.1.1 Field of use

PT2: disinfectants and algaecides not intended for direct application to humans or animals.
C(M)IT/MIT biocide is claimed as an antimicrobial product for the preservation of air conditioning and air washing systems, and for chemical toilets.

2.1.2.1.2 Function

C(M)IT/MIT may function as a bacteristat and a fungistat.

2.1.2.1.3 Mode of action

C(M)IT/MIT biocide utilizes a two-step antimicrobial mechanism of action involving rapid binding (association) to cells and inhibition of growth and metabolism (within minutes), followed by irreversible cell damage resulting in loss of viability (hours). Growth inhibition is the result of rapid disruption of essential metabolic pathways of the cell by inhibition of specific (thiol-containing) deshydrogenase enzymes involved in the Krebs (tricarboxylic acid) cycle and electron transport (NADH).

2.1.2.2 Objects to be protected, Target organisms

Data presented for the use in chemical toilets have been considered as insufficient for the approval of the active substance. Indeed, static activities demonstrated are not sufficient for this use.

On the other hand, the efficacy of C(M)IT/MIT on *Legionella pneumophila*, demonstrated in a lab test, is acceptable for the use in air conditioning and air washing systems with the defined dose below :

Dose active substance C(M)IT/MIT : 1 mg/L with a contact time of 48H

2 to 5 mg/L with a contact time of 24H

It shall be noted that the shock dose of 15 mg/L in 30 min, claimed by the applicant, has not been demonstrated in this dossier.
Nevertheless, for the use in air conditioning and air washing systems, additional field data have to be submitted at product authorisation stage.

2.1.2.3 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.
Microbial resistance to C(M)IT/MIT has been described in the literature and should lead to special attention during the evaluation of product authorisation dossiers.

2.1.3 Classification and Labelling

2.1.3.1 Current classification

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

Directive 67/548/EEC	
Class of danger	T - Toxic C – Corrosive N - Dangerous for the environment
R phrases	R23/24/25: Toxic by inhalation, in contact with skin and if swallowed. R34: Causes burns. R43: May cause sensitization by skin contact. R50-53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S phrases	S2: Keep out of the reach of children. S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.
Specific concentration limit	C, R34: Causes burns C ≥ 0.6%

	Xi, R36/38: Irritating to eyes and skin 0.06% ≤ C < 0.6% Xi; R43: May cause sensitization by skin contact C ≥ 0.0015%
Regulation 1272/2008	
Hazard classes and categories / hazard statements	Acute Tox. 3/H331: Toxic if inhaled Acute Tox. 3/H311: Toxic in contact with skin Acute Tox. 3/H301: Toxic if swallowed Skin Corr. 1B/H314: Causes severe skin burns and eye damage Skin Sens. 1/H317: May cause an allergic skin reaction Aquatic Acute 1/H400: Very toxic to aquatic life Aquatic chronic/H410 Very toxic to aquatic life with long lasting effects.
Specific concentration limit	Skin Corr. 1B; H314: Causes severe skin burns and eye damage C ≥ 0.6% Eye Irrit. 2; H319: Causes serious eye irritation Skin Irrit. 2; H315: Causes skin irritation 0.06% ≤ C < 0.6% Skin Sens.Cat 1A/H317: May cause an allergic skin reaction C ≥ 0,0015%

2.1.4 Proposed classification

- Active substance (C(M)IT/MIT 14%) and active ingredient (C(M)IT/MIT 100%)

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 environment	T+: Very toxic C: Corrosive Xi: Irritant N: Dangerous for the environment
R phrases	R20/21/22: Harmful by inhalation, in contact with skin and if swallowed R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact	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

	R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	adverse effects in the aquatic environment.
S phrases	S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.	
Specific concentration limit	C, R34: Causes burns C ≥ 0.6% Xi, R36/38: Irritating to eyes and skin 0.06% ≤ C < 0.6% Xi; R43: May cause sensitization by skin contact C ≥ 0.0015% This specific concentration limit is considered relevant for this dossier.	
Regulation 1272/2008		
Hazard classes and categories	Acute Tox 4 for acute oral hazard Acute Tox 3 for acute dermal hazard Acute Tox 4 for inhalation hazard Skin Corr. 1B** Skin Sens. 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. 1A STOT SE 3 Aquatic acute 1 Aquatic Chronic 1
Hazard statements	H332: Harmful if inhaled H312: Harmful in contact with skin H302: Harmful if swallowed H 314: Causes severe skin burns and eye damage** H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=10	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

	H410: Very toxic to aquatic life with long lasting effects M-factor=10	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 inhalative routes. No 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-C(M)IT 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 C(M)IT 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 C(M)IT. 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 that M15 may have been formed in the intestine. All of the ten metabolites found in bile accounted for less than 5% of the dose.

- Excretion

MIT and C(M)IT are both rapidly excreted. Urine and faeces are equal major routes of excretion for C(M)IT whereas bile is a minor route of excretion (4.74%). On the contrary, MIT is largely excreted in urine and in a lesser extent in faeces, of which the major part came from the bile (29.09%).
No parent compound is present in excreta.

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 92.4 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 Dow and Thor result in a classification Xn; R20 'Harmful by inhalation' (corr. to T+; R26 'Very toxic by inhalation' for C(M)IT/MIT 100%) 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 (RD_{50}). C(M)IT/MIT should therefore be classified as Xi; R37-Irritating to respiratory system according to the directive 67/548/EC and STOT SE 3, H 335: May cause respiratory irritation according to the regulation 1272/2008/EC.

C(M)IT/MIT is a skin sensitizer according to a GPMT, a Buehler test, an open epicutaneous test and two LLNAs. A classification Xi; 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..

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

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 Dow, 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 Dow study shows some methodological limitations: the tested substance was not analytically checked in the dosing solutions for concentration or stability and there were 6 animals/sex/group rather than the recommanded 10/sex/group (OECD 411).
Therefore, considering the elements above, in the absence of any systemic effects, 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* genotoxicity studies 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 to be non mutagenic when tested in a bacterial gene mutation assay (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 as 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 in rat and 2860 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 development study in rabbits is also available (Dow). It did not reveal any 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

Kathon™ 886F Biocide is a biocidal product used for private area and public health area disinfection (PT2). This product is formulated into final end-use products ultimately utilized by professionals only. A summary of the major end-use PT2 applications and the relevant routes of potential exposure are shown in Table 2.2.1-1.

Table 2.2.1-1– Relevant Routes of Potential Exposure

	Exposure path	**Industrial use**	**Professional use**	**General public**
Air Conditioners/Washers	Inhalation	Yes	Yes	Yes
	Dermal	Yes	Yes	No
	Oral	No	No	No

C(M)IT/MIT does not induce directly systemic effects but local effects according to the available toxicological studies. Therefore, quantitative risk assessment was performed for both systemic effects and local effects (inhalation), comparing the estimated exposure with relevant reference values (AELs/AECs).

As the specific threshold for sensitisation is taken into account for risk assessment of local effects, PPE for dermal protection can only be taken into account on a qualitative basis.

PRIMARY EXPOSURE

- Professional application of biocidal products into air conditioning/air washer systems.

SECONDARY AND INDIRECT EXPOSURE

- Secondary exposure of the general public – air conditioners/washers.
- Secondary exposure of the professional workers – air washers.
- Indirect exposure to residues via environmental compartments (Consumers Indirect Exposure).

2.2.1.3.1 Primary exposure

Production/formulation of active substance and formulation of product

The applicant has assessed exposures of worker during these tasks but it is not required by the Regulation (EU) No 528/2012 on the placing of biocidal products on the market so these scenarios have not been integrated in the risk assessment.

Professional Users Exposure Scenarios – Air Washers

- Description of the application

C(M)IT/MIT is used as a preservative to control the growth of bacteria, algae and fungi in the sump water of air conditioning and air washer systems. This end-use application corresponds to the Biocidal Product Directive (BPD) Product Type 2 (Private area and public health area disinfectants), and more specifically to the sub-product type PT2.03 (Biocidal products to be used in air conditioning systems). The TNsG states for PT 2.03, "there is no information available on the use of products within this type". The guidance provided in the TNsG suggests that there is considerable overlap between PT 2.03 (Biocidal products to be used in air conditioning systems) and PT 11.02 (Preservatives used in recirculating systems). The background information for PT 11.02 in the TNsG indicates one of the uses within this category includes the treatment of evaporative condensers that are attached to air conditioning systems. Therefore, where appropriate, the guidance provided in the TNsG (2002) for PT 11.02 will be utilized to assess potential exposure scenarios.

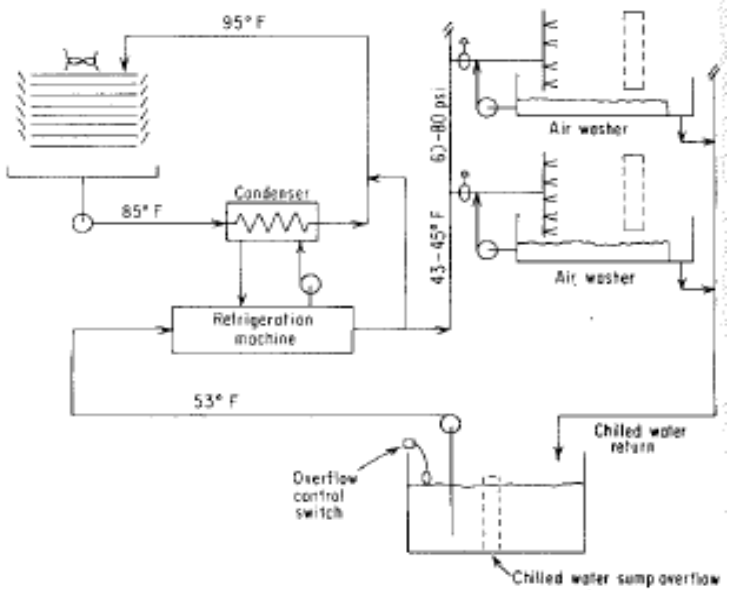
Air conditioning has been described as the process of treating air to control its temperature, humidity and cleanliness, and distributing this air to meet the needs of the conditioned space. Air conditioning systems utilizing water may be classified into three general categories: open recirculating cooling, air washers, and closed or open chilled water systems (Betz, 1980). The focus of this assessment will be **air washer systems** since this application is thought to represent the highest exposure potential.

The following description of the air washer system is based mainly on information from the Nalco Water Handbook (1998). Figure 2.2-1 and Figure 2.2-2 describe schematically a typical air washer system.
Air washers are used extensively in tobacco and textile facilities to clean and temper the air. Airborne material from the work environment is transferred to the water by the air washer requiring water treatment technology to maintain these systems. These systems consist of a number of components which typically includes the air washers, a chilled water

system, and a cooling tower. Depending on the plant design, there can be a single cooling tower circuit and a single chilled-water system, or several smaller systems, which provide water to air washers, process-heat exchangers and small office air-conditioning units. Air washers are by far the largest user of chilled water. The average textile plant with 1200 to 2400 tons of air conditioning capacity may have six to eight air washers. Refrigeration units operate in warm weather and supply chilled water (5 to 10°C) to air washer units. These chilled water systems typically have a high-level float switch on the chilled-water sump.

During summer months, the chilled water in the air washer dehumidifies the plant air causing the volume of water in the chilled water system to increase as water condenses from the makeup air. When the sump water reaches a certain level, it diverts excess chilled water (which is essentially condensate) to the cooling tower as makeup. In facilities where refrigeration is not required during the winter months, air washers operate independently, continually recirculating water from the sump through the spray nozzles. In winter months, evaporation occurs in air washer systems, eliminating overflow and requiring the addition of makeup water. During these months, air washers help provide humidified air to the work environment. In dusty manufacturing environments, such as in tobacco and textile facilities, air washers are used to remove particulates from the ambient air, and it should therefore be considered that the treated air is supplied throughout the entire year.

Figure 2.2-1: Typical textile air-washer system (from Nalco Water Handbook [3])



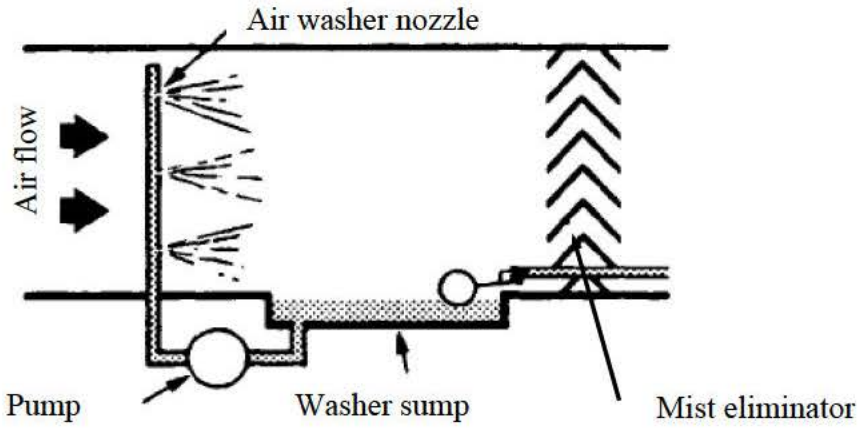


Figure 2.2-2: Schema of a air-washer (from Preventex, Volume 19, n°6, Dec.2002)

Most air washer systems automatically blend some outside air into the system. The mixture of work environment air and outside air enters the washing section of the air washer where vertically mounted spray nozzles are spaced evenly across the area of air flow. These nozzles are mounted on opposite sides so that incoming air must pass through a barrier of water droplets 2 to 3 feet thick removing airborne particles from the air. The spray nozzle headers are connected to a recirculating pump that has a capacity of 1 to 5 m^3/min. The main pump located at the chilled-water sump continually supplies each individual air-washer sump. Water returns to chilled-water sump by overflow and gravity. Each air-washer sump has a capacity of 2 to 10 m^3. The air then passes through mist eliminator blades to remove moisture and aerosol.
Some units are equipped with steam reheat coils to temper the cooled air to suit a particular textile process. Fans and blowers are used to distribute the "washed" air throughout the plant ductwork.

The high degree of recirculation in air washers leads to a variety of problems including slime formation, deposits, corrosion and odours. The deposits are mainly microbial slimes combined with dirt, corrosion products and crystalline matter. In order to control the fouling and deposition problems that occur, chilled water is treated with biocidal products, and air washers are periodically shut down and washed out. The intervals between successive shutdowns and washouts vary from one to 5-6 weeks, depending on the severity of the problems.

Water that is contaminated by process particulates is routinely filtered and recovered solids are disposed of as solid waste. The water is circulated continuously through the system. A portion is routinely released through a blowdown process to control the amount of dissolved salts that would otherwise build up. Waste water from air washing systems is released to site equilibration/remediation facilities (if available) prior to release to municipal sewer, then finally STP.

- Exposure scenarios

The TNsG (2002) identify for PT 2.03 (Biocidal products to be used in air conditioning systems) three basic worker exposure task scenarios including mixing/loading, application and post-application (including disposal). The mixing and loading phase involves changing

out the dip tube. The application phase involves dispensing the product to the sump. The post-application phase includes disposal to waste.
The TNsG (2002) identify for PT 11.02 (Preservatives used in recirculating systems) only the mixing/loading and post application as potential exposure scenarios. For this product type, mixing and loading involves manually dispensing a measure quantity into the sump or automated administration which includes changing out the dip tube. The post-application phase includes sampling process liquid (dip slide), system inspection and cleaning the dispensing pump for maintenance.
For the purpose of this exposure assessment, the mixing/loading and application phases have been combined for this product type, since the application phase includes dispensing (i.e., loading) the biocide into the sump. Therefore, two primary exposure task scenarios were identified for the use of biocidal products in air-washer systems:

- Mixing/Loading: Manual or automated administration of the biocidal product (containing C(M)IT/MIT) to the chilled water sump;
- Post-application (maintenance and disposal): Cleaning the dispensing pump, inspecting and monitoring the system, cleaning a fouled system and disposal of waste.

No data were available in the TNsG (2002) for the frequency and duration of administering biocide to air conditioning/air washer sumps for PT 2.03. However, the TNsG (2002) for product type 11.02 (Preservatives used in recirculation systems) provides guidance for these parameters and these data have been incorporated for air washer systems. The following task descriptors and associated parameters (i.e. frequency and duration) were obtained directly from Part 2 of the Technical Notes for Guidance (TNsG) on Human Exposure to Biocidal Products.

- PPE (personal protective equipments)

As the AEC for dermal local effect is expressed as ppm, exposure will be expressed in the same units; PPE will not reduce the exposure concentration but the occurrence of the event of exposure. So PPE for dermal protection against local effects can only be taken into account on a qualitative basis.
The active ingredient (C(M)IT/MIT) in Kathon™ 886F is irritating, corrosive and a potential skin sensitizer. For all mixing/loading and other tasks involving handling Kathon™ 886F and formulated biocidal products containing 1.5 to 5% active ingredient, the use of chemical resistant gloves, goggles and apron or coveralls is highly recommended by Material Safety Datasheets and labels of the products.

- Summary of exposure estimates

Table 2.2.1-2: Exposure estimates for water treatment service worker using biocidal products in air-washer systems

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 886F in chilled-water systems (water treatment service worker) - daily**				
Tier 1 : Without PPE	1.44×10^{-3}	2.40×10^{-4}	140000	7.96×10^{-1}	7.96×10^{-1}
Tier 2 : With gloves and impermeable coveralls	1.44×10^{-3}	2.40×10^{-4}	140000	7.18×10^{-2}	7.18×10^{-2}
Task – time frame :	**Cleaning Kathon 886F dispensing pumps (water treatment service worker) – daily**				
Tier 1 : Without PPE	negligible	negligible	140000	2.57	2.57
Tier 2 : With gloves and impermeable coveralls	negligible	negligible	140000	2.12×10^{-1}	2.12×10^{-1}
Tier 2 + rinse: With gloves and impermeable coveralls	negligible	negligible	1400	1.06×10^{-3}	1.06×10^{-3}
Task – time frame :	**Cleaning air-washer systems (water treatment service worker) – daily**				
Tier 1 : Without PPE	negligible	negligible	15	2.48×10^{-3}	2.48×10^{-3}

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 2 : With gloves and impermeable coveralls	negligible	negligible	15	2.04×10^{-4}	2.04×10^{-4}
Task – time frame :	**System monitoring and waste disposal (water treatment service worker) - daily**				
Covered by above scenarios.					
Task – time frame :	**Combined = loading + cleaning pumps (water treatment service worker) - daily**				
Tier 1 : Without PPE	1.44×10^{-3}	2.40×10^{-4}	Not relevant	3.37	3.37
Tier 2 : With gloves and impermeable coveralls	1.44×10^{-3}	2.40×10^{-4}	Not relevant	2.84×10^{-1}	2.84×10^{-1}
Tier 2 + rinse: With gloves and impermeable coveralls	1.44×10^{-3}	2.40×10^{-4}	Not relevant	7.31×10^{-2}	7.33×10^{-2}

Assumptions:

Biocidal product concentration: C(M)IT/MIT 14%

Concentration in chilled water: 15 ppm a.i

Task duration and frequency (maximum for a water treatment service worker) : 4 facilities visited per day, with up to 3 loadings (2 minutes) and 1 pump cleaning (5 minutes) per facility.

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

Dermal absorption: concentration > 0.6%: 100 %; diluted solutions (< 0.6%): 50%

2.2.1.3.2 Secondary exposure

- **Secondary exposure to General Public from Air Washers/Conditioners**

Biocidal products used in air washers are recommended and sold for professional use only, and air washers are not used in non-industrial applications. Therefore, general public is unlikely to be exposed to treated air from air washers.

Exposure to the general public from large air conditioning systems used for shopping centers, cinemas, hospitals, apartment buildings, etc. is not anticipated. Commercial air conditioning systems are typically internally closed systems and the circulating water is sent to outdoor cooling towers to dissipate heat. This cooled water is returned to the closed system where it is condensed and further chilled, and circulated through the closed system. Since the treated water does not come in contact with the air that is being conditioned, secondary inhalation exposure to the general public is not anticipated.

- **Secondary Exposure to Workers from Air Washers – Inhalation (chronic)**

Exposure to humidified or washed air containing residual biocide represents a potential secondary inhalation exposure scenario for workers, e.g. in textile factories.

Nevertheless, this exposure is thought to be negligible as air washer systems are designed to remove water aerosols from washed air (by mist eliminators) and C(M)IT/MIT concentration in aerosol is low.

Vapour phase

Indeed, regarding the extremely high solubility of C(M)IT/MIT (>3000 g/l[6]), the low vapour pressure of pure constituents (3.9 Pa at 25°C) and the very low concentration in water (up to 5 ppm (i.e. mg/L) in usual conditions), the volatility of C(M)IT/MIT is extremely low. In other words, the quantity of substance that can transfer from water to air is extremely low.

A worst case scenario has been developed extrapolating the air concentration of active substance from the concentration in water and the Henry's law constant ($<10^{-4}$ Pa.m^3.mol^{-1}).

Aerosol phases

There is no model for assessing exposure to the aerosol part of the air washing system. As a worst case approach, the exposure to the aerosol of such systems is supposed to be lower than the application of liquid by spraying. The worst case value of the different spraying model of the TNsG 2002 has been chosen for the tier 1 assessment. The worst case value, 405 mg product /m^3, is from the spraying model 1 page 145 considering spraying with a compression sprayer at 1 to 3 bars.

- **Summary of secondary exposures following use of C(M)IT/MIT containing products in PT2 intended uses.**

The secondary exposures following use of C(M)IT/MIT containing products in PT2 intended uses (in air washing/conditioning systems) are summarised in following Table 2.2.1-3.

[6] See Document IIA, section 1.3.

Table 2.2.1-3: Secondary exposure following use of C(M)IT/MIT in air-washer/conditioner systems

Inhalation exposure		Dermal exposure		Total exposure
External concentration	Systemic dose	Deposit on skin	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
Inhaling residues of C(M)IT/MIT in washed air (workers in factories) - daily				
Considering that aerosols are removed by mist eliminators and the very low potential of volatilisation of CMIT/MIT, residues in washed air is assumed to be negligible. A very worst-case estimation resulted in following exposure :				
6.28×10^{-3}	1.05×10^{-3}	negligible	negligible	1.05×10^{-3}
Inhaling residues of C(M)IT/MIT in conditioned air (general public) - daily				
Considering that air conditioners in public areas are internally closed systems (i.e. without contact between chilled water and air), there is no potential exposure to general public following such use.				

Assumptions: Concentration in chilled water: maximum 15 ppm
Task duration and frequency: 8 hours for workers

2.2.1.4 Risk characterisation

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

Table 2.2.1.4-1: 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 corrected with the oral absorption factor and 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. This value is used as reference margin of exposure (MOE_{ref}).

The following AELs were therefore derived:
- Acute/medium-term AEL= (22/100) x 50% = 0.11 mg ai/kg bw/d
- Long-term AEL= (17.2/100) x 50% = 0.09 mg ai/kg bw/d

In the AEL approach, a risk is considered 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 $\leq$ MOE_{ref}, the risk is not considered as acceptable,
- If the MOE > MOE_{ref}, the risk is considered as acceptable.

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

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

AEC = NOAEC / assessment factors

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

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

Table 2.2.1.4-2: Critical endpoints for the determination of the AEC

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 a.i./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 (MOEref).

The following AECs were therefore derived for inhalation route:

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

Derivation of the 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 the 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.

Risk characterisation for primary exposure scenarios

For each scenario, the risk characterisation is considered for both systemic effects and local effects (inhalation).

- ***Quantitative risk assessment for systemic effects***

For the systemic exposure, the MOE and %AEL are presented in the table below:

Table 2.2.1.4-3: MOE and %AEL calculated for systemic exposure

	Total exposure (mg a.i/kg bw/f)	Relevant NOAEL* (mg a.i./kg bw/d)	MOE_{ref} (sum of AFs)	MOE	AEL (mg a.i./kg bw/d)	%AEL
Task– time frame :	**Loading Kathon 886F in chilled-water systems (water treatment service worker) - daily**					
Tier 1 : Without PPE	7.96×10^{-1}	8.6	100	**10.8**	0.09	**885**
Tier 2: With gloves and impermeable coveralls	7.18×10^{-2}	8.6	100	119.8	0.09	80
Task – time frame:	**Cleaning Kathon 886F dispensing pumps (water treatment service worker) – daily**					
Tier 1: Without PPE	2.57	8.6	100	**3.3**	0.09	**2852**
Tier 2: With gloves and impermeable coveralls	2.12×10^{-1}	8.6	100	**40.6**	0.09	**235**
Tier 2 + rinse: With gloves and impermeable coveralls	1.06×10^{-3}	8.6	100	8113	0.09	1.2
Task – time frame:	**Cleaning air-washer systems (water treatment service worker) – daily**					
Tier 1: Without PPE	2.48×10^{-3}	8.6	100	3467	0.09	3
Task – time frame:	**System monitoring and waste disposal (water treatment service worker) - daily**					
Covered by above scenarios.						
Task – time frame :	**Combined = loading + cleaning pumps (water treatment service worker) - daily**					
Tier 1 : Without PPE	3.37	8.6	100	**2.55**	0.09	**3739**
Tier 2: With gloves and impermeable coveralls	2.84×10^{-1}	8.6	100	**30.3**	0.09	**316**
Tier 2 + rinse: With gloves and impermeable coveralls	7.33×10^{-2}	8.6	100	117.3	0.09	81

* NOAEL corrected by the oral absorption factor of 50%

Except the cleaning phase of the air washer-system, where no PPE are needed, all other primary exposure scenarios require that PPE are worn for being considered as safe (MOE > MOE_{ref} and %AEL>100%). Moreover, the combined scenario even requires a rinse before cleaning in addition to the PPE.

- ***Quantitative risk assessment for local effects***

For the exposure by inhalation, the MOE and %AEC are presented in the table below:

Table 2.2.1.4-4: MOE and %AEC calculated for exposure by inhalation

	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 886F in chilled-water systems (water treatment service worker) - daily**					
Tier 1 : Without PPE	1.44×10^{-3}	0.34	16	236	0.02	7.2
Task– time frame :	**Cleaning pumps**					
Tier 1 : Without PPE	Negligible	0.34	16	∞	0.02	Negligible
Task – time frame :	**Combined = loading + cleaning pumps (water treatment service worker) - daily**					
Tier 1 : Without PPE	1.44×10^{-3}	0.34	16	236	0.02	7.2

Whatever the scenario considered, the MOE is higher than MOE_{ref} and the %AEC is lower than 100%. This means that no unacceptable risk can be identified for workers primarily exposed by inhalation to C(M)IT/MIT.

- **<u>Qualitative risk assessment for local effects</u>**

<u>Dermal exposure</u>

Table 2.2.1.4-5: 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 Kathon 886F in chilled-water systems (water treatment service worker) - daily**	
Tier 1 : Without PPE	140 000	15
Tier 2 : With PPE	140 000	15
Task – time frame :	**Cleaning Kathon 886F dispensing pumps (water treatment service worker) - daily**	
Tier 1 : Without PPE	140 000	15
Tier 2 : With rinse Without PPE	1400	15
Tier 2 : With rinse and refined assessment factors Without PPE	1400	15
Task – time frame :	**Cleaning air-washer systems (water treatment service worker) - daily**	
Tier 1 : Without PPE	15	15

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 above the concentration that would lead to sensitisation (15 ppm a.i.).

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

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 of C(M)IT/MIT is therefore still possible, provided such risk mitigation measures are implemented.

Risk characterisation for secondary exposure scenarios

The secondary exposure to C(M)IT/MIT is limited to the inhalation of washed air, which is considered as very unlikely because of the removal of water aerosols by mist eliminators and the very low volatility of C(M)IT/MIT from water.

Risk characterisation considering systemic effects

When quantified on the basis of the Henry's law constant (< 10^{-4} Pa.m^3.mol^{-1}), the exposure dose-level of C(M)IT/MIT should not exceed 1.05 x 10^{-3} mg ai/kg bw/d.

Table 2.2.1.4-6: MOE and %AEL calculated for secondary exposure considering systemic effects

Scenarios	Exposure concentration (mg ai/kg bw/d)	NOAEL (mg ai/kg bw/d)	MOE	MOE_{ref}	AEL (mg ai/kg bw/d)	%AEL
Workers breathing washed air	1.05 x 10^{-3}	8.6	8190	100	0.09	1.17

Risk characterisation considering local effects

When quantified on the basis of the Henry's law constant (< 10^{-4} Pa.m^3.mol^{-1}), the exposure concentration of C(M)IT/MIT should not exceed 6.28 x 10^{-3} mg/m^3.

Table 2.2.1.4-7: MOE and %AEC calculated for secondary exposure considering local effects

Scenarios	Exposure concentration (mg a.i./m^3)	NOAEC (mg a.i./m^3)	MOE	MOE_{ref}	$AEC_{inhalation}$ (mg a.i./m^3)	%AEC
Workers breathing washed air	< 6.28 x 10^{-3}	0.34	>54.2	16	0.02	< 31.4

This worst case of workers chronically exposed to washed air clearly shows that there is no unacceptable risk related to a secondary exposure, when considering systemic or local effects.

It has to be noted that this assessment is a very worst case situation as air washer are equipped by mist eliminators that have not been taken into account in these calculations.

Risk characterisation for combined exposure

As far as a water treatment professional who is directly exposed to C(M)IT/MIT while at work (mixing/loading and post application in air-washer systems) is not supposed to be secondarily exposed *via* air treated by an air washer. No combined exposure to C(M)IT/MIT was considered.

Overall conclusion of the risk characterisation for human health

No unacceptable risks related to possible systemic effects were identified whatever the scenario considered.

Unacceptable risks of local effects were identified following dermal exposure to Kathon™ 886F, corresponding to a solution of C(M)IT/MIT (3:1) at 14% in water, during the loading of the products in air-washer systems and the cleaning of dispensing pumps. The exposure during loading phase was estimated conservatively using a model for manual loading. If appropriate PPE is used while handling biocidal products during formulation, mixing/loading, and post application, the exposure concentration is not reduced but only the probability of occurrence. However, the exposure to concentrated products should be prevented.

Therefore, as the product is classified and labelled as corrosive and sensitising, it should 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 specialised operators, it may be assumed that dermal exposure would occur only in accidental circumstances.

Therefore, the RMS considers that Kathon™ 886F can be used in air-washer systems provided that appropriate risk mitigation measures are applied during the loading of the products and the cleaning of the dispensing pumps. Possible measures (not exhaustive list) are:

- The containers of the products are designed to prevent spillages during pouring,
- Automated systems preventing contacts with the product are used,
- 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. These RMMs are summarized in the tables below.
Other dermal exposure scenarios (cleaning, monitoring and waste disposal) are in contrast considered as safe since the operator will be exposed to a diluted solution (maximum 15 ppm).
Unlike dermal exposure, no unacceptable risk was identified for the respiratory tract, whatever the scenario considered. This applies for both primary and secondary exposure scenarios where exposures are lower than $AEC_{inhalation}$.

Table 2.2.1.4-8: Primary exposure – Use of the concentrated product (Mixing and loading phase)

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 Kathon 886F in chilled-water systems (water treatment service worker)										
High	Skin Corr 1B (H314), Skin Sens 1A (H317)	-	2	Industrial and professional users	Manual loading of the biocidal product (14% a.s.) to the chilled water sump	Skin	daily	<u>Manual loading:</u> Small exposure to spills <u>Semi automated and fully automated loading systems:</u> Accidental exposure to spills during connection of container to the pumping system	**Organizational RMM** • Restriction of manual loading to only small quantities. High quantities should be restricted to semi-automated or automated processes. **Personal protective equipment** • 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)	Acceptable: + Minimization of manual phases; + Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.

									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).	

Table 2.2.1.4-9: Primary exposure – Use of the concentrated and the diluted product (cleaning phase)

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**
Cleaning Kathon 886F dispensing pumps (water treatment service worker) – Use concentrated product										
High	Skin Corr 1B (H314), Skin Sens 1A	-	2	Industrial and professional users	Cleaning the dispensing pump containing product (14% a.s.)	Skin	daily	Direct contact with residues in pump	**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,	Acceptable: + Professionals adding a rinse step of the device with water before cleaning;

	(H317)								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) **General safety and hygiene measures** Do not inhale gases/vapours/aerosols. Avoid contact with the skin, eyes and clothing. Handle in accordance with good industrial hygiene and safety practice. Wearing of closed work clothing is recommended. When using, do not eat, drink or smoke. Hands and/or face should be washed before breaks and at the end of the shift. At the end of the shift the skin should be cleaned and skin-care agents applied. Gloves must be inspected regularly and prior to each use. Replace if necessary (*e.g.*, pinhole leaks).	+ Professionals using PPE; + Professionals following instructions for use; + Good standard of personal hygiene.
Cleaning air-washer systems (water treatment service worker) – Use diluted product										
High	Skin Sens 1A	-	2	Industrial and professional	Cleaning the air washer system	Skin	daily	Direct contact with	**Organisational RMM** • Rinsing of the system before opening and cleaning.	+ Professionals using PPE;

	(H317)			users	containing diluted product (end – use concentration 15 ppm)			residues in system	**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. • 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).	+ Professionals following instructions for use; + Good standard of personal hygiene.

2.2.2 Environment risk assessment

2.2.2.1 Fate and distribution in the environment

2.2.2.1.1 Hydrolysis as a function of pH

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

2.2.2.1.2 Photolysis in water

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

2.2.2.1.3 Photolysis in air

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

2.2.2.1.4 Biodegradation

In the Dow Chemical dossier, the 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), 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 assessement on environmental organisms (active substance)

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

2.2.2.2.1 Aquatic compartment (including water, sediment and STP)

Aquatic organisms

Available valid aquatic ecotoxicological data provided by the two applicants (Dow Chemical and Thor) have been used to derive the PNEC for the aquatic (freshwater) compartment. Additionally, as the species sensitivity between freshwater and marine fish and algae is within a factor of 10, data from fresh and marine water have been pooled to derive the PNEC for the aquatic (freshwater) compartment.
The most sensitive endpoint validated 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 **$PNEC_{fresh\ surface\ water}$** 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 $PNEC_{marine\ water}$ is therefore estimated to be 0.0098 µg a.i./L.**

For **MIT**, the $PNEC_{fresh\ surface\ water}$ 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 $PNEC_{microorganisms}$ is derived from the respiration inhibition test according to OECD guideline 209. The NOEC obtained (0.91 mg a.i./L) divided by an assessment factor of 10 leads to a **$PNEC_{microorganisms}$** of **0.091 mg a.i./L.** Whereas the lowest EC50 (4.5 mg a.i./L) divided by an assessment factor of 100 leads to a lower **$PNEC_{microorganisms}$** 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 $PNEC_{microorganisms}$ for MIT is considered (issued from MIT dossier) to be **$PNEC_{microorganisms}$ = 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 **$PNEC_{sediment}$** of 0.027 mg a.i./$kg_{dry\ sediment}$ corresponding to **0.0058 mg a.i./$kg_{wet\ sediment}$**.

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.

2.2.2.2.3 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 **$PNEC_{soil}$** of 0.01 mg a.i./$kg_{drysoil}$ corresponding to **0.009 mg a.i./$kg_{wet\ soil}$**.
As stated at the 32nd Competent Authority meeting, as degradation half-life is < 2 days, for the risk assessment the initial PNEC is compared to the initial PEC calculated without taking into account any degradation. Nevertheless, for intended uses leading to continuous release to the soil, PNEC twa has been calculated to be 0.0004 mg a.i./$kg_{wet\ soil}$ taking into account of a half life in soil of 0.78 d at 20°C.
For release through the spreading of STP sludge, the initial $PNEC_{soil}$ for MIT is considered to be **PNEC soil = 0.0417 mg/$kg_{wet\ soil}$** from EC_{50} of 18 mg/$kg_{dry\ soil}$ issued from a plant tests and an assessment factor of 1000 (issued from MIT dossier).

2.2.2.3 Summary of PNEC values

Table 2.2.2-1: Summary of the selected PNEC values used for the risk characterisation part

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

2.2.2.4 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.

2.2.2.5 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.

2.2.2.5.1 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 > 40 days 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 water/sediment are less than 6 days at 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.

2.2.2.5.2 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.

2.2.2.5.3 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.

2.2.2.6 Environmental exposure assessment

The risk characterisation has been carried out for the representative product: Kathon™ WT (Dow Chemical). 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.

Manufacture and formulation of the active substance is currently carried out both within the EU and outside the EU. According to the applicant, in most EU countries, chemical manufacturing installations are subject to planning and environmental laws and regulations and process operators are required to operate them in accordance with the conditions of the approval. The implementation EC Directive 96/61/EC, the Integrated Pollution Prevention and Control Directive (IPPC) means that operators are strictly regulated on permitted emissions, and manufacturing processes are typically "zero-loss" systems. Thus for the manufacture of C(M)IT/MIT and the initial formulation phase of Kathon™ 886F Biocide zero loss emissions are assumed.

The intended use for Kathon™ 886F is application in air conditioning and air washing systems to preserve the sump water and control the growth of bacteria, algae and fungi. The "use stage" of the formulated product is therefore considered as the time the biocide containing solution is used within air conditioning system. An ESD[7] for disinfection of air conditioning systems, corresponding to the existing scenarios for PT11 with small

[7] Supplement to the Emission Scenario Document for Product Type 2: Private and public health area disinfectants and other biocidal products, January 2009, SCC for UBA.

amendments, was adopted as a basis for the exposure analysis. The open re-circulating cooling system was chosen for the model calculations since its dimensions and operating conditions are most comparable for the application here. It was proposed to calculate the emission of dosing in the open recirculating cooling system with a continuous dosing to maintenance levels of 1 to 5 ppm C(M)IT/MIT in the sump water.

Some of the solution in the air conditioner/air washer system is discharged, via blowdown, and directed to STP. These processes are considered as the "disposal phase" for C(M)IT/MIT. Discharge to STP is the only route of disposal. Secondary compartments considered for the risk assessment were surface water, soil and groundwater.

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

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

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

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

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

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

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

2.2.2.7 Risk characterisation

To allow for a quantitative risk assessment for the environment when Kathon™ 886F is used as a preservative to control the growth of bacteria, algae and fungi in the sump water of air conditioning and air washer systems (PT02.03), the PEC values are compared to the respective PNEC values for the different compartments, resulting in the following PEC/PNEC ratios. When releases occur through the STP, the $PEC_{MIT}/PNEC_{/MIT}$ ratios have been considered.

Table 2.2.2-2: PEC/PNEC ratios for Kathon™ 886F use for air conditioning / air washing systems

PEC_{MIT} / $PNEC_{MIT}$	Continuous dose	
	5 ppm	**1 ppm**
TIER I		
Sewage treatment plant	1.59E-02	3.18E-03
Surface water	9.38E-02	1.88E-02
Sediment	NR	NR
Agricultural Soil	1.97E-01	3.93E-02
Groundwater	**> 0.1 µg L^{-1}**	< 0.1 µg L^{-1}
Air	NR	NR
TIER II		
Agricultural Soil	2.14E-03	4.27E-04
Groundwater	< 0.1 µg L^{-1}	< 0.1 µg L^{-1}

NR: not relevant

2.2.2.7.1 Aquatic compartment

Estimated risks from use of Kathon™ 886F in air conditioning and air washer systems are considered as acceptable whatever the dose.
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, risk assessment for sediment is considered as not relevant.

2.2.2.7.2 Sewage treatment plant organisms

No risks are expected for sewage treatment plant organisms.

2.2.2.7.3 Atmosphere

No risks are expected due to extremely low volatility of C(M)IT/MIT.

2.2.2.7.4 Terrestrial compartment

In Tier I and Tier II approaches and considering the agricultural soil, the risk are deemed acceptable for a use of Kathon™ 886F in air conditioning and air washer systems at the dose rates of 5 ppm or 1 ppm (continuous dosing to maintenance level).

2.2.2.7.5 Groundwater

For groundwater, the concentrations of MIT expected after sludge applications onto agricultural soil are below the trigger value of 0.1 µg/L set for pesticides in drinking water in Tier II approach and whatever the dose. The risk for groundwater is therefore considered as acceptable at the dose rates of 5 ppm or 1 ppm (continuous dosing to maintenance level).

2.2.2.8 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 potential 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 CMIT 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 as air conditioning/air washing systems preservative 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

SCENARIO		Human primary exposure		Human secondary exposure		STP	Aquatic compartment	Terrestrial compartment	Groundwater	Air	Secondary poisoning
		Professional	Non professional	Worker	General public						
PROFESSIONAL APPLICATION in air conditioning system and air washer system											
Continuous dose	**5 mg ai L^{-1}**	Acceptable*	NR	Acceptable	NR	Acceptable	Acceptable	Acceptable	Acceptable	NR	NR
	1 mg ai L^{-1}	Acceptable*	NR	Acceptable	NR	Acceptable	Acceptable	Acceptable	Acceptable	NR	NR
Overall conclusions: An acceptable risk has been considered for trained professionals wearing appropriate PPE whatever the conditions of use (shock dose and continuous dose).											

NR: Not relevant

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

2.2.5 Data requirement for the representative product

- Concerning the efficacy, only an efficacy against *Legionella pneumophila* in a lab test has been performed for the preservation of air conditioning and air washing systems. At product authorisation stage, tests showing an efficacy against *L. pneumophila* performed under realistic in use conditions have to be provided. Generally, if a microbiocide activity is claimed (as for chemical toilets) at the product authorisation stage, then it should be entirely proved in the use conditions, in accordance with the requirements of PT2 efficacy guidance.

2.3 OVERALL CONCLUSIONS

The outcome of the assessment for C(M)IT/MIT in product-type 2 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 [8]

Note: The owner of data is marked before or after endpoints where relevant: T = THOR, DOW (previously Rohm & Haas). However, please note that for PT2, only Dow is considered as applicant.
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

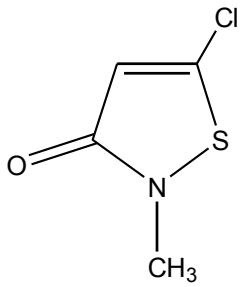
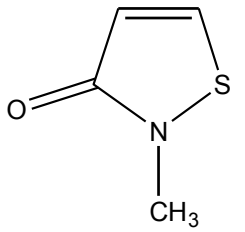
Active substance (ISO Common Name)	No ISO name accepted or proposed. The active ingredient common name used is: C(M)IT/MIT (3:1)
Function (*e.g.* fungicide)	Broad spectrum preservative biocide. Bactericide and fungicide.

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%

[8] 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 chloride and magnesium nitrate
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)	<u>C(M)IT</u>: melting onset at 51.3°C, with a peak at 54.9°C (purity = 99.86%) (DOW) 46.6-48.9°C (purified) (T) <u>MIT:</u>

	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. 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. 1A STOT SE 3 Aquatic acute 1 Aquatic Chronic 1
Hazard statements	H332: Harmful if inhaled H312: Harmful in contact with skin H302: Harmful if swallowed H 314: Causes severe skin burns and eye damage H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=10 H410 very toxic to aquatic life M-factor = 10	H 330: Fatal if inhaled H 310: Fatal in contact with skin H 301: Toxic if swallowed H 314: Causes severe skin burns and eye damage H 317: May cause an allergic skin reaction (H 335: May cause respiratory irritation) H400: Very toxic to aquatic life M-factor=100 H410 very toxic to aquatic life M-factor=100
Specific concentration limit	Skin Corr. 1B; H314: Causes severe skin burns and eye damage C ≥ 0.6%** Eye Irrit. 2; H319: Causes serious eye irritation Skin Irrit. 2; H315: Causes skin irritation 0.06% ≤ C < 0.6% Skin Sens. 1, H 317 : May cause sensitization by skin contact 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 for the environment
R phrases	R20/21/22: Harmful by inhalation, in contact with skin and if swallowed R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.	R26/24/25: Very toxic by inhalation, toxic in contact with skin and if swallowed. R34: Causes burns. (R37 : Irritating to the respiratory tract) R43: May cause sensitization by skin contact. R50/53: Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
S phrases	S26: In case of contact with eyes, rinse immediately with plenty of water and seek medical advice. S28: After contact with skin, wash immediately with plenty of water S36/37/39: Wear suitable protective clothing, gloves and eye/face protection. S45: In case of accident or if you feel unwell, seek medical advice immediately (show the label where possible). S60: This material and its container must be disposed of as hazardous waste. S61: Avoid release to the environment. Refer to special instructions/Safety data sheets.	
Specific concentration limit	C, R34: Causes burns C ≥ 0.6% Xi, R36/38: Irritating to eyes and skin 0.06% ≤ C < 0.6% Xi; R43: May cause sensitization by skin contact C ≥ 0.0015% This specific concentration limit is considered as relevant for this dossier.	

Chapter 2: Methods of Analysis

Analytical methods for the active substance

Technical active substance (principle of method) (Annex IIA, point 4.1)	DOW: Reversed Phase High Performance Liquid Chromatography with UV detection (254 nm) Thor: HPLC-UV (275 nm)
Impurities in technical active substance (principle of method) (Annex IIA, point	DOW: Titration and GC-FID

4.1)	Validation data are missing on some impurities and should be provided Thor: Titration and NMR-spectroscopy Validation data on the impurities are missing.

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. Thor: No method submitted.
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 Thor: 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 Thor: No method submitted
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 Thor: No method submitted

Chapter 3: Impact on Human Health

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

	DOW	THOR
Rate and extent of oral absorption:	**C(M)IT: 49 %** MIT: 78%	C(M)IT: 44-47% MIT: 67-69%.
Rate and extent of dermal absorption:	➔ **50%** for aqueous solution below corrosive concentration; ➔ **100%** for corrosive concentration (> 0.6% the specific concentration limit)	➔ **50%** for aqueous solution below corrosive concentration; ➔ **100%** for corrosive concentration (> 0.6% the specific concentration limit)
Tissue Distribution study:	4 days after exposure: 4.72% of dosed radioactivity found in tissues (rat) Highest amount of radioactivity in blood	
Potential for accumulation:	After oral administration, no evidence of accumulation in the animal body	After dermal exposure C(M)IT/MIT is largely (>80%) absorbed. However, a large part remains tightly bound to the skin
Rate and extent of excretion:	Following oral administration, C(M)IT and MIT are both rapidly excreted: - C(M)IT: urine and faeces are equal major routes of excretion whereas bile is a minor (4.74%) - MIT: largely excreted in urine and in a lesser extent in faeces of which the major part came from bile (29.09%) No parent compound in excreta.	All the C(M)IT/MIT is rapidly metabolized after oral absorption: no parent compound is found in the excreta. The first step in metabolism was glutathione conjugation, resulting in four major metabolites for MIT and two major metabolites for C(M)IT. The open literature points to the formation of malonic acid, malonamic acid, *N*-methylmalonamic acid and other small polar organic acids.
Toxicologically significant metabolite	None of the metabolites are considered to be of concern.	None of the metabolites are considered to be of

	concern.

Acute toxicity (Annex IIA, point 6.1)

	DOW	THOR
Rat LD_{50} oral C(M)IT/MIT 14% (values for C(M)IT 100% between brackets)	**457 mg/kg bw (corr. to 64 mg a.i./kg bw)**	472 mg/kg bw (corr. to 66 mg a.i./kg bw)
Rat LD50 oral, N-(methyl) malonamic acid (NMMA)	3550 mg NMMA/kg b.w. in males 4100 mg NMMA/kg b.w. in females	
Rat; Rabbit LD_{50} dermal C(M)IT/MIT 14% (values for C(M)IT 100% between brackets)	**Rabbit= 660 mg/kg bw (corr. to 92.4 mg a.i./kg bw)**	Rat > 1007 mg/kg bw (corr. to 141 mg a.i./kg bw)
Rat LC_{50} inhalation C(M)IT/MIT 14% (values for C(M)IT 100% between 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 C(M)IT/MIT 100%)	Irritant	**Corrosive**
Eye irritation (rabbit) C(M)IT/MIT 14% (and C(M)IT/MIT 100%)	**Corrosive**	Not tested, but C(M)IT/MIT is considered to pose a risk of serious damage to the eyes
Airway irritation C(M)IT/MIT 14%	RD_{50}= 69µg/L (corr. to 9.66 µg a.i/L)	-
Skin sensitization (test method used and result) C(M)IT/MIT 14% (and C(M)IT/MIT 100%)	Sensitising	Sensitising
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** -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.)**	**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 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. equivalent to 0.7 mg/kg bw/d (corr. to 0.1 mg a.i/kg bw/d) based on systemic and local effects observed at this dose. Mouse, 30 months NOAEL = 2857 ppm (corr. to 400 ppm a.i. corr. to 0.25 mg a.i./kg.bw/d)	**Rat, 90 days** - NOEL = 18.75 mg/kg/d (corr. to 2.61 mg a.ikg bw/day) based on no systemic effects **- NOAEC = 12500 ppm (corr. to 1740 ppm a.i) based on local effects**
Lowest relevant inhalation NOAEL / LOAEL	**Rat, 90 days** **NOAEC = 2.4 mg/m^3 (corr. to 0.34 mg a.i./m^3 based on irritation to the respiratory tract)**	**Rat, 90 days (Letter of access)** **NOAEC = 2.4 mg/m^3 (corr. to 0.34 mg a.i./m^3 based on irritation to the respiratory**

	tract)

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

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

Genotoxicity (Annex IIA, point 6.6)	Genotoxic *in vitro* (Ames, mammalian cell gene mutation test) Not a genotoxic *in vivo* (*in vivo* unscheduled DNA synthesis, *in vivo* chromosome aberration assay)	Genotoxic *in vitro* (Ames, mammalian chromosome aberration test, mammalian cell gene mutation test) Not a genotoxic *in vivo* (*in vivo* unscheduled DNA synthesis, *in vivo* bone marrow micronucleus test)
Genotoxicity of C(M)IT/MIT metabolites (Annex IIA, point 6.6)	N-methyl malonamic acid (NMMA): **Not mutagenic** (Bacterial Gene Mutation Assay test)	-

Carcinogenicity (Annex IIA, point 6.4)

	DOW	**THOR**
Species/type of tumour	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	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

	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	
lowest dose with tumours	No evidence of carcinogenicity	No evidence of carcinogenicity

Reproductive toxicity (Annex IIA, point 6.8)

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

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

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

	DOW	**THOR**
Species/	No evidence of neurotoxicity in	No evidence of neurotoxicity in

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

Other toxicological studies (Annex IIIA, VI/XI)

....	none

Medical data (Annex IIA, point 6.9)

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

Summary (Annex IIA, point 6.10)

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

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 22°C MIT, $DT_{50\ (dissipation)}$= 0.03-0.04 day at 22°C $DT_{50\ (mineralisation)}$= 1.69 days at 22°C	Tested as ACTICIDE® 14 CIT: elimination >96% MIT: elimination >80% Tested on MIT only MIT: $DT_{50\ (dissipation)}$ = 0.02 day

	<u>Sewage Treatment Plant</u> **<u>CMIT</u> DT_{50} = 0.27 day at 22°C** **<u>MIT</u> DT_{50} = 0.04 day at 22°C**	
Biodegradation in Sewage Treatment Plant (metabolites)	Not relevant	No relevant
Biodegradation in surface water	<u>Estuarine water</u> <u>CMIT</u>, 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 <u>MIT</u>, 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 <u>Marine water</u> <u>CMIT</u>, 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 <u>MIT</u>, DT_{50} = 3.6 for threshold and 8.3 for PEC calculation (10 µg/L) – 12.3 days (100 µg/L) at 20°C DT_{50} = 6.8 for threshold and 15.7 for PEC calculation (10 µg/L) – 23.3 days (100 µg/L) at 12 °C DT_{50} = 8.7 for threshold and 20.0 for PEC calculation (10 µg/L) – 29.7 days (100 µg/L) at 9 °C	<u>Estuarine water</u> Not available <u>Marine water</u> <u>CIT</u> (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 <u>MIT</u> (87.5 µg/L): DT_{50} = 3.9 days at 15°C DT_{50} = 5.0 days at 12°C DT_{50} = 6.3 days at 9°C
	<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% in the Cedar Hill water: sediment system, (3.3% at day 30).	<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). Their identity was not elucidated, despite efforts with LC/MS analysis <u>Aerobic, MIT</u> One metabolite detected but not identified in both water:sediment system: - low organic matter water: sediment system, maximum 48.5% by day 4 and 11.4% by day 38 - high organic matter water:

		sediment system, maximum 36.9% by day 8 and not detected by day 58.
Non-extractable residues	C(M)IT, aerobic: 45.4-69.5 % of the applied ^{14}C-activity with 60.4 % at study termination (30 days) and 34.6-44.4 % with 42.2 % at study termination (30 days) for the Almhouse and Cedar Hill water:sediment systems, respectively). MIT, aerobic: 45.2-60.2 % of the applied ^{14}C-activity with 57.7 % at study termination (30 days) and 27.2-62.6 % with 62.6 % at study termination (30 days) for the Almhouse and Cedar Hill water:sediment systems, respectively).	C(M)IT, aerobic: - low organic matter water: sediment system, from 17.0% of applied activity by day 1 to 43.9% by day 58 - high organic matter water: sediment system, from 17.8% of applied activity by day 1 to 51.4% by day 31.5 MIT, aerobic: - low organic matter water: sediment system, from 12.6% of applied activity by day 1 to 53.7% by day 38 - high organic matter water: sediment system, from 15.8% of applied activity by day 1 to 42.0% by day 39

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

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

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

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

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

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

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

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

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

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

Chapter 5: Effects on Non-target Species

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

Species	Time-scale	**DOW**	**THOR**
		Endpoint	Endpoint
Freshwater Fish			
Rainbow trout (*Oncorhynchus mykiss*)	Acute-96 hr US-EPA 72-1 Flow through	96 hr LC_{50} 1.36 mg/L (eq. to 0.19 mg a.i./L) 96 hr NOEC 0.93 mg /L (eq. to 0.13 mg ai/L) (mean measured concentration)	
	Acute-96 hr OECD 203 Static		96 hr LC_{50} 1.57 mg /L (eq. to 0.22 mg ai/L) (nominal concentration)
Bluegill sunfish (*Lepomis macrochirus*)	Acute-96 hr US-EPA 72-1 Flow through	96 hr LC_{50} 2.00 mg /L (eq. to 0.28 mg ai/L) 96 hr NOEC 1.57 mg /L (eq. to 0.22 mg ai/L) (mean measured concentration)	
Rainbow trout (*Oncorhynchus mykiss*)	Prolonged Toxicity Test -14 Day OECD 204 Flow through	14 d NOEC 0.36 mg /L (eq. to 0.05 mg ai/L) (mean measured concentration)	
	Mortality test -28 Days OECD 215 Semi Static		28d NOEC 0.70 mg /L (eq. to 0.098 mg ai/L) (nominal concentration)
Fathead minnow (*Pimephales promelas*)	Early life stage toxicity-36 days US-EPA 72-4 Flow through	NOEC, egg hatch, survival, length 0.86 mg /L (eq. to 0.12 mg ai/L) NOEC, weight 0.14 mg /L (eq. to 0.02 mg ai/L) (mean measured concentration)	
Saltwater Fish			

Sheepshead minnow (*Cyprinodon variegatus*)	Acute-96 hr Static	96 hr LC_{50} 2.14 mg ./L (eq. to 0.30 mg ai/L) 96 hr NOEC 1.29 mg /L (eq. to 0.18 mg ai/L) (nominal concentration)	
	Acute-96 hr Flow through		96 hr LC_{50} 3.43 mg /L (eq. to 0.48 mg ai/L) (nominal concentration)
Freshwater Invertebrates			
Daphnia magna	Acute-48 hr US-EPA 72-2 Flow through	48 hr EC_{50} 1.14 mg /L (eq. to 0.16 mg ai/L) 48 hr NOEC 0.86 mg ./L (eq. to 0.12 mg ai/L) (mean measured concentration)	
	Acute-48 hr OECD 202 Static		48 hr LC_{50} 4.71 mg ./L (eq. to 0.71 mg/L C(M)IT /MIT 14% a.i. and 0.10 mg ai/L) (issued from 2.1% source) (nominal concentration)
Daphnia magna	Chronic-21 days US-EPA 72-4	NOEC, survival of first generation[1], 0.71 mg ./L (eq. to 0.10 mg ai/L) EC_{50}, survival of first generation[1], > 1.29 mg ./L (eq. to 0.18 mg ai/L) (mean measured concentration)	
	Chronic-21 days OECD 202		NOEC reproduction 0.172 mg./L (eq. to 0.026 mg/L C(M)IT /MIT 14% a.i. and 0.0036 mg ai/L) (issued from 2.1% source)

[1]: most sensitive parameter

Saltwater Invertebrates			
Mysid (*Americamysis bahia*)	Acute-96 hr US-EPA OPPTS 850.1035 Flow through	96 hr EC_{50} 2.01 mg ./L (eq. to 0.282 mg a.i./L) 96 hr NOEC 0.21 mg./L (eq. to 0.030 mg a.i./L) (mean measured concentration)	

	Acute-96 hr US-EPA FIFRA 72-3 Flow through		96 hr EC_{50} 2.36 mg ./L (eq. to 0.33mg ai/L) (nominal concentration)
(Acartia tonsa)	Acute-48 hr ISO TC 147/SC 5 WG 2: and PARCOM Ring Test Protocol Static	48 hr EC_{50} 0.05 mg ./L (eq. to 0.007 mg ai/L) (nominal concentration)	
Crassostrea virginicia (Eastern oyster)	Acute-96 hr US-EPA FIFRA 72-3 Flow through		96 hr LC_{50} 0.29 mg ./L (eq. to 0.041mg ai/L) (nominal concentration)
Freshwater Algae			
Selenastrum capricornutum	120 hr OECD 201 US-EPA FIFRA 122-2 Static	24 hr NOErC 35.3 µg/L (eq. to 4.955 µg ai/L) (Initial measured concentration (LOQ/2))	
	72 hr OECD 201 US-EPA OPPTS 850.5400 Static		72 hr NOErC 8.29 µg ./L (eq. to 1.16 µg ai/L) 72 hr EbC50 69.50 µg /L (eq. to 9.73 µg ai/L) 72 hr ErC50 382.1 µg /L (eq. to 53.5 µg ai/L) (mean measured concentration)
Saltwater Algae			
Skeletonema costatum	48 hr OECD 201 US EPA OPPTS 850.5400 Static	48 hr NOE_rC 3.5 µg/L (eq. to 0.49 µg a.i./L) 48 hr ErC50 37.1 µg/L (eq. to 5.2 µg a.i./L) (mean measured concentration)	Available but no reliable

Freshwater sediment dwelling organisms			
Midge larvae (Chironomus riparius)	Chronic-28 days OECD 218	28 d NOEC, survival 23.79 mg/kg (eq to 3.33 mg a.i./kg) dry sediment 28 d LC_{50}, survival 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment 28 d NOEC, adult emergence 27 mg/kg (eq to 3.78 mg a.i./kg) dry sediment 28 d EC_{50}, adult emergence 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment 28 d NOEC, developmental rate > 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment 28 d EC_{50}, developmental rate > 50.21 mg/kg (eq to 7.03 mg a.i./kg) dry sediment (mean measured concentration)	Not Available
Lumbriculus variegatus	Chronic-28 days Draft OECD	28d EC50 survival 2.64-3.29 mg/kg dry sediment (eq to 0.37 - 0.46 mg a.i./kg dry sediment) 28d NOEC survival 1.93 mg/kg (eq to 0.27 mg a.i./kg) dry sediment (mean measured concentration)	Not Available
Hyalella azteca	Chronic-28 days US-EPA OPPTS 850.1735	28d EC50 survival 13.07-45.39 mg/kg dry sediment (eq to 1.83- 6.34 mg a.i./kg dry sediment) 28d NOEC survival 7.93 mg/kg (eq to 1.11mg a.i./kg) dry sediment (mean measured concentration)	Not Available

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

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

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

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

***No data provided by THOR**

Effects on earthworms or other soil non-target organisms

	DOW	**THOR**
	OECD 207, 14-days mortality	OECD 207, 14-days mortality
Acute toxicity to Earthworm (*Eisenia foetida*) (Annex IIIA, point XIII.3.2)	- <u>Nominal</u> : 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) <u>- Twa:</u> 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)	- <u>Nominal</u> : 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 <u>- Twa:</u> NOEC (survival) = 14.47 mg/kg (eq to 2.09 mg a.i/kg) dw LC_{50} (survival) > 80.38

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

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

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

Effects on terrestrial vertebrates

	DOW	**THOR**
Acute toxicity to mammals (Annex IIIA, point XIII.3.3)	LD_{50} oral : 457 mg/kg bw (rat) (eq. to 64 mg a.i. /kg bw) LD_{50} dermal : 660 mg./kg bw (rabbit) (eq. to 92.4 mg a.i./kg bw) 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 Red Clover :	660 mg /kg dry soil (eq. to 92.4 mg ai/kg) 218.57 mg /kg dry soil (eq. to 30.6 mg ai/kg) 68.9 mg /kg dry soil (eq. to 9.65 mg ai/kg) 214.3 mg /kg dry soil (eq. to 30 mg ai/kg) 64.3 mg /kg dry soil (eq. to 9.0 mg ai/kg) 19.3 mg /kg dry soil (eq. to 2.7 mg ai/kg) 28.04 mg /kg dry soil (eq. to 3.93 mg ai/kg) 9.29 mg /kg dry soil (eq. to 1.30 mg

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

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

Appendix II: List of intended uses[9]

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 as/L min max	water L/m^2 min max	g as/m^2 min max	
Air conditioning/air washing systems	EU	C(M)IT/MIT containing biocidal products Kathon ™ 886F (Kathon ™WT)	*Legionella Pneumophila*	Aqueous concentrate	14% Kathon ™ 886F (Kathon ™WT).	Dose by pouring or by pumping using metered addition. Air conditioning/air washing systems:in a reservoir or a location to provide uniform mixing	Dosed as needed to maintain control of the system	As needed, to be determined on a case by case basis	1-5 ppm Shock dose : 15 ppm (not proved in the efficacy part)	N/A	N/A	

[9] adapted from: EU (1998a): European Commission: Guidelines and criteria for the preparation of complete dossiers and of summary dossiers for the inclusion of active substances in Annex I of Directive 91/414/EC (Article 5.3 and 8,2). Document 1663/VI/94 Rev 8, 22 April 1998

Appendix III: List of studies

Reference list sorted by section:

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)[10]	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
A3/04	Broughton, H.S.	1993	Characterization of test substance Kathon™ 886F, an MUP, to be used for submission to regulatory agencies in Europe,	Y(ii)	Rohm and Haas

[10] 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).

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
			(December 15, 1993), GLP, Unpublished.		
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

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
A4.1.a/01:	Berrios, Efrain	2006	"CIS Dept. Test method #06-111-01, Reverse phase HPLC analysis of Kathon™ 886 Technical for active ingredients" July 20, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.a/02:	Berrios, Efrain	2006	"CIS Dept. Test method #06-111-02, Reverse phase HPLC analysis of Kathon™ 886 Technical for active ingredients" October 3, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.a/03:	Berrios, Efrain	2006	"GLP validation of CIS analytical test method #06-111-01 for the analysis of Kathon™ Tech for active ingredient" under protocol # GLP 24P-2006-106" Rohm and Haas Report # GLP-2006-085, September 12, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/01:	Doshi, Deepak,	2001	"CIS Dept. Test method #89-03-03, Reverse phase HPLC analysis of Kathon™ Formulations for active ingredients" March 5, 2001, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/02:	Doshi, Deepak	2001	"GLP report on validation of CIS test method #89-03-03 (Draft) for the analysis of Kathon™ formulations for active ingredients under protocol # GLP 24P-2000-026" Rohm and Haas Report # GLP-2001-006, February 15, 2001, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/03:	Doshi, Deepak	2003	"Round robin study for the analysis of active ingredients in Kathon™ formulations in support of European Biocidal Product Directives", Rohm and Haas Report # GLP-2002-072, April 1, 2003, Unpublished.	Y(ii)	Rohm and Haas
A4.1.b/04:	Eisenschmied, Mark A	2006	"GLP LC-MS peak identity verification of AI in Kathon™ CG and Kathon™ 886F as detected by CIS TM 89-03-03", CAs Technical document	Y(ii)	Rohm and Haas

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
			# TD2006-182. July 19, 2006, Unpublished.		
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,	Y(ii)	Rohm and Haas

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
			Unpublished.		
A4.1.d/02:	Berrios, Efrain	2006	CIS Dept. Test method #06-110-02, "Analysis of Kathon™ 886F for % magnesium chloride using potentiometric titration", August 2, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.1.d/03:	Berrios, Efrain	2006	"GLP validation and revision of of CIS analytical test method #06-110-01 for the determination of magnesium chloride in Kathon 886F ", protocol # 24P-2006-097, Rohm and Haas Report # GLP-2006-046, July 25, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.2.a/01:	Marbo, M	2005	Validation of CIS analytic methods to determine RH-886 and RH-573 in soil and sediment Samples. Performed at Rohm and Haas Technical Center, Spring House, PA, USA, Technical Report N°. GLP-2005-009, December 12, 2005, Unpublished.	Y(ii)	Rohm and Haas
A4.2.b/01:	Dr. Krainz Alexander	2006	Test method for the determination of 2-methyl-4-isothiazolin-3-one (RH-573) and 5-chloro-2-methyl-4-isothiazolin-3-one (RH-651) the active ingredients in RH-886 and RH-573 formulations, in air, Test method 857665, June19, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.2.b/02:	Dr. Krainz, Alexander	2006	Development and validation of residue analytical methods for determination of 2-methyl-4-isothiazolin-3-one (RH-573) and 5-chloro-2-methyl-4-isothiazolin-3-one (RH-651) the active ingredients in RH-886 and RH-573 formulations, in air, RCC Ltd., Study # 857665, Rohm and Haas Study # GLP-2005-012, June19, 2006, Unpublished.	Y(ii)	Rohm and Haas
A4.2.c/01:	Dr.	2004	Development and validation of	Y(ii)	Rohm and

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
	Stefan Wolf		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.		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	Y(ii)	Rohm and Haas

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
			stimulants), RCC Ltd, Study # B25626, August 29, 2007, Unpublished.		
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)[11]	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-	Y(ii)	Rohm and Haas

[11] 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.

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
			1039 (November 13, 1972 original report; April 13, 2006 additional data), unpublished.		
A6.1.2/01:	[redacted]	1993 b	Kathon™ 886 all-magnesium formulation: acute dermal toxicity study in male rabbits, Rohm and Haas Company, Rohm and Haas Report N° 76R-056A, July 23, 1993, unpublished.	Y(i)	Rohm and Haas
A6.1.3.a/01:	[redacted]	1991 a	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 91R-018, July 10, 1991, Unpublished.	Y(i)	Rohm and Haas
A6.1.3.a/02:	[redacted]	1991 b	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018A, August 12, 1991, Unpublished.	Y(i)	Rohm and Haas
A6.1.3.a/03:	[redacted]	1992	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018B, June 9, 1992, Unpublished.	Y(i)	Rohm and Haas
A6.1.3.b/01:	Papagiannis C.N.	1993	Kathon™ 886F biocide: evaluation of the upper airway irritation potential (RD_{50}), International Research and Development Corporation Project ID: 285-047, Rohm and Haas Report N° 91RC-047, April 23, 1993, Unpublished.	Y(i)	Rohm and Haas
A6.1.4.a/01:	[redacted]	1986	Kathon™ 886 – 13.9 %: determination of the acute dermal irritation or corrosion in male rabbits, [redacted] Protocol N° BT0102, Rohm and Haas Report N° 86RC-1005, November 26, 1986, Unpublished.	Y(ii)	Rohm and Haas

A6.1.4.a/03:	[redacted]	1985	Kathon™ 886 1.5 % Biocide: skin irritation study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 84R-244A, B, C, D, January 16, 1985, Unpublished.	Y(i)	Rohm and Haas
A6.1.4.b/01 :	Longacre, S.L.	1995	Kathon™ 886 Biocide: revised acute toxicity reports, Rohm and Haas Company, Rohm and Haas Report N° 76-56B, March 20, 1995, Unoublished.	Y(i)	Rohm and Haas
A6.1.5/01:	House R.V.	2000 a	Murine local lymph node assay with Chloromethylisothiazolinone and Methylisothiazolinone, Covance Laboratories Study ID: 6228-145, Rohm and Haas Report N° 00RC-148A, November 7, 2000, Unpublished.	Y(ii)	Rohm and Haas
A6.1.5/02:	[redacted]	2001	Chloromethylisothiazolinone/Methylisothiazolinone 3:1 - Open epicutaneous test in guinea pigs, [redacted] Project ID N 31H0367/002132, US Ref N° 01RC-1030, July 12, 2001, Unpublished.	Y(ii)	Rohm and Haas
A6.1.5/03:	House R.V.	2000 b	Murine local lymph node assay to evaluate Chloromethylisothiazolinone/Methylisothiazolinone, Covance Laboratories Study ID: 6228-146, Rohm and Haas Report N° 00RC-148B, November 7, 2000, Unpublished.	Y(ii)	Rohm and Haas
A6.1.5/04:	[redacted]	2000	Chloromethylisothiazolinone and Methylisothiazolinone 3:1: Dermal sensitization study in guinea pigs Maximization test, Rohm and Haas Company Report N° 00R-140, September 28, 2000, Unpublished.	Y(i)	Rohm and Haas
A6.1.5/06:	[redacted]	1982	Kathon™ 886: a study of the concentration-dependent delayed contact hypersensitivity in guinea pigs, Rohm and Haas Company, Rohm and Haas Report N° 81R-66, August 24, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.1.5/06bis:	[redacted]	1983	Kathon™ Biocide: Manifestation of delayed	N	Rohm and

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

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

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
			epidermis, Central Toxicology Laboratory Study N°: JV1870, Rohm and Haas Report N°: 05RC-055, October 20, 2005, Unpublished.		
A6.2.c/01:	[redacted]	1997	^{14}C-Kathon biocide toxicokinetic study in rats, Rohm and Haas Company, Rohm and Haas Report N° 97R-1058, March 14, 1997, Unpublished.	Y(i)	Rohm and Haas
A6.3.1/01:	[redacted]	1984	Kathon™ 886 MW: one month oral toxicity study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 84R-095, August 31, 1984, Unpublished.	Y(i)	Rohm and Haas
A6.4.1.a/01:	[redacted]	1982	Kathon™ 886 NAR three month rat drinking water study and one generation reproduction study, Rohm and Haas Company, Rohm and Haas Report N° 81R-162, September 9, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.4.1.a/02:	[redacted]	1975	RH-886T, RH-35,375 and RH-00,345: three month subchronic oral safety evaluation study in rats (metabolite). [redacted] Study N°: 285-010, Rohm and Haas Report N°: 75RC-1001 (February 17, 1975), Unpublished.	Y(ii)	Rohm and Haas
A6.4.1.b/01:	[redacted]	1975	RH-886: Three month subchronic oral safety evaluation study in Beagle dogs, [redacted] Study N° 285-008, Rohm and Haas Report N° 75RC-1002, February 19, 1975, Unpublished.	Y(ii)	Rohm and Haas
A6.4.2/01:	[redacted]	1982	Kathon™ 886 MW: 90-day percutaneous toxicity study in rabbits. Rohm and Haas Company, Rohm and Haas	Y(i)	Rohm and Haas

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
	[redacted]		Report N° 80R-119, August 31, 1982, Unpublished.		
A6.4.3/01:	[redacted]	1984	Kathon™ 886 MMPA Process: thirteen-week inhalation toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 82R-245, December 10, 1984, Unpublished.	Y(i)	Rohm and Haas
A6.5/01:	[redacted]	1994	Kathon biocide: 24-month drinking water chronic/oncogenic study in rats, Rohm and Haas Company, Rohm and Haas Report N° 90R-149, January 24, 1994, Unpublished.	Y(i)	Rohm and Haas
A6.5/02:	[redacted]	1983	Kathon™ CG: 30-month dermal carcinogenesis study in male mice, Rohm and Haas Company, Rohm and Haas Report N° 81R-288, January 14, 1983, Unpublished.	Y(ii)	Rohm and Haas
A6.6.1/01:	Fujii M. and Sugita N.	1982	Microbial mutagenicity study on Kathon WT, Takeda Chemical Industries, Japan, Rohm and Haas Report N° 82RC-1019, January 1982, Unpublished.	Y(ii)	Rohm and Haas
A6.6.1/02:	Sames J.L., Frank J.P.	1990	Kathon™ 886: Salmonella typhimurium gene mutation assay, (Screening test in TA98 and TA1537), Rohm and Haas Company, Rohm and Haas Report N° 90R-0142, July 24, 1990, Unpublished.	Y(ii)	Rohm and Haas
A6.6.1/03:	San R.H.C. and VanDyke M.R.	2005	N-Methyl Malonamic Acid: bacterial reverse mutation (Ames) assay, BioReliance Study N°: AB13CE.503.BTL, Rohm and Haas Report N°: 05RC-045, September 9, 2005, Unpublished.	Y(ii)	Rohm and Haas
A6.6.2/01:	McGlynn A.M. and McCarthy K.L.	1981	Kathon™ 886 mammalian cell transformation test, Rohm and Haas Company, Rohm and Haas Report N° 81R-110, June 29, 1981, Unpublished.	Y(i)	Rohm and Haas

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
A6.6.3/01:	[redacted]	1981	Mutagenicity evaluation of TD-81-155 in the mouse lymphoma forward mutation assay, [redacted] Project N° 20989, Rohm and Haas Report N° 81RC-153, December 1981, Unpublished.	Y(i)	Rohm and Haas
A6.6.3/02:	[redacted]	1991	Kathon™ 886 M.W. biocide: Test for chemical induction of unscheduled DNA synthesis in rat primary hepatocyte cultures by autoradiography, [redacted] Study N° 0159-5100, Rohm and Haas Report N° 90RC-168, April 24, 1991, Unpublished.	Y(i)	Rohm and Haas
A6.6.4/01:	[redacted]	1997	Kathon™ 886F biocide: measurement of unscheduled DNA synthesis in rat liver using an in vivo/in vitro procedure, [redacted] Report N° 616/21-1052, Rohm and Haas Report N° 97RC-055, October 1997, Unpublished.	Y(i)	Rohm and Haas
A6.6.4/02:	[redacted]	1992	Acute test for chemical induction of chromosome aberration in mouse bone marrow cells in vivo, [redacted] Study N° 0202-1541, Rohm and Haas Report N° 92RC-0054, October 15, 1992, Unpublished.	Y(i)	Rohm and Haas
A6.6.5/01:	Valencia R.	1982	Drosophila sex-linked recessive lethal test on Kathon biocide, Zoology Department, University of Wisconsin, Madison, WI, USA, Laboratory Project N° 100, Rohm and Haas Report N° 82RC-94, December 22, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.7/01:			Refer to the A6.5.1/01 study above.		
A6.7/02:			Refer to the A6.5.2/01 study above		
A6.8.1.a/01:	[redacted]	1980	Kathon™ 886: Teratology	Y(i)	Rohm

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
	[redacted]		study in rats, [redacted] Project N° 417-399, Rohm and Haas Report N° 80RC-81, September 25, 1981, Unpublished.		and Haas
A6.8.1.b/01:	[redacted]	1992	Kathon™ biocide: oral (gavage) developmental toxicity study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 91R-074, April 28, 1992, Unpublished.	Y(i)	Rohm and Haas
A6.8.2.a/01:	[redacted]	1982	Kathon™ 886 NAR three month rat drinking water study and one generation reproduction study, Rohm and Haas Company, Rohm and Haas Report N° 81R-162, September 9, 1982, Unpublished.	Y(i)	Rohm and Haas
A6.8.2.b/01:	[redacted]	1998	Kathon™ 886F biocide: two-generation reproductive toxicity study in rats, Rohm and Haas Company, Rohm and Haas Report N° 96R-189, August 7, 1998, Unpublished.	Y(i)	Rohm and Haas
A6.12.6/05:	Scott F.	1979	Repeated Insult Patch Test of Kathon™ 886, Hill Top Research Report N° 78-1011-70 and 79-0129-70, Rohm and Haas Report N° 79RC-0014 (February 1, 1979), Unpublished.	Y(ii)	Rohm and Haas
A6.12.6/06:	Maibach H.I.	1984d	Repeated insult patch test with Kathon™ CG 50 ppm active ingredient, University of California, San Francisco Study N° HIM 83 – R&H D-1, Rohm and Haas Report N° 84RC-011 (February 29, 1984), Unpublished.	Y(ii)	Rohm and Haas
A6.12.6/07:	Maibach H.I.	1984e	Human repeat insult patch test Kathon™ CG 100 ppm active ingredient, University of California, San Francisco Study N° HIM 83 – R-H D-2, Rohm and Haas Report N° 84RC-051 (September 21, 1984), Unpublished.	Y(ii)	Rohm and Haas

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
A6.12.6/08:	Schwartz S.R.	1990	A double-blind study to determine the topical contact sensitization potential of three test products, International Research Services, Inc. Study N° 743RH1289, Rohm and Haas Report N° 90RC-0017 (May 11, 1990), Unpublished.	Y(ii)	Rohm and Haas
A6.12.6/09:	Maibach H.I.	1990	Modified Draize Skin Sensitization Study, University of California, San Francisco Study N° HIM 89-R&H-D-1&2, Rohm and Haas Report N° 90RC-016 (July 6, 1990), Unpublished.	Y(ii)	Rohm and Haas
A6.15/01	Quérou R. and Lévy R.	2007	Calculation of the maximum loading of CMIT/MIT in food contact packaging materials in a worst case situation Rohm and Haas Company, Report N° 0704_RQ (13 March 2007), unpublished.	Y(ii)	Rohm and Haas
A6.16/01:	[redacted]	2005	Neutral red uptake phototoxicity assay in BALB/C 3T3 mouse fibroblasts, [redacted] Study N° 04AF51.140058, Rohm and Haas Report N° 04RC-059 (May 11, 2005), Unpublished.	Y(ii)	Rohm and Haas
A7.1.1.1.1/01:	Jalali-Araghi, K and Shepler, K.	1993	Hydrolysis of ^{14}C RH-651 (the major component of RH-886) at pH 5, 7, and 9; Pharmacology and Toxicology Research Laboratory-West, Richmond, CA USA, PTRL Report N° 225W-1 Rohm and Haas Company, Technical Report N° 34-93-07 (18 February 1993), unpublished.	Y(i)	Rohm and Haas
A7.1.1.1.1/02:	Mazza, L.	1998	Identification of Hydrolytic Degradates of ^{14}C RH-651 at pH 9; Rohm and Haas Company Technical Report N° Biocides TR-98-039 (11 November 1998), Unpublished.	Y(ii)	Rohm and Haas
A7.1.1.1.1/	Marx, M,	1992	Hydrolysis of ^{14}C RH-573 at	Y(i)	Rohm

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

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

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

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
			Rohm and Haas Report N° GLP-2002-081 (April 22, 2003), Unpublished.		
A7.1.2.3/02 :	Seyfried, B.	2003 b	Ready Biodegradation of N-methyl Acetamide in a CO2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study No.: 843967, Rohm and Haas Report N° GLP-2003-031 (November 5, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.3/03 :	Seyfried, B.	2003 c	Ready Biodegradation of Malonamic Acid in a CO_2 Evolution (Modified Sturm) Test; RCC Ltd, CH-4452 Itingen, Switzerland, RCC Study No.: 843968, Rohm and Haas Report N° GLP-2003-032 (November 5, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.3/04 :	Jacobson A.	2007	Memo: Status of ready biodegradation study of metabolite. Support section A7.1.2.3. Not GLP, Unpublished.	Y(ii)	Rohm and Haas
A7.1.2.3/05 :	Seyfried B.	2007	Study plan (Protocol) : Sodium salt of 2-(methylcarbamoyl) ethene sulfonic acid, RCC Ltd. B44098, Rohm and Haas company GLP24P-2007-068 (2007), Unpublished.	Y(ii)	Rohm and Haas
A7.1.3.a/01 :	Swales, S.	2002 a	^{14}C-RH-651: Activated Sludge Adsorption Isotherm; Covance Laboratories Ltd., North Yorkshire England, Covance Report N°: 616/32-D2149, Rohm and Haas Report N°: 02RC-0030 (December 23, 2002a), Unpublished.	Y(ii)	Rohm and Haas
A7.1.3.a/02 :	Swales, S.	2002 b	^{14}C-RH-573: Activated Sludge Adsorption Isotherm; Covance Laboratories Ltd., North Yorkshire England, Covance Report No. 616/31-D2149, Rohm and Haas Report N° 02RC-0031 (December 23,	Y(ii)	Rohm and Haas

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
			2002b), Unpublished.		
A7.1.3.b/01:	Wang, W.W.	1991	Soil Adsorption and Desorption of ^{14}C RH-651 in Four Soils and One Sediment; XenoBiotic Laboratories, Inc., Princeton, NJ, USA. XBL Report No. RPT0046, Rohm and Haas Technical Report N° 31-91-09 (May 31, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.1.3.b/03:	Gillings, E.	2006	RH-573: Adsorption and Desorption to Soil; Brixham Environmental Laboratories, Brixham, Devon, UK. Brixham Report N°. BL8308/B, Rohm and Haas Technical Report N° 06-058 (29 August 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.2.1.a/01:	Guo, I and Eisenschmid, M.	2006	Aerobic Transformation of RH-651 in Soil. Performed at Rohm and Haas Technical Center, Spring House, PA, USA, Technical Report N°. GLP-2006-024, (December 18, 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.2.1.a/02:	Wang, W.W.	1991	Aerobic Soil Metabolism of ^{14}C RH-651; Xenobiotic Laboratories, Inc (XBL), Plainsboro, New Jersey, USA, XBL Report N°. RPT0045, Rohm and Haas Technical Report N°. 34-91-03 (April 11, 1991), Unpublished.	Y(ii)	Rohm and Haas
A7.2.1.b/01:	Guo, I	2006	Aerobic Transformation of RH-573 in Soil. Performed at Rohm and Haas Technical Center, Spring House, PA, USA, Technical Report N°. GLP-2006-012, (December 12, 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.2.3.1/01:	Reynolds, J.L.	1996	Aged Leaching of ^{14}C-RH-651 in Four Soils. XenoBiotic Laboratories, Inc., Plainsboro, New Jersey, USA, XBL Report N°. RPT00171, Rohm and Haas Technical Report N° 34-95-91 (July, 18, 1996),	Y(ii)	Rohm and Haas

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

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

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
			Rohm and Haas Report No 01RC-301 (August 13, 2002), Unpublished.		
A7.4.1.2.c/02:	Rhodes J.E.	2002b	Acute toxicity of N-methyl acetamide to the water flea, *Daphnia magna*, determined under static test conditions. (metabolite), ABC Laboratories Study N° 47184, Rohm and Haas Report N° 01RC-304 (August 5, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.2.c/03:	Madsen T.	2002d	Acute toxicity of malonamic acid to the water flea, *Daphnia magna,* determined under static test conditions (metabolite), ABC Laboratories Study N° 47181, Rohm and Haas Report N° 01RC-307 (September 10, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.3.a/01:	Boeri R.L, Kowalski P.L. and Ward T.J.	1995a	Acute Toxicity of Kathon™ WT 14 % to the freshwater alga, *Selenastrum capricornutum*, TR Wilbury Study N° 658-RH, Rohm and Haas Report N° 95RC-0061 (August 2, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.3.b/01:	Boeri R.L., Kowalski P.L. and Ward T.J.	1995b	Acute toxicity of Kathon WT 14 % to the marine alge, *Skeletonema costatum*; TR Wilbury Study N° 659-RH, Rohm and Haas Report N° 95RC-0062 (August 21, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.4.1.3.b/03	-	2009	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1: A 96-hour toxicity test with the marine diatom (Skeletonema costatum), Wildlife International Project N° 129A-226, Rohm and Haas Report N° 09RC-009 (July 29, 2009), GLP, Unpublished	Y(i)	Rohm and Haas
A7.4.1.3.c/01:	Madsen T.	2002e	Toxicity of N-methyl malonamic acid to the	Y(ii)	Rohm and

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
			unicellular green alga, *Selenastrum capricornutum*, (metabolite), ABC Laboratories Study N° 47179, Rohm and Haas Report N° 01RC-302 (September 9, 2002), Unpublished.		Haas
A7.4.1.3.c/02:	Rhodes J.E.	2002c	Toxicity of N-methyl acetamide to the unicellular green alga, *Selenastrum capricornutum*, (metabolite), ABC Laboratories Study N° 47186, Rohm and Haas Report N° 01RC-305 (September 5, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.3.c/03:	Madsen T.	2002f	Toxicity of malonamic acid to the unicellular green alga, *Selenastrum capricornutum*, (metabolite), ABC Laboratories Study N° 47183, Rohm and Haas Report N° 01RC-308 (September 20, 2002), Unpublished.	Y(ii)	Rohm and Haas
A7.4.1.4/01:	Ward T.J., Kowalski P.L. and Boeri, R.L.	1995	Activated sludge respiration inhibition test with Kathon ™ WT 14 %; TR Wilbury Laboratories Study N° 665-RH, Rohm and Haas Report N° 95RC-0063 (June 27, 1995), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.1.a/01:	[redacted]	1991a	Acute flow-through toxicity of Kathon™ 886 biocide to the rainbow trout, *Oncorhynchus mykiss* – 14 day prolonged test, [redacted] Study Nº 9006-RH, Rohm and Haas Report Nº 89RC-0348 (June 19, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.2.a/01:	[redacted]	1991b	Early life stage toxicity of Kathon™ 886 biocide to the fathead minnow, *Pimephales promelas*; [redacted] Study N° 9004-RH, Rohm and Haas Report N° 89RC-0347 (June 21, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.3.1.a/01:	[redacted]	1996	RH-651 Bioconcentration and Elimination of ^{14}C-Residues by Bluegill Sunfish (In-Life), [redacted]	Y(ii)	Rohm and Haas

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
	[redacted]		[redacted] Unpublished [redacted] Study N°42387, 6 August 1996, Rohm and Haas Technical Report N° 34-96-40, Unpublished.		
A7.4.3.4.a/01:	Ward T.J. and Boeri R.L.	1991c	Chronic toxicity of Kathon™ 886 biocide to the daphnid, *Daphnia magna*, EnviroSystems Study N° 9005-RH, Rohm and Haas Report N° 89RC-0346 (June 17, 1991), Unpublished.	Y(i)	Rohm and Haas
A7.4.3.5.1a/01	Aufderheide J.	2006	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1 (supplied as Kathon™ 886F): chronic toxicity in whole sediment to the freshwater midge, *Chironomus riparius;* ABC Laboratories Study N° 49248, Rohm and Haas Report N° 04RC-080 (February 15, 2006), Unpublished.	Y(ii)	Rohm and Haas
A7.4.3.5.1a/02	Thomas S.T., Krueger H.O., Kendall T.Z., and Nixon W.B.	2007	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1: A sediment-water *Lumbriculus* toxicity test using spiked sediment, Wildlife International Ltd Project N° 129A-211A, Rohm and Haas Report N° 06RC-216 (December 3, 2007), GLP, Unpublished.	Y(ii)	Rohm and Haas
A7.4.3.5.1a/03	Thomas S.T., Krueger H.O., Kendall T.Z., and Nixon W.B.	2008	Mixture of 5-Chloro-2-methyl-4-isothiazolin-3-one and 2-methyl-4-isothiazolin-3-one in a ratio of 3:1: A prolonged sediment toxicity test with *Hyalella azteca* toxicity test using spiked sediment, Wildlife International Ltd Project N° 129A-212B, Rohm and Haas Report N° 06RC-217 (February 29, 2008), GLP, Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.1/01	Schaefer	2003	Kathon™ 886F biocide: soil	Y(ii)	Rohm

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
:	E.C. and Flaggs R.S.	a	microorganisms: carbon transformation test. Wildlife International Project N° 129E-108, Rohm and Haas Report N° 02RC-0210, (November 3, 2003), Unpublished.		and Haas
A7.5.1.1/02:	Schaefer E.C. and Flaggs R.S.	2003 b	Kathon™ 886F biocide: soil microorganisms: nitrogen transformation test. Wildlife International Project N° 129E-109, Rohm and Haas Report N° 02RC-0028, (October 31, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.2/01:	Armstrong K. and White D.	2000	Kathon™ 886F determination of acute toxicity (LC_{50}) to the earthworms, Inveresk Research Project N°: 396112, Inveresk Report N° 18165, Rohm and Haas Report N°: 99RC-0210 (February 28, 2000), Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.3/01:	Porch, J.R., Martin, K.H., Krueger, H.O.	2003 a	Kathon™ 886F biocide: a toxicity test to determine the effects of the test substance on seedling emergence and growth of three species of plants, Wildlife International Project N°: 129-179, Rohm and Haas Report N°: 02RC-0027A (January 9, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.5.1.3/02:	Porch, J.R., Martin, K.H., Krueger, H.O.	2003 b	Kathon™ 886F biocide: a toxicity test to determine the effects of the test substance on vegetative vigour of three species of plants, Wildlife International, Ltd., Project N° 129-180, Rohm and Haas Report N° 02RC-0027 (January 20, 2003), Unpublished.	Y(ii)	Rohm and Haas
A7.5.3.1.1/01:	[redacted]	1990 a	Kathon™ 886 biocide: 21-day acute oral LD_{50} study in bobwhite quail. [redacted] Project ID: BLAL 90 QD 148, Rohm and Haas Report N° 89RC-0339 (August 14, 1990), Unpublished.	Y(ii)	Rohm and Haas

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
A7.5.3.1.2/01:	[redacted]	1990b	Kathon™ 886 biocide: 8-day acute dietary LC_{50} study in Mallard ducklings. [redacted] Project ID: BLAL 90 DC 145. Rohm and Haas Report N° 89RC-0341 (October 18, 1990), Unpublished.	Y(ii)	Rohm and Haas
A7.5.3.1.2/02:	[redacted]	1990c	Kathon™ 886 biocide: 8-day acute dietary LC_{50} study in bobwhite quail. [redacted] Project ID: BLAL 90 QC 148. Rohm and Haas Report N° 89RC-0340 (October 18, 1990), Unpublished.	Y(ii)	Rohm and Haas

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
B03/01: covering section IIIB 3.7	M. L. Bates	2005	Kathon™ 886 MW Biocide: Two Year Ambient Temperature Storage Stability, Covance Laboratories Ltd., Harrogate, UK. Technical Report N°: 0616/034-D2149. Rohm and Haas Compagny, Report N°: 24P-2002-037 (December, 2005), GLP-2005-038, Unpublished.	Y(ii)	Rohm and Haas
B03/02: covering sections IIIB 3.3, 3.5, 3.6, 3.7 (Low temp), 3.8	M. L. Bates	2003	Kathon™ 886 MW Biocide: Evaluation of Chemical and Technical Properties (Active Ingredient, Content, pH, Acidity, Relative Density, Foaming, Persistence, Low Temperature Stability,	Y(ii)	Rohm and Haas

			Oxidising Properties), Covance Laboratories Ltd., Harrogate, UK. Technical Report N° : 616/33-D2149. Rohm and Haas Compagny, Report N°: 24P-2002-037 (19 November 2003), GLP-2003-015, Unpublished.		
B03/03: covering section IIIB 3.7	M. L. Bates	2004	Kathon™ 886 MW Biocide: Evaluation of the stability to light. Covance Laboratories Ltd., Harrogate, UK.Technical Report N°: 0616/38-D2149. Rohm and Haas Compagny, Report N°: 24P-2004-046 (December 2004), GLP-2004-046, Unpublished.	Y(ii)	Rohm and Haas
B03/04: covering section IIIB 3.9	T. Ghosh	1997	A Summary of our Knowledge on the Conditions and Mechanism of Isothiazolone Degradation. Rohm and Haas Biocides Research Technical Report. TR-97-28, Dr. Tirthankar Ghosh, July 10, 1997.	Y(i)	Rohm and Haas
B03/05: (**cross reference to Doc IIIA ref A3/01)** covering section IIIB 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.10	R. B. Petigara	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, Research Laboratories, Spring House, USA. Technical Report N°.: TR-01-058 (December 2001).	Y(ii)	Rohm and Haas
B4.1.a/01 (A4.1.b/01)	Doshi, Deepak,	2001	"CIS Dept. Test method #89-03-03, Reverse phase HPLC analysis of Kathon™ Formulations for active ingredients" March 5, 2001, Unpublished.	Y(ii)	Rohm and Haas

B4.1.a/02 (A4.1.b/02)	Doshi, Deepak	2001	"GLP report on validation of CIS test method #89-03-03 (Draft) for the analysis of Kathon™ formulations for active ingredients under protocol # GLP 24P-2000-026" Rohm and Haas Report # GLP-2001-006, February 15, 2001, Unpublished.	Y(ii)	Rohm and Haas
B4.1.a/03 (A4.1.b/03)	Doshi, Deepak	2003	"Round robin study for the analysis of active ingredients in Kathon™ formulations in support of European Biocidal Product Directives", Rohm and Haas Report # GLP-2002-072, April 1, 2003, Unpublished.	Y(ii)	Rohm and Haas
B4.1.a/04 (A4.1.b/04)	Eisenschmied, Mark A	2006	"GLP LC-MS peak identity verification of AI in Kathon™ CG and Kathon™ 886F as detected by CIS TM 89-03-03", CAs Technical document # TD2006-182. July 19, 2006, Unpublished.	Y(ii)	Rohm and Haas
B5.10/01	Diehl MA	2006 a	The antimicrobial activity of CMIT/MIT: Frame formulation minimum inhibitory concentration (MIC) studies versus Bacteria and Fungi, Rohm and Haas Technical Report Nr TR-06-001, January 10, 2006, GLP, Unpublished.	Y(ii)	Rohm and Haas
B5.10/02 (cross ref A5.3.1/02)	Diehl MA	2006 b	Seed of kill (SOK) and multipke challenge efficacy test with CMIT/MIT in a in-can model preservative system, Rohm and Haas Report BPD-06-017, 23 May 2006, GLP, Unpublished.	Y(ii)	Rohm and Haas
B5.10_03	Thery F. and Lens C.	2007	Evaluation of basic bactericidal and fungicidal activities of CMIT/MIT active substance. Keybio laboratory –France.Study 46340701. Study was conducted according to GLP	Y(ii)	Rohm and Haas

			Procedure 98-1312 Decree (12/31/1998).		
B5.10_04	Walker, JT	1999	Determination of the bactericidal activity against *Legionella pneumophila*. Centre for Advanced Microbiology and Research (CAMR), Report No. 98Q/029 (January 5, 1999), NOT GLP unpublished	Y(ii)	Rohm and Haas
B6.1.1/01 Cross reference: 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)	Rohm and Haas
B6.1.2/01 Cross reference: 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
B6.1.3/01 Cross reference: 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
B6.1.3/01 Cross reference: A6.1.3.a/01	[redacted]	1991 b	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018A, August 12, 1991, Unpublished.	Y(i)	Rohm and Haas
B6.1.3/02 Cross reference: A6.1.3.a/02	[redacted]	1992	Kathon™ 886F biocide: acute inhalation toxicity study in rats, Report Supplement, Rohm and Haas Company, Rohm and Haas Report N° 91R-018B, June 9, 1992, Unpublished.	Y(i)	Rohm and Haas
B6.1.3/03 Cross	Papagiannis C.N.	1993	Kathon™ 886F biocide: evaluation of the upper	Y(i)	Rohm and

reference: A6.1.3.a/03			airway irritation potential (RD_{50}), International Research and Development Corporation Project ID: 285-047, Rohm and Haas Report N° 91RC-047, April 23, 1993, Unpublished.		Haas
B6.2/01 Cross reference: A6.1.4.a/01:	[redacted]	1986	Kathon™ 886 – 13.9 %: determination of the acute dermal irritation or corrosion in male rabbits, [redacted] Protocol N° BT0102, Rohm and Haas Report N° 86RC-1005, November 26, 1986, Unpublished.	Y(ii)	Rohm and Haas
B6.2/03 Cross reference: A6.1.4.a/03	[redacted]	1985	Kathon™ 886 1.5 % Biocide: skin irritation study in rabbits, Rohm and Haas Company, Rohm and Haas Report N° 84R-244A, B, C, D, January 16, 1985, Unpublished.	Y(i)	Rohm and Haas
B6.2/04 Cross reference: A6.1.4.b/01 :	Longacre, S.L.	1995	Kathon™ 886 Biocide: revised acute toxicity reports, Rohm and Haas Company, Rohm and Haas Report N° 76-56B, March 20, 1995, Unoublished.	Y(i)	Rohm and Haas
B6.3/01 Cross reference: A6.1.5/01	House R.V.	2000a	Murine local lymph node assay with Chloromethylisothiazolinone and Methylisothiazolinone, Covance Laboratories Study ID: 6228-145, Rohm and Haas Report N° 00RC-148A, November 7, 2000, Unpublished.	Y(ii)	Rohm and Haas
B6.3/02 Cross reference: A6.1.5/02	[redacted]	2001	Chloromethylisothiazolinone/Methylisothiazolinone 3:1 - Open epicutaneous test in guinea pigs, [redacted] Project ID N 31H0367/002132, US Ref N° 01RC-1030, July 12, 2001, Unpublished.	Y(ii)	Rohm and Haas
B6.3/03 Cross reference:	House R.V.	2000b	Murine local lymph node assay to evaluate Chloromethylisothiazolinone	Y(ii)	Rohm and Haas

A6.1.5/03			/Methylisothiazolinone, Covance Laboratories Study ID: 6228-146, Rohm and Haas Report N° 00RC-148B, November 7, 2000, Unpublished.		
B6.3/04 Cross reference: A6.1.5/04	[redacted]	2000	Chloromethylisothiazolinone and Methylisothiazolinone 3:1: Dermal sensitization study in guinea pigs Maximization test, Rohm and Haas Company Report N° 00R-140, September 28, 2000, Unpublished.	Y(i)	Rohm and Haas
B6.3/06 Cross reference: A6.1.5/06	[redacted]	1982	Kathon™ 886: a study of the concentration-dependent delayed contact hypersensitivity in guinea pigs, Rohm and Haas Company, Rohm and Haas Report N° 81R-66, August 24, 1982, Unpublished.	Y(i)	Rohm and Haas
B6.4/02 Cross reference: A6.2.a/04	[redacted]	2003	2-Methyl-4-isothiazolin-3-one: In vitro percutaneous absorption through rat skin, Rohm and Haas Company, Rohm and Haas Company Report No. 00R-066, August 22, 2003, Unpublished.	Y(ii)	Rohm and Haas
B6.4/03 Cross reference: A6.2.b/04	Ward R.J.	2005	2-Methyl-4-isothiazolin-3-one (MI): in vitro absorption from water and three formulations through human epidermis, Central Toxicology Laboratory Study No: JV1839, Rohm and Haas Report N° 04RC-066 (August 16, 2005), Unpublished.	Y(ii)	Rohm and Haas
B6.4/04 Cross reference: A6.2.b/05	Ward RJ	2005	5-Chloro-2-methyl-4-isothiazolin-3-one (CMIT)/2-Methyl-4-isothiazolin-3-one (MIT): in vitro absorption of CMIT from an aqueous solution and three formulations through human epidermis, Central Toxicology	Y(ii)	Rohm and Haas

			Laboratory Study N°: JV1870, Rohm and Haas Report N°: 05RC-055, October 20, 2005, Unpublished.		
B6.4/0 Cross reference: A6.2.c/01	[redacted]	1997	^{14}C-Kathon biocide toxicokinetic study in rats, Rohm and Haas Company, Rohm and Haas Report N° 97R-1058, March 14, 1997, Unpublished.	Y(i)	Rohm and Haas