

Draft Assessment Report

Metam

Volume 1

August 2007

Revision August 2010

**Report and
Proposed Decision**

Rapporteur Member State: Belgium

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LEVEL 1

Metam

**Statement of subject matter and purpose for which
the monograph was prepared**

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

1.1 Purpose of the monograph (Document A)

This revised DAR is submitted to support the first inclusion of the existing active substance metam-sodium (incl. salts metam-sodium and metam-potassium) in Annex I. It is however noted that the majority of data provided in the dossier evaluated by the RMS belongs to the variant metam-sodium. It should be noted that studies provided for metam-potassium (Annex B and Annex C) were evaluated by the RMS, but were not taken into account for the conclusions.

Two dossiers were submitted in the framework of the EU review process:

- Taminco submitted a dossier that has been considered sufficiently complete to perform the detailed evaluation. The present DAR is only based on the Taminco dossier.

- The European Metam Sodium Task Force that is made up of the companies FMC Foret and Lainco submitted a dossier that was considered incomplete. In the original DAR, the rapporteur checked whether the a.s. source of the European Metam Sodium Task Force is comparable to the a.s. source proposed by Taminco.

Although the European Metam Sodium Task Force did not resubmit a dossier in the framework of the accelerated procedure according to Regulation (EC) No. 33/2008, the RMS has revisited the equivalence assessment of the FMC Foret and Lainco source taking into account changes in the identity section for the Taminco reference source.

Added in August 2010:

Metam is one of the 84 substances of the third stage Part B of the review programme covered by Commission Regulation (EC) No 1490/2002. Belgium being the designated rapporteur Member State submitted the DAR on metam in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 10 September 2007.

The peer review was initiated on 4 October 2007 by dispatching the DAR for consultation of the Member States and the main notifier Taminco. Subsequently, the comments received on the DAR were examined and responded by the rapporteur Member State in the reporting table. This table was evaluated by the EFSA to identify the remaining issues. The identified issues as well as further information made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in June – July 2008. A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in October 2008 leading to the conclusions as laid down in the EFSA Conclusion issued on 26 November 2008 (EFSA Scientific Report (2008) 203).

In the absence of a favourable opinion of the Standing Committee on the Food Chain and Animal Health, the Commission was unable to adopt the provisions it envisaged under the procedure laid down in Article 19 of Council Directive 91/414/EEC.

On the 28th of July 2009, the Council Decision of 13 July 2009 (2009/562/EC) concerning the non-inclusion of metam in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance was published in the Official Journal of the European Union.

The notifier Taminco N.V. made a resubmission application for the inclusion of metam in Annex I under the 'Accelerated Procedure', i.e. in accordance with the provisions laid down in Chapter III (Articles 13 to 19) of Commission Regulation (EC) No. 33/2008.

Details of the reason for the non-inclusion are provided in the EFSA Scientific Report (2008) No 203:

<<

List of studies to be generated, still ongoing or available but not peer reviewed

- Revised specification to include the relevant impurity MITC Taminco (relevant for all uses evaluated, data gap identified by EFSA August 2008, proposed submission date unknown, refer to chapter 1).
- Spectra for the relevant impurity DMTU (relevant for all uses evaluated, data gap identified by EFSA August 2008, proposed submission date unknown, refer to chapter 1).
- Flash point for metam-sodium TK (relevant for all uses evaluated, data gap identified by meeting of experts June 2008, proposed submission date unknown, refer to chapter 1).
- Storage stability data with analysis of the relevant impurities before and after storage (relevant for all uses evaluated, data gap identified by EFSA August 2008, proposed submission date unknown, refer to chapter 1).

- Information on operator, worker and bystander exposure during drip irrigation application in greenhouse is missing (relevant for greenhouse uses, data gap identified at the meeting of experts residues July 2008, proposed submission date unknown, refer to chapter 2.12)
- Further metabolism studies in plants. However, the need for these studies is dependant on the outcome of the data gaps identified for fate and behaviour. Should the fate studies confirm that there are no other significant metabolites in soil then further plant metabolism studies would not be required. (relevant for all uses evaluated, data gap identified at the meeting of experts residues July 2008, proposed submission date unknown, refer to chapter 3).
- The 2 significant organic impurities in the technical material should be addressed with regard to consumer exposure given the high rate of application (relevant for all uses evaluated, data gap identified at the meeting of experts residues July 2008, proposed submission date unknown, refer to chapter 3).
- Sufficient residue trials according to GAP to support the non-residue situation have been identified as a data gap. A sufficiently sensitive method should be used and also given that MITC is volatile the samples should be analysed as soon as possible after harvest. (relevant for all uses evaluated, data gap identified at the meeting of experts residues July 2008, proposed submission date unknown, refer to chapter 3).
- A data gap has been identified by EFSA after the meeting of experts to address the fate of DMTU in soil in order to obtain adequate input parameters for ground water modelling (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.1.2).
- A data gap was identified by the meeting of experts to address the range of half-lives available for metam and MITC and whether they are applicable to metam EU risk assessment. The notifier should address the different variables that might impact on the degradation in soil, such as method of application dose rate and soil adaptation (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.1.2).
- The meeting of experts proposed a data gap for a new soil adsorption / desorption study conducted with consideration of the volatility and the low adsorption properties of MITC (eg. with shorter equilibration times, soil solution ratios of 1:1, high organic carbon soils) (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.1.3).
- A new data gap has been identified by EFSA after the meeting of experts to address the mobility of impurity DMTU in soil, in order to obtain adequate input parameters for ground water modelling (relevant for all uses evaluated, data gap identified after the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.1.3).
- A data gap was identified by the meeting of experts to address the effect of temperature on the dissipation of MITC from water by volatilization (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.2.1).
- A data gap for worst case PEC_{SW} estimations of MITC taking into consideration short range transport and deposition to surface water bodies and potential exposure via drainage with adequate input parameters was identified by the meeting of experts (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.2.1).
- A data gap was identified by the meeting of experts to recalculate MITC PEC_{GW} with adequate input parameters (when available) using FOCUS GW or higher tier approach if appropriate (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.2.2).
- A new data gap has been identified by EFSA after the meeting of experts, to address the potential ground water contamination of impurity DMTU (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.2.2).
- A data gap to address the atmospheric fate and behaviour of MITC including global warming ozone depletion, long range transport and deposition, and to address the potential contamination of surface water and soil by deposition in the vicinity of the applied areas was identified by the meeting of experts (relevant for all uses evaluated, data gap identified at the meeting of experts PRAPeR 52, proposed submission date unknown, refer to point 4.3.).
- Acute risk assessment for metam-sodium and MITC to birds and mammals that feed invertebrates is required (relevant for all out-door uses; submission date proposed by the notifier: unknown; data gap was identified during the PRAPeR 53; refer to point 5.1).
- A data gap for the submission of a new risk assessment to mammals based on the agreed endpoint of 100 mg/ kg bw has been identified (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; data gap identified by EFSA after the PRAPeR 53 meeting refer to point 5.1).

- The aquatic risk assessment needs to be revised when the new PEC_{sw} will be available. The reliability of the chronic exposure of the aquatic organisms should be confirmed after data gaps in fate and behaviour are solved; in case MITC DT₅₀ > 2 d, then the chronic risk assessment to aquatic organisms would have to be performed (relevant for all representative out-door uses evaluated; submission date proposed by the notifier: unknown; data gap was identified during the experts meeting; refer to point 5.2).
- Notifier to provide a semi-field or field study to address the recovery potential of the non-target arthropods after exposure to metam and MITC (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; data gap was identified in the DAR by RMS refer to point 5.4)
- Notifier to address concerns on the recovery/recolonisation of earthworms this should include considerations on effects on recovery of different ecological groups as well known data on migration distances (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; data gap was identified in the DAR by RMS; refer to point 5.5).
- A semi-field or field study to address the recovery potential of the soil non-target macro-organisms after exposure to metam and MITC (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; data gap was identified in the DAR by RMS; refer to point 5.6).
- A new data gap was identified by EFSA after the meeting of the experts to provide ecotoxicological data to address the equivalence of the relevant impurity DMTU compared with metam-sodium.

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The complementary dossier for resubmission was received by the RMS on 28 January 2010 and comprised a comprehensive assessment of each of the points in the “List of the studies to be generated, still available or available but not peer reviewed”. These assessments are supported by data and risk assessments, which have been evaluated in this amended DAR version (‘additional report’ in the format of an updated DAR).

The revised DAR is a stand-alone document that contains the evaluations already displayed in the original DAR and in the peer-reviewed addenda (under the mention “added in June 2008 - peer reviewed”), as well as the new evaluation and assessments produced in 2010 (under the mention “added in August 2010” or “revised in August 2010”). The new information (i.e. not yet peer-reviewed before) is highlighted in yellow in the work version.

1.2 Summary and assessment of information relating to the collective provision of dossiers (Document B)

“Taminco N.V. claimed that all reasonable steps were taken in order to make a joint dossier on Metam to support its inclusion in Annex I of Directive 91/414/EC.”

Taminco provided a detailed chronology of the contacts with FMC Foret and Lainco.

“FMC Foret and Lainco originally undertook notification of Metam sodium in Europe for first inclusion of the existing active substance (Metam sodium) in Annex I of Directive 91/414/EEC. FMC Foret and Lainco are currently working together through the European Metam Sodium Task Force for EU re-registration of Metam sodium. Commission Regulation (EC) No. 451/2000 of August 14, 2002 identifies FMC Foret and Lainco as notifiers of Metam sodium in Europe.

The European Metam Sodium Task Force is made up of the following companies:

FMC Foret, S.A.
Plaza Xavier Cugat, 2, Edificio C, planta 3ª
Parque de Oficinas Sant Cugat Nord
08174
Sant Cugat del Vallès
Barcelona
Spain

Lainco, S.A.
Polígono Can Cardí
Avda. Bizet, 8-12
08191 Rubí
Barcelona
Spain

The company Taminco and the European Metam Sodium Task Force were not able to reach an agreement to prepare a common dossier

1.3 Identity of the active substance (Annex IIA 1)

1.3.1 Name and address of applicant(s) for inclusion of the active substance in Annex I (Annex IIA 1.1)

Name: Taminco N.V.

Address: Panterschipstraat 207,
B-9000 Gent
Belgium

Telephone: [REDACTED]
Fax: [REDACTED]

Contact person: [REDACTED]
Telephone: [REDACTED]
Fax: [REDACTED]
E-mail: [REDACTED]

Alternative
contact person: [REDACTED]
Telephone: [REDACTED]
Fax: [REDACTED]
E-mail: [REDACTED]

1.3.2 ISO common name and synonyms (Annex IIA 1.3)

ISO common name: Metam

Variant 1:

Common name: metam-sodium

synonyms: metham-sodium, metham-Na

Variant 2:

Common name: metam-potassium

synonyms: metham-potassium, metham-K

1.3.3 Chemical name (Annex IIA 1.4)

IUPAC name: methylthiocarbamic acid

CA name: methylthiocarbamic acid

Variant 1: Metam-sodium

IUPAC: sodium N-methylthiocarbamate

CA: Methylthiocarbamic acid sodium salt

Variant 2: Metam-potassium:

IUPAC: potassium N-methylthiocarbamate

CA: Methylthiocarbamic acid potassium salt

1.3.4 Manufacturer's development code number (Annex IIA 1.5)

Not applicable

1.3.5 CAS, ECC and CIPAC numbers (Annex IIA 1.6)

CAS no: 144-54-7

CIPAC: 20

Variant 1: Metam-sodium

CAS no: 137-42-8

EEC: 205-293-0

CIPAC: 20.011

Variant 2: Metam-potassium

CAS no: 137-41-7

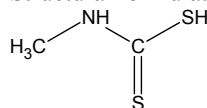
EEC: 205-292-5

CIPAC: 20.019

1.3.6 Molecular formula, molecular mass and structural formula (Annex IIA 1.7)

Molecular formula: $C_2H_5NS_2$

Structural formula:

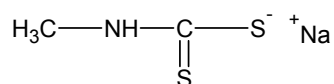


Molecular mass: 107.2 u

Variant 1: Metam-sodium

Molecular formula: $C_2H_4NNaS_2$

Structural formula:

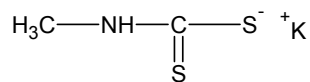


Molecular mass: 129.19 u

Variant 2: Metam-potassium

Molecular formula: $C_2H_4KNS_2$

Structural formula:



Molecular mass: 145.3 u

1.3.7 Manufacturer of the active substance (Annex IIA 1.2)

Name: Faminco N.V.

Contact:

Address:

Location of plant:

Telephone:

Fax:

1.3.8 Method or methods of manufacture (Annex IIA 1.8)

Confidential information, see Annex C

1.3.9 Specification of the purity of the active substance (Annex IIA 1.9)Metam-sodium TK (Technical concentrate, i.e. SL-formulation):

Declared metam-sodium content: 510 g/L at 20°C (42.1 % w/w)

Metam-sodium content: min. 400 g/kg – max. 442 g/kg (corresponding to range 485 – 536 g/L at 20°C)

→ FAO specification Code 20.1Na/13/S/15, published in AGP:CP/82 (1979), applicable to Metam-sodium aqueous solutions: “The metam-sodium content shall be declared (g/L at 20°C or % w/w). When the combined carbon disulphide is determined and expressed as metam-sodium the content obtained shall not differ from that declared by more than $\pm 5\%$ of the declared content.”

Min. purity of dry weight basis (calculated): 983 g/kg (cf. Vol.4, C.1.2.2)

Metam-potassium TK (Technical concentrate, i.e. SL-formulation):

Declared metam-potassium content: 690 g/L at 20°C (54.0 % w/w)

Metam-potassium content: min. 520 g/kg – max. 560 g/kg (approximately corresponding to the range 665 – 715 g/L at 20°C, which is in accordance with the FAO tolerance of ± 25 g/L from the declared content 690 g/L)

Min. purity of dry weight basis (calculated): 990 g/kg (cf. Vol.4, C.1.2.2)

1.3.10 Identity of inactive isomers, impurities and additives (Annex IIA 1.10)

Confidential information, see Annex C

→ FAO specification Code 20.1Na/13/S/15, published in AGP:CP/82 (1979), applicable to Metam-sodium aqueous solutions: “Insoluble material: maximum 0.2% retained on a 125 μ m test sieve.”

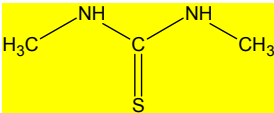
Compliance of the TK with the FAO specification for this parameter has been demonstrated by a wet sieve test: see Vol.3 B.2.2.25. [peer-reviewed in June 2008]

Reference: Re-submission dossier - Doc. J dated June 2010

During the first peer review of metam, the EFSA considered MITC (methyl isothiocyanate) to be a relevant impurity in the technical grade active ingredient and as a consequence, the applicant Taminco was requested to provide a revised specification in which MITC is listed with a maximum content value. The requested specification was presented in the resubmission dossier. The maximum content levels proposed for MITC are based on the 5-batch analysis results (using the thumb rule ‘mean + 3*SD’).

	MITC
IUPAC name:	Methyl isothiocyanate
CA name :	Methyl isothiocyanate
CAS No.:	556-61-6
EINECS No.:	209-132-5
molecular formula:	C ₂ H ₃ NS
structural formula:	CH ₃ -N=C=S
molecular mass:	73.11 u
max. content:	0.09 g/kg in metam-sodium TK (corresponding to 0.22 g/kg on dry weight basis); 0.22 g/kg in metam-potassium TK (corresponding to 0.42 g/kg on dry weight basis);

Also **DMTU** (N,N'-dimethylthiourea or 1,3-dimethylthiourea) is to be regarded as an impurity of potential toxicological relevance (cf. Vol.4 C.1.2.2):

1	DMTU
IUPAC name:	N,N'-dimethylthiourea
CA name :	Thiourea, N,N'-dimethyl-
CAS No.:	534-13-4
EINECS No.:	208-588-2
molecular formula:	C ₃ H ₈ N ₂ S
structural formula:	
molecular mass:	104.2 u
max. content:	2.9 g/kg in metam-sodium TK (corresponding to 7 g/kg on dry weight basis); 2.9 g/kg in metam-potassium TK (corresponding to 6 g/kg on dry weight basis);

1.3.11 Analytical profile of batches (Annex IIA 1.11)

Confidential information, see Annex C

1.4 Identity of the plant protection product (Annex IIA 3.1; Annex IIIA 1)

1.4.1 Current, former and proposed trade names and development code numbers (Annex IIIA 1.3)

Metam-sodium 510 g/L:

Different tradenames are used in different EU member states: Solasan, Terrasan, Monam, Nemasol, Traitam Sol, Metam sodio, etc.

Manufacturer's code number: not applicable

1.4.2 Manufacturer or manufacturers of the plant protection product (Annex IIIA 1.2)

Manufacturer of the preparations and the active substances:

Name: Taminco N.V.
 Contact: [REDACTED]
 Address: [REDACTED]
 [REDACTED]
 [REDACTED]
 Location of plant: [REDACTED]
 [REDACTED]
 [REDACTED]
 Telephone: [REDACTED]
 Fax: [REDACTED]

1.4.3 Type of the preparation and code (Annex IIIA 1.5)

Physical state : Soluble concentrate (SL)

1.4.4 Function (Annex IIIA 1.6)

Soil fumigant (nematicide, fungicide, herbicide, insecticide)

1.4.5 Composition of the preparation (Annex IIIA 1.4)Metam-sodium 510 g/L:

Technical active substance: 100 %
The preparation is identical to the technical grade active ingredient (metam-sodium as manufactured).

Pure active substance: 510 g/L $\pm$ 25 g/L (as determined with CIPAC method 20/13M/1.3)

Additives: see Annex C (Confidential information)

Metam-potassium 690 g/L:

Technical active substance: 100 %
The preparation is identical to the technical grade active ingredient (metam-potassium as manufactured).

Pure active substance: 690 g/L $\pm$ 25 g/L (as determined with CIPAC method 20/13M/1.3)

Additives: see Annex C (Confidential information)

1.5 Uses of the plant protection product**1.5.1 Fields of use (Annex IIA 3.3; Annex IIIA 3.1)**

Agriculture, horticulture (Field and protected crops)

1.5.2 Effects on harmful organisms (Annex IIA 3.2; Annex IIIA 3.2)

Metam-sodium acts as fumigant through rapid degradation to Methylisothiocyanate (MITC), which is active on living organisms present in the soil at the time of the application.

1.5.3 Summary of intended uses (Annex IIA 3.4; Annex IIIA 3.3 to 3.7, 3.9)

See listing of endpoints; Summary of representative uses evaluated

1.5.4 Information on authorizations in EU Member States (Annex IIIA 12.1)

Table 1.5.4-1: Authorizations and Registrations in the EU

Metam-sodium

Authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)	Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)
Belgium crops: soils, potting soils harmful organisms: nematodes, fungi, secondary effect as herbicide rates of application: 5 to 7.5 l/are number of applications: 1 timing of application: 3 weeks before planting/sowing	

Authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)	Actual uses, if current practice is known to deviate from the authorized uses (crops, harmful organisms, rates of application, number of applications, timings of applications - growth stages and where appropriate, season)
Cyprus crops: potatoes, carnations, seed beds, other crops (vegetables, etc) harmful organisms: nematodes: free nematodes (Pratylenchus, Tylenchorynchus), root nematodes (Meloidogyne, Heterodera), stem nematodes (Ditylenchus), Fungi (Pythium, Fusarium, Rhizoctonia, Phytophthora, Verticillium, Sclerotinia) Soil insects Weeds: annual and perennial (seeds, rhizomes, bulbs, tubers) rates of application: potatoes: 300-400 l/ha, carnations: 1500 l/ha, seed beds: 60-80 ml/m ² , other crops (vegetables etc.): 600-1000 l/ha number of applications: 1 timing of application: 3-4 weeks	
France crops: soils (general), tomatoes, carnations harmful organisms: Botrytis, Fusarium, Pythium, Rhizoctonia, Sclerotinia, Phoma, Nematodes, Phialophora (carnations) rates of application: 1200 l/ha number of applications: 1 timing of application: not specified	
Germany crops: potato harmful organisms: potato nematodes rates of application: 300 l/ha number of applications: 1 timing of application: when needed, late summer, before planting	

Greece crops: soils before culture, potting soil harmful organisms: nematodes (except cyst nematodes such as Heterodera); soil fungi (Phytophthora, Pythium, Sclerotinia, Fusarium, Verticillium, Rhizoctonia); weeds (emerged seeds of weeds until 25 cm of depth: Purslane, wild tomato, etc.) rates of application: normal soils: 1-1.25 l in 10 l of water/10 m². Heavy and wet soils: 1.5 l in 10 l of water/10 m². Very heavy-coherent soils: 2 l in 10 l of water/10 m² For the weeds: 0.5 l in 10 l of water for 10 m² of soil, for oxalys 0.5 l in 20 l of water/10 l of water/10 m². Potting soils: 1.25 l in 10 l of water/10 m². number of applications: 1 timing of application: before culture	
Hungary crops: vegetables, ornamentals, potatoes harmful organisms: use as soil fumigant rates of application: 1200 l/ha number of applications: 1 timing of application: before culture	
Ireland crops: soils harmful organisms: use as soil sterilant rates of application: 800 l/ha timing of application: no later than 21 days before preparation for the next crop	
Italy crops: bare soil intended for sowing or the transplanting of horticultural, ornamental and industrial crops, nurseries, seed-beds, mushroom-beds, glasshouses harmful organisms: fungi, nematodes rates of application: normally 750 litres/ha 1300-1500 litres/ha in heavy soils or where infected by Verticillium wilts (<i>Verticillium</i> spp.) Brown foot rot and ear blight (<i>Fusarium</i> spp.) <i>Phialophora</i> spp. number of applications: 1 timing of application: min. 8-14 days before planting or sowing	

Netherlands crops: potatoes, beets, strawberries, onions, perennial plants harmful organisms: nematodes crops: vegetables, flower bulbs, ornamentals, tree nursery harmful organisms: nematodes, fungi crops: soil harmful organisms: <i>Cyperus esculentus</i> L., <i>Cyperus tuberosus</i> Pursh crops: orchards harmful organisms: general soil disinfection before re-planting rates of application: 300 l/ha: potatoes, beets, onions 600-750 l/ha: strawberries, vegetables, perennial plants, flower bulbs, ornamentals, nursery trees, orchards 700 l/ha: control of cyperus number of applications: 1 timing of application: 3 to 6 weeks before planting or sowing	
Poland crops: soils harmful organisms: soil fungi, nematodes, germinating weeds rates of application: 70 ml/m² number of applications: 1 timing of application: 1.5-5 weeks before planting or sowing	
Portugal crops: all crops (before planting or sowing) harmful organisms: nematodes (<i>Ditylenchus</i>, <i>Meloidogynes</i>, <i>Aphelenchoides</i>, <i>Tylenchulus</i>) fungi (<i>Pythium</i>, <i>Rhizoctonia</i>, <i>Phytophthora</i>, <i>Verticillium</i>, <i>Fusarium</i>) rates of application: 750 - 1150 l/ha number of applications: 1 timing of application: min. 2-4 weeks before planting or sowing	
Spain crops: Seeding beds, nursery soils, vegetables harmful organisms and rates of application: soil fungi, soil insects, nematodes: 750-1200 l/ha annual weeds, oxalis: 2000 l/ha number of applications: 1 timing of application: before planting or sowing for light disinfection - potatoes: 200 l/ha	
UK crops: potting soils and other soils (indoor and outdoor) harmful organisms: nematodes, soil-borne diseases, weed seeds and seedlings, soil pests rates of application: potting soils: 1.05 l/5 m³ other soils: 1.8 l/20 m² timing of application: before planting edible or non-edible crops	

LEVEL 2

Metam

**Reasoned statement of the overall conclusions drawn by
the Rapporteur Member State**

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

2.1.1 Identity

Metam-sodium as manufactured by the main applicant Taminco (i.e. reference source) is a technical concentrate (TK) with an active ingredient (metam-sodium) content in the range of 400 to 442 g/kg. The minimum purity on dry weight basis (derived by calculation from the TK specification) is 983 g/kg.

Two impurities were identified as relevant, i.e. methyl isothiocyanate (MITC) and N,N'-dimethylthiourea (DMTU). Maximum contents were established based on the amounts of these impurities observed in the metam-sodium from the reference source (Taminco).

The technical specification proposed by Taminco was sufficiently supported by analytical data (5-batch analysis) and was considered acceptable from a toxicological, ecotoxicological and environmental point of view. Compliance with the current FAO specification (Code 20.1Na/13/S/15, published in AGP:CP/82 (1979)) was also demonstrated.

The applicant Taminco also provided a full data package on the identity of another variant of metam, namely the potassium salt of metam. The RMS evaluated this information and appropriate specifications supported by 5-batch analysis were set for the metam-potassium TK (containing 520 – 560 g/kg metam-potassium), as well as on dry weight basis. On the basis of a Tier II assessment, Taminco's metam-potassium source is considered equivalent to the metam-sodium reference source.

Furthermore, the RMS has considered two alternative sources of metam-sodium (FMC Foret and Lainco) for their equivalence to the Taminco reference source.

For the Lainco source, the provided data concerning the analytical profile did not enable an equivalence assessment and therefore, this source was not further considered. Regarding the FMC Foret source, equivalence could not be concluded on based on Tier I criteria. With the information available for a Tier II assessment, equivalence to the reference source could also not be concluded on.

2.1.2 Physical and chemical properties

Pure metam-sodium is a white crystalline powder with a sweet onion-like smell and a relative density (D_4^{20}) of 1.44. Its melting point is in the range 86.5 – 90.5 °C and decomposition has been observed at 150°C and at 215°C. It is moderately volatile (vapour pressure = $5.75 \cdot 10^{-2}$ Pa at 25°C) and readily soluble in water (578.29 g/L at 20°C) and thus, slightly volatile from water ($\alpha = 8.34 \times 10^{-6}$ Pa.m³.mol⁻¹ at 20°C). Metam-sodium is also readily soluble in methanol, but in other organic solvents, solubility is relatively low (< 0.26 g/L). It is not a surface-active compound (surface tension of 1 g/L aqueous solution at 21°C: 72.0 mN/m). In diluted concentrations, metam-sodium is subject to fast hydrolysis (estimated half-lives at 25°C ranging from few hours to few days). Main degradation products are MITC, methylamine and MCDT (sodium methylcarbamodithioperoxothioate). Hydrolysis appears to be accelerated with decreasing pH. In pH 7-buffered solution, metam-sodium is very rapidly degraded by direct phototransformation into N-methylthioformamide, MITC, methylamine and MCDT (photochemical half-life: $DT_{50} = 12$ min, equivalent to 27.8 min of natural sunlight at latitude 38° N). With a log Pow < -2.9, it is not critical with respect to bioaccumulation. It is not considered as highly flammable or auto-flammable and has no explosive or oxidising properties. Metam-sodium is expected to be very rapidly degraded in air.

The preparation **Metam-sodium 510 g/L (soluble concentrate, SL)** is identical to the technical product active ingredient as manufactured. It is a clear, yellowish solution with a weak CS₂ and H₂S odour and has a relative density (D_4^{20}) of 1.21 (at 20°C). Furthermore, metam-sodium 510 g/L is not considered auto-flammable and is not expected to have explosive or oxidising properties. The preparation has a pH around 9.6 and is not surface-active. No significant physical/chemical changes were observed after storage for 14 days at 54°C or for 7 days at 0°C. Moreover, the preparation was shown to remain stable after storage for 2 years at ambient conditions.

The flash point was determined to be > 97°C and thus, compliance with FAO specification (Code 20.1Na/13/S/15) (requiring flash point ≥ 66°C) was demonstrated. The amount of insoluble material retained on a 125µm test sieve meets the FAO spec. (i.e. max. 0.2% w/w).

A GLP storage stability study with analysis of the relevant impurities before and after storage (cf. data gap identified in EFSA conclusion of 26 November 2008) is ongoing.

Metam-potassium is another variant (salt) of metam. Based on the chemical similarity with metam-sodium, it is expected that hydrolysis, photolysis, octanol-water partition, **dissociation in water**, flammability, explosive and oxidising properties of metam-potassium will be comparable to that/those of Metam-sodium.

Purified metam-potassium is a pale yellow, crystalline/amorphous powder with a slightly acrid, sulphurous odour and a relative density (D_4^{20}) of 1.58. It decomposes (before melting) at a temperature of approximately 150°C. The determined octanol/water partition coefficient (log Pow of -3.47) reconfirms that bioaccumulation of metam-(potassium) in the environment is not to be expected.

The preparation **Metam-potassium 690 g/L (soluble concentrate, SL)** is identical to the technical metam-potassium as manufactured. It is a clear, light yellow liquid with a pungent, sulphurous odour and a relative density of 1.278 (at 20°C). The preparation has Newtonian fluid behaviour and is surface-active (surface tension of neat formulation and 1g/L aqueous solution: 51.5 and 55.1 mN/m at 20°C, respectively). A 1% (w/w) aqueous dilution has a pH of 7.69 (at 25°C). Furthermore, the preparation is not flammable (flash point > 102°C), not auto-flammable and no explosive or oxidising properties are to be expected.

Metam-potassium 690 g/L was found to be physically stable to storage at 0 °C for 7 days. The preparation was also shown to remain stable after storage for 2 years at ambient conditions. No persistent foam is formed when the preparation is diluted in water.

The amount of insoluble material retained on a 125µm test sieve meets the FAO spec. (i.e. max. 0.2% w/w).

A GLP storage stability study with analysis of the relevant impurities before and after storage (cf. data gap identified in EFSA conclusion of 26 November 2008) is ongoing.

MITC (impurity/main degradation product of metam):

Purified MITC is a colourless, crystalline solid. It is highly volatile (vapour pressure at 20°C: 1739 Pa) and readily soluble in water (8.94 g/L at 20°C) and thus, moderately volatile from water ($H = 14.2 \text{ Pa.m}^3/\text{mol}$ at 20°C). MITC has a log Pow of 1.05 and hence, bioaccumulation of MITC in the environment is not expected. Hydrolysis of MITC was found to be significant and appeared to be more extensive at higher temperatures and at higher pH (concomitant with higher hydroxyl ion concentration). Estimated half-lives at 25°C were 40, 50 and 11 days at pH 4, pH 7 and pH 9, respectively. Major degradation products were identified as dimethylurea (DMU), N,N'-dimethyl thiourea (DMTU) and methylthiocarbamic acid (MDTCA, i.e. metam). Furthermore, there were indications that volatile degradation products were formed at pH 4 (and pH 7).

DMTU (impurity):

DMTU is a highly volatile substance (vapour pressure of 832.95 Pa at 20°C). It is moderately volatile from water ($H = 0.149 \text{ Pa.m}^3/\text{mol}$ at 20°C), in which it is readily soluble ($\geq 581.98 \text{ g/L}$ at room temperature). Its low octanol/water partition coefficient (log Pow = - 0.23) indicates that bioaccumulation of DMTU in the environment is not to be expected.

2.1.3 Details of use and further information

Details of use

Metam-sodium is a soil disinfectant, which, is intended for use in the production of vegetables (in greenhouse and open field), Nurseries (trees, strawberry, tobacco), Ligneous plants (grape vines, fruit trees), Ornamentals (bulbs, cut flowers) to control soil-borne pest organisms. The soil-borne pest organisms to be controlled include fungi, nematodes, soil insects and weeds. The uses supported by available data are carrot (F), corn salad (=lamb's lettuce) (F), cucumber (G), eggplant / aubergine (G), pepper (G), potato (F), strawberry (F), tomato (F, G), grape (F) at the application rate of 153-612 kg a.s./ha before plantation. (local application of 1020 kg a.s./ha in the case of grape replanting)

Metam-sodium acts as fumigant through rapid degradation to Methylisothiocyanate (MITC), which is active on living organisms present in the soil at the time of the application.

The metam-sodium aqueous solutions are generally used without further dilution.

Application is done by direct injection or through drip-irrigation system.

- *Injection.* Metam-sodium is injected in the field at 15 cm depth and immediately homogenised within the soil by spading or roto-tilling in a depth of 25 cm; this allow a good diffusion of the metam-sodium in the whole mass of soil, thus enabling MITC to reach all infested sites. Soil surface is sealed with a roller in order to keep the fumes longer in the soil.
In grape vines, metam-sodium is applied occasionally and very locally by injection in the soil at 40 cm depth at the site of the de-rooted vine (0.2 L/m²). It should be noted that the corresponding dose rate of 1020 kg a.i./ha, as given in the GAP table below, refers to the specific spot treated and thus, the application rate on full field basis will be considerably lower.
- *Drip-irrigation.* Metam-sodium is directly injected in the drip-irrigation system by mean of a dosing pump or a venturi set, thus applied as a dilution. Application occurs under plastic mulch to keep the active fumes longer in contact with the organisms to be controlled.

After a waiting period of 13-45 days (depending on soil temperature, soil type), the soil is aerated by means of a cultivator and a cress germination test is performed in order to check the absence of phytotoxic MITC residues in the soil.

Details of intended uses supported by available data are summarized in the listing of endpoints.

Further information

Acceptable information has been provided for the active substance as manufactured and the plant protection product (recommendations concerning handling/storage/transport/fire, emergency measures in case of an accident, packaging, resistance of the packaging material to its contents, cleaning procedures, procedures for destruction or decontamination and methods for decontamination of water in case of an accident).

2.1.4 Classification and Labelling

Table 2.1.4-1 : Classification and labelling of Metam-sodium made by the Rapporteur

Classification :	Repr.Cat 3; R63; Carc. Cat 3; R 40: Xn; R20/22: C; R31:R34: R43; N, R50/53	
Hazard symbols :	C, Xn, N	
Indication of danger :	Corrosive, Harmful, Dangerous for the environment	
Risk phrases :	R20/22	Harmful by inhalation and if swallowed
	R31	Contact with acids liberates toxic gases
	R34	Causes burns
	R43	May cause sensitisation by skin contact
	R40	Limited evidence of a carcinogenic effect
	R63	Possible risk of harm to the unborn child
	R50	Very toxic to aquatic organisms
Safety phrases:	R53	May cause long-term effects in the aquatic environment
	S28	After contact with skin, wash immediately with plenty of water and seek medical advice

	S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
	S36/37/39	Wear suitable protective clothing, gloves and eye/face protection
	S42	During fumigation wear suitable respiratory equipment
	S45	In case of accident or if you feel unwell, seek medical advice immediately
	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

Table 2.1.4-2 : Classification and labelling of MITC made by the Rapporteur

Classification :	C ; R34 : T; R23/25: Xn ; R21 : R43; N, R50/53	
Hazard symbols :	C, T, N	
Indication of danger :	Corrosive, Toxic, Dangerous for the environment	
Risk phrases :	R23/25	Toxic by inhalation and if swallowed
	R34	Causes burns
	R43	May cause sensitisation by skin contact
	R21	Harmful in contact with skin
	R50	Very toxic to aquatic organisms
	R53	May cause long-term effects in the aquatic environment
Safety phrases :	S28	After contact with skin, wash immediately with plenty of water and seek medical advice
	S26	In case of contact with eyes, rinse immediately with plenty of water and seek medical advice
	S36/37/39	Wear suitable protective clothing, gloves and eye/face protection
	S42	During fumigation wear suitable respiratory equipment
	S45	In case of accident or if you feel unwell, seek medical advice immediately
	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

2.2 Methods of analysis

2.2.1 Analytical methods for analysis of the active substance as manufactured

The provided CS₂-evolution method based on CIPAC method 20/13/M/1.3 allows the determination of the a.i. content in the technical active ingredients, i.e. aqueous metam-sodium solution (TK) and aqueous metam-potassium solution (TK).

Fully validated analytical methods (HPLC-UV, titration, ion chromatography) are provided for the determination of the content of significant and relevant impurities in the technical active ingredient, i.e. aqueous metam-sodium solution (TK) and aqueous metam-potassium solution (TK).

2.2.2 Analytical methods for formulation analysis

The provided CS₂-evolution method based on CIPAC method 20/13/M/1.3 allows the determination of the a.i. content in the preparations, i.e. aqueous metam-sodium solution (TK) and aqueous metam-potassium solution (TK).

2.2.3 Analytical methods for residue analysis

The GC-MS method 234/2 has been sufficiently validated (incl. ILV) for the determination of MITC in **food/feed of plant origin** commodities with high water content and with high acid content. The LOQ of the method is 0.01 mg/kg. [added and peer-reviewed in June 2008]

No MRL's are proposed for **food of animal origin** and therefore, no enforcement method is required.

The LOQ of the GC-NPD method (Rooseboom-Reimers, 2002 – Report No. V4211), i.e. 0.02 mg/kg, is sufficiently low for enforcement of the general upper limit of 0.05 mg/kg for MITC in **soil**.

The LOQ of the GC-NPD method (Rooseboom-Reimers, 2002 – Report No. V4440), i.e. 0.1 µg/L, is sufficiently low for enforcement of the (drinking) water limit of 0.1 µg/L for MITC in **water**. Furthermore, all relevant concentrations that have an impact on non-target organisms were found to be above the LOQ.

Fully validated GC-NPD method (Schouten, 2007) allows determination of MITC in **air** with a LOQ of 0.5 µg/m³ and thus enables enforcement of the relevant residue limit (C = 1.2 µg/m³, based on proposed AOEL_{sys-temic} of 0.004 mg/kg b.w./day).

The submitted HPLC-MS method 557/8 allows determining the **acetyl cysteine conjugate of MITC** (i.e. N-acetyl-S-[(methylamino) carbothioyl]cysteine) in **body fluids** (blood plasma and urine) at a LOQ of 0.05 mg/L.

The fully validated GC-NPD method (Wolf, 2006) allows determining MITC in **liver** at a LOQ of 0.1 mg/kg.

2.3 Impact on human and animal health

2.3.1 Effects having relevance to human and animal health arising from exposure to the metam sodium or to their transformation products.

Absorption, distribution, metabolism and excretion:

Oral absorption of metam and its main metabolite MITC is rapid and important reaching a mean value of 85% and 90% of metam or MITC, respectively. Comparing the results from the high and low dose levels, it is clear that metabolism of metam sodium may be saturated at high dose levels resulting in a reduced breakdown of MITC, which is then excreted unchanged via exhaled air.

Tissue distribution is important and suggests that thyroid could be a target organ. Approximately 2.3% of the dose was still detected at 168 h in tissues. Half-life of elimination from plasma ranged from 60.8 to 74.1 hours.

Metabolism is extensive and rapid, suggesting a decomposition of metam into MITC, CO₂, and COS. MITC is further conjugated to GSH and excreted in urine while CO₂ and COS are excreted via expired air. The other significant pathway for metam is the release of CS₂, which could be related to the acidic conditions existent in the stomach of the rat (pH 3.8-5) following oral ingestion.

From published studies in the open literature, it appears that, although similar metabolites were identified in rats

and mice, non identified part of polar metabolites are more important in mice than in rats suggesting that metabolism of metam and MITC after ip administration, is quantitatively and qualitatively different. The majority of the material given was excreted within 24-48 h after administration with minor portions excreted up to 168 h after dosing.

Acute toxicity studies:

Metam breaks down to MITC, which is the ultimate toxicant. The gaseous decomposition of metam sodium into MITC under acidic conditions justifies the need for a R31.

Acute oral exposure to metam or MITC led to pilo-erection, hunched posture, abnormal gait, lethargy, decreased respiration rate, ptosis, and pallor of extremities, increased salivation, and clonic convulsions. Metam and MITC should be classified as harmful or toxic by ingestion, respectively.

After dermal exposure, hypothermia was reported after metam sodium while quite similar signs as those reported after oral exposure was seen after MITC dermal exposure. MITC should be classified as harmful by skin exposure.

After whole body inhalation exposure to metam, signs consistent with exposure to an irritant and toxic aerosol were noted. Histopathology of the lungs showed bronchiolar epithelial necrosis with inflammatory exudates. Classification as harmful by inhalation and R20 is required according to this study. A nose and head only inhalation exposure was realized where reddish discharges from nose and eyes were reported and animals had high stepping gait. According to the results of this latter study, metam should not be classified for inhalation toxicity. Clinical signs reported after exposure to MITC by inhalation were quite similar to those seen after metam. MITC requires a classification as toxic by inhalation (whole body inhalation study).

Metam and MITC were corrosive in the skin irritation test. No irritation effects were seen in the eye irritation test. Skin sensitization potential was seen for metam sodium and for MITC.

Table B.2.3.1-1: Summary of acute toxicity of Metam sodium

Type of test Test species	Test substance purity	Results	References
Acute oral, rat	Batch n°? 510 g/L	Combined: 896 mg/kg bw harmful Xn, R22	Baldrick and Healing, 1991a
Acute dermal, rat	Batch n°? 510 g/L	LD50 >2000 mg/kg bw	Baldrick and Healing, 1991b
Acute inhalation, rat whole body	Batch n°? 510 g/L	LC50combined= 2.54 mg/L Xn, R20	Jackson and Hardy, 1992
Acute inhalation, rat head and nose	42.2% batch ZH 130585	LC50 > 6.8 mg/L	Gelbke and Klimisch, 1986
Acute skin irritation, rabbit	Batch n°? 510 g/L	Corrosive : C, R34	Ligget and McRae, 1991a
Acute eye irritation, rabbit	Batch n°? 510 g/L	Non irritant	Ligget and McRae, 1991b
Skin sensitization- M&K test.	Batch n°? 510 g/L	Skin sensitizer, R43	Parcell and Danton, 1991

Table B.2.3.1-2: Summary of acute toxicity of Metam potassium

Type of test Test species	Test substance purity	Results	References
Acute oral, rat	batch n° V814/2207KF, 54.7% w/w	1000 mg/kg bw harmful Xn, R22	Sulaiman, 2004
Acute dermal, rat	V814/2207KF, 54.7% w/w	LD50 > 2000 mg/kg bw	Sulaiman, 2002
Acute inhalation, rat head and nose	batch n° V814/2207KF, 54.7% w/w	LC50combined= 3.04 mg/L Xn, R20	Venugopala Rao, 2002
Acute skin irritation, rabbit Metam sodium	Batch n°? 510 g/L	Corrosive : C, R34	Liggett and McRae, 1991a
Acute eye irritation, rabbit	batch n° V814/2207KF, 54.7% w/w	Non irritant	Prakash, 2002
Skin sensitization- M&K test	batch n° V814/2207KF, 54.2% w/w	Not sensitizer	Merkel, 2002

Table B.2.3.1-3: Summary of acute toxicity of MITC

Type of test Test species	Test substance purity	Results	References
Acute oral, rat	MITC; lot n° 6205 MK, 98%	Combined: 147 mg/kg bw. Toxic T, R25	Kieczka and Kirsch, 1986
Acute dermal, rat	Lot n° 6205 MK, 98%	1290 mg/kg bw Xn, R21	Kirsch and Hildebrand, 1987
Acute inhalation, rat whole body	98%	LC50 = 0.54 mg/L T, R23 Xi, R37	Jackson et al, 1981
Acute skin irritation, rabbit	Lot n° 6205 MK, 98%	Corrosive : C, R34	Kirsch and Kieczka, 1986
Acute eye irritation study		No study is required.	
Skin sensitization- M&K test	Batch n° 6205MK, 98%	Skin sensitizer; R43	Kieczka and Kirsch, 1986

Summary of short term-toxicity studies:

Drinking water range finding studies were performed with metam sodium for short periods of exposure in mice (6-8 days) and in rats (21 days). The studies were used to set dose levels for the subsequent 90 -day studies.

Rats and mice received metam sodium in drinking water for a 90-day period. Due to the instability of metam sodium in water, the doses of metam sodium actually received were recalculated assuming maximum degradation. In rats, at 18-20 mg/kg bw/d, the olfactory epithelium in the posterior nasal passage was affected and Bowman's glands were prominent and/or vacuolated and disorganized. The NOAEL was set at 0.79 mg/kg bw/d. In mice, at 36-38 mg/kg bw/d, mucosal hyperplasia and epithelial eosinophilia was apparent in the urinary bladder. Nasal cavity was not affected. A NOAEL at 0.49 mg/kg bw/d is proposed.

In a 65-day inhalation study, at 45 mg/m³ metam sodium (12 mg/kg bw/d), rats nasal passages presented a mild degree of mucigenic epithelial hyperplasia as well as lymphocytic rhinitis. Pulmonary histiocytosis and gastric erosions of the stomach were seen in both sexes at 160mg/m³ (42 mg/kg bw/d). The NOAEL was set at 6.5 mg/m³.

In dogs, metam sodium was given in capsules for 90 days and caused treatment related hepatitis at 5mg/kg bw/d onwards, resulting in the early termination of two dogs in the top dose group due to adverse clinical signs. Treatment-related hepatitis was associated with progressive inappetence and weight loss. There was a variety of changes, secondary to hepatotoxicity or indicative of generalized toxicity or poor clinical conditions. Consider-

able reversal of both macroscopic and microscopic changes in the liver had taken place between cessation of treatment with metam sodium and termination of the study. After 1-year, hepatotoxicity was more evident in female dogs as suggested by increased ALT and some liver histopathological findings. The NOAEL was set at 0.1mg/kg bw/d.

Rabbits did not show systemic toxicity after dermal exposure for 21 days to metam sodium. Local skin reactions such as erythema edema and rhagades and epidermis-dermatitis were seen at 62.5 and 125 mg/kg bw/d. NOAEL for local effects = 31.25 mg/kg bw/d.

A 4-week inhalation rat study was performed with MITC. At doses of 100 mg/m³, lung weight was increased, and was associated with bronchopneumonia and epithelial proliferation in bronchi and bronchiole. At this dose level, proliferation in tracheal epithelial cells and inflammatory changes in the nasal cavity and atrophy of the olfactory epithelium as well as focal metaplasia of squamous epithelial cells in the area of respiratory epithelium were reported. The company proposed a NOAEL = 20 mg/m³ (5.76 mg/kg bw/d). A NOAEL for systemic effects is proposed at 5 mg/m³.

In a 90-day dog study by gavage with MITC, at the dose level of 2 mg/kg bw/d body weight decrease, haematological findings and blood chemistry were observed.

As severe toxic effects are reported at doses lower than 50 mg/kg bw/d, RMS considers that metam sodium should be classified as R48/22.

According to the company, based on the provisions of EU Directive 2001/59/EC (28th ATP) and taking into account the NOAEL derived in the 90-day rat study, it is principally justified to classify metam with R48/22. However, there was no serious damage or even overt toxicity/mortality seen in the 90-day and/or one-year dog studies. The most pronounced effect in the 90-day study was hepatitis and a drastic increase in liver enzyme parameters.

These effects on liver and liver enzyme parameters were shown to be completely reversible with full recovery observable, which was agreed upon in the evaluation of the RMS. In light of the reversibility of effects on liver and liver enzymes, in the absence of other severe systemic effects and in view of the occurrence of effects in an individual animal only (see metam one-year study), a classification with R48/22 is not considered to be appropriate. Effects mediated by local contact at the site of first contact will be mitigated by consideration of suitable protective equipment and are not within the scope of the R48. Such effects are rather addressed by R phrases applicable for local effects (i.e. R34/35-R38/37/38).

Table B.2.3.1-4: Summary of short term-toxicity of Metam-sodium

Type of test Test species	Test sub- stance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
90-day drinking water study, mice at 0.018, 0.088, 0.35, 0.62 mg/ml	ref n° Y06930/007 and Y06930/008, 525.54 g/L	0.018 mg/ml = 0.8 mg/kg bw/d	0.088mg/ml = 4.5 mg/kg bw/d	↓water consumption, hematological changes, histopathological changes in bladder	Whiles, 1991
Oral 90-day drinking water study in rat at 0.018, 0.089 and 0.443 mg/ml	batch n° Y06930/007 and Y03930/008; 525.54 g/L	0.018 mg/ml = 0.5 mg/kg bw/d	0.089mg/ml = 3.1 mg/kg bw/d	↓ body weight, food and water consumption; nasal histopathological findings at top dose	Allen, 1991
Oral 90-day gavage study in dog at 1, 5 and 10 mg/kg bw/d	ref n° BAS 005 00N with CTL ref n° Y06930/008 at 43.15%	1 mg/kg bw/d	5 mg/kg bw/d	Clinical signs of toxicity, hepatitis, urinary bladder cell increased mitosis	Brammer, 1992
Oral 1-year dog study by gavage at 0.05, 0.1 or 1 mg/kg bw/d	batch reference n° BAS/005/00N 90-2; CTL n° Y06930/008; 525.54 g/L	0.1mg/kg bw/d	1mg/kg bw/d	Hepatotoxicity (blood chemistry and histopathological findings)	Brammer, 1993

Type of test Test species	Test sub- stance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
	(43.148% w/w)				
Inhalation 90-day rat study at 6.5, 45, 160 mg/m ³	Vapam technical: lot n° EHC 0355-21; containing 32.7% metam sodium.	Metam: 6.5 mg/m ³ = 1.75 mg/kg bw/d	45 mg/m ³ = 12 mg/kg bw/d	Liver and nasal toxicity	Knapp, 1983
Percutaneous 21 day rabbit study at 31.25, 62.5 or 125 mg/kg bw/d	BAS 00500 N; 42.4%	NOAEL local effects = 31.25 mg/kg bw/d NOAEL systemic effects	62.5 mg/kg bw/d >125 mg/kg bw/d	Local dermal effects: erythema, edema, rhagades; epidermodermatitis No systemic toxicity.	Leuschner, 1979

Table B.2.3.1-5: Summary of short term-toxicity of MITC

Type of test Test species	Test sub- stance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
MITC: 4-week inhalation study in rats at 5, 20, 100 mg/m ³	Batch n° 6205MK, 96.9%	5mg/m ³ (1.7 ppm)	20mg/m ³ = 6.8 ppm	Nasal cavity atrophy	Klimisch, 1987
MITC: 90-day dog study gavage at 0.04, 0.4 or 2 mg/kg bw/d	MITC: batch n° BX340178 AD11308, 95.96% and batch n° BX 340178 AD11328 at 95.96% formulation CR 20593/AD11331	0.4 mg/kg bw/d	2 mg/kg bw/d	body weight decrease, haematological findings and blood chemistry	Harling et al, 1986

Summary of genotoxicity

Metam-sodium was evaluated for possible mutagenic/genotoxic effects in *in vitro* test systems using bacterial and mammalian cells and in *in vivo* test systems using hamsters and mice.

In the bacterial revertant assay, employing the standard plate test as well as the preincubation test method Metam-sodium was negative in the presence or absence of metabolic activation towards *S. typhimurium* strains TA 92, TA 98, TA 100, TA 1535, TA 1537 and TA 1538.

In the HGPRT assay in CHO cells, slight increases in mutation rates cannot be ruled out completely although the results are not dose-related.

Metam-sodium revealed a slight clastogenic activity in the presence and absence of metabolic activation in the first chromosome aberrations test and in the presence of metabolic activation system in the second test, both performed in human lymphocytes. Increases in structural chromosomal aberrations were observed at concentrations that had cytotoxic effects on chromosomal morphology which prevented metaphases from accurate analysis for structural chromosomal aberrations.

In the *in vitro* UDS assay to assess DNA damage in freshly isolated primary rat hepatocytes metam-sodium did not induce unscheduled DNA synthesis even at concentration being cytotoxic as demonstrated by the net nuclear grain count and the percentage of nuclei with more than 6 or 20 grains.

Metam-sodium did not induce micronuclei in bone marrow polychromatic erythrocytes in male and female CD-1 mice and does not possess clastogenic activity in the mouse bone marrow micronucleus test.

In the *in vivo* chromosome aberration test performed in Chinese hamsters, Metam-sodium is not clastogenic.

In conclusion, Metam-sodium induced equivocal results in *in vitro* tests evaluating mammalian gene mutations and chromosomal aberrations.

Metam sodium did not induce unscheduled DNA synthesis in primary hepatocytes. *In vivo* cytogenic investigations were negative. Overall, it can be concluded that metam sodium is not genotoxic *in vivo*.

Table B.2.3.1-6: Summary of genotoxicity of Metam-sodium

Type of test Cell/Test species	Conditions	Test substance purity	Results	References
In vitro tests				
<i>Salmonella typhimurium</i> strains TA 92, TA 98, TA 100, TA 1535, TA 1537 and TA 1538	Standard plate test: 20 – 5,000 µg/plate (+ S9/-S9) Preincubation test: 4 – 5,000 µg/plate (+ S9/-S9)	Batch n° ZH130585; 42.2%	Negative	Engelhardt, (1987)
CHO cells (HGPR) locus	0.0000464 - 0.01mg/mL (+/-S9)	Batch n° ZH130585; 42.2%	Equivocal	Engelhardt, (1987)
CA in human lymphocytes	+ S9: 10 – 40 µg/mL - S9: 1 – 20 µg/mL	Batch n° ZH130585; 42.2%	Positive	Gelbke and Engelhardt, (1987)
CA in human lymphocytes	+ S9: 5 – 40 µg/mL - S9: 2.5 – 30 µg/mL	Batch n° WCR 14989-13-01 ; 32.3%	Equivocal	Mackay, (1996)
<i>in vitro</i> UDS	primary rat hepato- cytes 0.5 – 250 nL/mL	Batch n° ZH130585; 42.2%	Negative	Cifone, (1987)
In vivo tests				
Micronucleus test Bone marrow cells CD1-mice	single oral dose males and females: 500 mg/kg bw bone marrow sampling 24 and 48 h after dosing	Batch n° WCR 14989-13-01 ; 32.3%	Negative	Barber and Mackay (1996)
Cytogenetic study <i>in vivo</i> Bone marrow cells of male and female Chinese hamsters	single oral dose (gavage) males and females: 0, 150, 300 and 600 mg/kg bw bone marrow sampling 6, 24 and 48 h after dosing	Batch n° ZH130585; 42.2%	Negative	Gelbke and Engelhardt (1987)

MITC was not mutagenic in *Salmonella typhimurium* strains TA98, TA100, TA1535, and TA1537 in the presence and absence of metabolic activation.

MITC has no chromosomal damaging effects in an *in vitro* test using human lymphocytes.

MITC was further negative in recombination assays in *Bacillus subtilis* strains H17 and M45 with and without metabolic activation.

In the *in vivo* mouse micronucleus test, MITC did not increase the number of micronucleated polychromatic erythrocytes.

MITC is not genotoxic. From open literature, it was reported that MITC was not genotoxic.

Table B.2.3.1-7: Summary of genotoxicity of MITC

Type of test Cell/Test species	Conditions	Test substance purity	Results	References
in vitro tests				
<i>Salmonella typhimurium</i> strains TA98, TA100, TA1535 and TA1537	+ S9: 20 – 5,000 µg/plate - S9: 20 – 5,000 µg/plate	Batch n° 6205 MK. 98.1%	Negative	Engelhardt, and Gelbke, 1986
Recombination assays with <i>Bacillus subtilis</i> H17 (rec+) and M45 (rec-)	+ S9: 1 – 10,000 µg/plate - S9: 1 – 10,000 µg/plate	Id n° 85/231 charge 6205 MK. 98.1%	Negative	Jagannath, 1989
CA in human lymphocytes	+ S9: 0.05, 0.1, 0.5 µg/mL - S9: 0.1, 0.5, 1.0 µg/mL	Batch n° 6205 MK. 98.1%	Negative	Engelhardt and Gelbke, 1987
in vivo tests				
Micronucleus test Bone marrow cells CD1 Swiss mice	single oral dose males and females: 110 mg/kg bw bone marrow sampling 24, 48 and 72 h after dosing	Batch n° 340178 B19 and batch n° 340173 B23 at 95.86%	Negative	Allen et al (1985)

Summary of long-term studies:

Metam sodium was administered to rats in drinking water for 2 years. At 0.19 mg/ml, rats showed signs of systemic toxicity indicated by reduced bodyweight gain, specific lesion within the nasal passages, and changes in some hematology and spleen (hemosiderin depots) parameters and a slight increase in the severity but not of incidence of degenerative myopathy of the voluntary muscle. There were a few changes associated with the 0.056 mg/ml dose level, which were consistent with, but less marked than effects at the high dose. The incidence of hemangiosarcoma in males in the mesenteric lymph nodes was slightly higher than the control at the intermediate dose of 0.056 mg/ml but this effect was not observed at top dose. In view of the overall results obtained in this carcinogenicity study, it can be concluded that metam sodium is not carcinogenic in rats. A NOAEL was established at 0.019 mg/ml.

Mice received in their drinking water metam sodium at 0.019, 0.074 or 0.23 mg/ml for 24 months.

Both male and female mice had urinary bladder lesions and pathological significant changes were mainly present at 0.23 mg/ml. At 0.074 and 0.23mg/ml, there was an increased incidence of angiosarcoma in males and females. Metam sodium is carcinogenic in mice and the symbol **Xn** and risk phrase **R40** is proposed (limited evidence of a carcinogenic effect). A NOAEL systemic toxicity and carcinogenicity= 0.019mg/ml is proposed taking into account the increased incidence of urinary bladder epithelial hyperplasia, hepatocytic necrosis and increased incidence of angiosarcoma at 0.074 mg/ml.

The increased incidence of bladder neoplasia reported at top dose is associated with the treatment of metam sodium. The reason for this increase could be related to the induction of chronic hyperplasia in this organ. The extremely low incidence of neoplasia, however, indicates that the transition from hyperplasia to neoplasia is a rather rare event.

Rats received MITC via drinking water at 2, 10 or 50 ppm over 104 weeks. Reduced body weight of male rats, was more important at top dose at the end of the study period, white blood cell parameters, histopathological findings such as bone marrow hyperplasia, increased kidney microcalculi, liver effects, and spleen hyperplasia/increased haematopoiesis were reported at 50 ppm (1.6 mg/kg bw/d) and could be related to MITC exposure. MITC is not carcinogenic under these experimental conditions. A NOAEL=10 ppm (0.44 mg/kg bw/d) is proposed.

Mice received MITC in drinking water at 5, 20, 80 and 200 ppm. A NOAEL can be set at 20 ppm (3.3 mg/kg bw/d) taking into account the different slight effects seen at 80 ppm (12 mg/kg bw/d) such as the increased incidence of clinical signs, slight decreased body weight and body weight gain, slight effects in blood and altered organ weights. MITC is not carcinogenic in mice.

Table B.2.3.1-8: Summary of long-term toxicity and carcinogenicity of Metam-sodium

Type of test Test species	Test substance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
Rat, 104 week drinking water study at 0.019, 0.056 and 0.19 mg/ml	batch n° BAS/005/OON 90-2; 525.54 g/L = 43.148% w/w	0.019 mg/ml = 1.5 mg/kg bw/d	0.056 mg/ml = 4.3 mg/kg bw/d	nasal passages toxicity, ↓ body weight, changes in some hematological parameters	Allen, 1991 Rattray, 1994
Mice study at 0.019, 0.074 or 0.23 mg/ml in drinking water for 24 months	Batch n° BAS/005/00N 90*2; 525.54 g/L (43.148%)	0.019 mg/ml (1.9 mg/kg bw/d)	0.074 mg/ml (7.2 mg/kg bw/d)	Urinary bladder hyperplasia, incidence of angiosarcoma, and at top dose: urinary bladder neoplasm Xn, R40	Horner, 1994 Pistel, 1994

Table B.2.3.1-9: Summary of long-term toxicity and carcinogenicity of MITC

Type of test Test species	Test substance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
104 weeks rat study at 2, 10 or 50 ppm in drinking water	batch n° 28 166: 95.58%; batch n° 29 482: 95.41%; batch n° 29 482: 95.36% and batch n° 29 482: 96.06%	10 ppm (0.44 mg/kg bw/d)	50 ppm (1.6 mg/kg bw/d)	↓ body weight, altered WBC parameters, bone marrow hyperplasia, ↑ kidney microcalculi, liver effects, and spleen hyperplasia/ increased haematopoiesis	Brown, 1984 Brown, 1988 Iwan, Kaiser, and Hollihn, 1988
Mice, drinking water study at 5, 20, 80 and 200ppm	lot n° MS 25206; 93.14%	20 ppm (3.3 mg/kg bw/d)	80 ppm (12 mg/kg bw/d)	↑ clinical signs, ↓ body weight, body weight gain, slight effects in blood and altered organ weights	Satoh et al, 1980 Shigeshi Toyoshima, 1982 Kashima and Sato, 1985 Hiraide, 1988

Summary of reproduction toxicity studies:

In rats, metam sodium was tested in a multigenerational drinking water study corresponding to 1.4-21.6 mg/kg bw/d.

At top dose, body weight was decreased on occasion in males and in females during the different phases of the study. Food consumption was reduced. In females, minimal to marked Bowman's gland duct hypertrophy with loss of alveolar cells was detected in the olfactory mucosa lining the nasal septum and turbinate bones at all

levels of the nasal cavity. The changes in the Bowman's gland were accompanied by degeneration/ disorganization/atrophy of the olfactory epithelium. The nasal lesion was a direct consequence of the increased dose taken by females during lactation. Nasal passage of offspring of either generation at any dose level was not affected. The percentage of pups live born was in excess of 94% for each group in both generations. There were no litter losses. There was a reduction in individual pup weight and in total litter weight and a reduction of pup weight gain at top dose in both generations. One female pup of top dose had no ocular tissues. Bilateral anophthalmia seems to occur spontaneously in the Alpk: APfSD rat and this isolated incidence in one generation only are considered to be of no toxicological significance.

Developmental studies were performed in rats by gavage at doses ranging from 5 to 120 mg/kg bw/d.

Maternal toxicity started at 10 mg/kg bw/d as suggested by the reduced body weight gain going to a reduced body weight when the dose increases. Reproduction parameters were not affected. A significantly increased post-implantation loss was reported at 120 mg/kg bw/d. At 60 mg/kg bw/d, one female had complete resorption. At 120 mg/kg bw/d, the number of live fetuses was reduced and means fetal weight was significantly lower.

Fetotoxicity was evident at 80 mg/kg bw/d with a reduced mean fetal weight. At 40 mg/kg, bw/d there was also some evidence for fetotoxicity.

Major defects were reported at 120 mg/kg bw/d, two fetuses/litter exhibited a meningocele (neural tube closure defect) and another fetus had bilateral microphthalmia. At 80 mg/kg bw/d, one fetus/1 litter had a meningocele.

At 60 mg/kg bw/d 5 fetuses/5 litters were affected: defects of eyes (3 fetuses with other head defects); 1 fetus had a shortened jaw and cleft lip, 1 had meningocele, 1 fetus had unossified 2nd, 3rd and 4th arches of the cervical vertebrae, and one fetus displayed an abnormal zygomatic arch. None of which has been seen historically in controls in the laboratory. At 20 mg/kg, one fetus had four major defects, including a shortened lower jaw, which has not been seen in historical data. At 5 mg/kg bw/d, two fetuses in the 5 mg/kg group had abnormal zygomatic arch. Whilst this defect was not seen at 20 mg/kg, a single incidence was seen at 60 mg/kg.

The incidence of specific major defects and number of fetuses affected at 5 and 20 mg was small, not statistically significant, and did not form part of any dose-response relationship, although the possibility of a treatment-related effect cannot be completely dismissed.

Skeletal anomalies and variations were detected in the vertebral column and in sternum and the number affected litters were increased as compared to the control and sometimes higher at 40 mg/kg bw/d than at 120 mg/kg bw/d. These effects were assessed as sign of immaturity of fetuses. There was a dose-related effect for retardations. Retarded ossification of fetal skeletons, especially the incomplete ossification of skull bones could be connected with the mechanism of development of meningocele and influence of metam sodium cannot be excluded.

In rabbits, metam sodium was given by gavage at doses ranging from five up to 100 mg/kg bw/d.

Body weight gain of dams at 100 mg/kg bw/d was lower on most days of treatment. The influence on body weight gain partly corresponds with the diminished feed consumption. At 60 mg/kg bw/d, dams lost considerable weight after starting of dosing and food consumption was reduced. Similar but less marked changes were seen in the 20 mg/kg bw/d group.

At 100mg/kg bw/d, the number of dead implants was increased, especially due to the high number of early resorptions. Increased post implantation loss was seen at 100 and 60 mg/kg bw/d, and reduced number of live fetuses/pregnant female was seen at 30, 60 and 100 mg/kg bw/d. At 60 mg/kg bw/d, fetal weight was decreased. Percentage of male fetuses was reduced and litters containing five or less fetuses did not included males.

Two fetuses in two litters of 100 mg/kg bw/d showed a meningocele or spina bifida. These are rare anomalies in the strain of rabbits used in this study. There was a slight dose-related increase in sternebra asymmetry. The influence of metam sodium cannot be ruled out.

In each of the reported metam sodium studies, single cases of rare anomalies, reaching no statistically significant, were reported at maternal toxic doses and influence of metam sodium cannot be excluded. RMS proposes to classify metam sodium **Repr.Cat 3; R63**.

Similar defects affected head of rat and rabbits and were related to neural tube closure or eyes defects. Fetuses showed retarded ossification in head but also in limbs, thoracic vertebrae, sternum, and these effects were seen at doses with maternal toxicity.

Table B.2.3.1-10: Summary of reproductive toxicity and teratogenicity of Metam-sodium

Type of test Test species	Test substance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
2 generation rat study in drinking water at 0.01, 0.03 or 0.1 mg/ml	batch ref BAS/005/00N; 526 g/L or 43.148%/w; CTL n0 Y06930/008	NOAEL reproduction toxicity >0.1 mg/ml = 12 mg/kg bw/d. NOAEL fetotoxicity= 0.03 mg/ml = 4 mg/kg bw/d NOAEL parental toxicity= 0.03 mg/ml = 4mg/kg bw/d	- 0.1 mg/ml =12.3 mg/kg bw/d 0.1 mg/ml	- ↓ pup and litter weight ↓ body weight during premating, gestation and lactation	Milburn, 1993
Developmental rat study, gavage at 0, 10, 40 ,120 mg/kg bw/d day 6-15 gestation	metam sodium batch n° ZH 130585; 42.2% or 517.3 g/L	NOAEL maternal toxicity= 10 mg/kg bw/d NOAEL developmental toxicity=10 mg/kg bw/d	40 mg/kg bw/d 40 mg/kg bw/d	↓body weight, body weight gain, food consumption ↑incidence of variations and retardations at maternal toxic doses; rare anomalies at top dose	Hellwig and Hildebrand, 1987
Developmental rat study, gavage 0, 5, 20 or 60 mg/kg bw/d days 7- 16	metam sodium (ref n° BAS/005/00N, CTL n° Y06930/008; 43.15% w/w)	NOAEL parental toxicity= 5 mg/kg bw/d NOAEL developmental tox=5 mg/kg bw/d	20 mg/kg bw/d 20 mg/kg bw/d	- ↓body weight gain, food consumption, piloerection, salivation and urinary incontinence ↓ossification consistent with ↓ fetal weight Major defects were observed at 60 mg/kg bw/d Developmental toxicity: Cat 3, Xn, R 63	Tinston,1993

Type of test Test species	Test substance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
Developmental rabbit study, gavage 0, 5, 20 or 60 mg/kg bw/d days 8- 20	metam sodium (ref n° BAS/005/00N, CTL n° Y06930/008; 43.15% w/w)	NOAEL parental toxicity= 5 mg/kg bw/d NOAEL developmental tox=20 mg/kg bw/d	20 mg/kg bw/d 60 mg/kg bw/d	↓body weight gain, food consumption, piloerection, salivation and urinary incontinence ↓ fetal weight, altered sex ratio Major defects were observed at 60 mg/kg bw/d Developmental toxicity: Cat 3, Xn, R 63	Hodge, 1993
Developmental rabbit study, gavage 0, 10, 30 or 100 mg/kg bw/d days 6-18	metam sodium (ref n° 85/232, batch n° ZH130585; 42.2% w/w)	NOAEL parental toxicity= 10mg/kg bw/d NOAEL developmental tox=10 mg/kg bw/d	30 mg/kg bw/d 30 mg/kg bw/d	↓body weight gain ↓ number live fetuses; ↑dead implants Major defects were observed at 100 mg/kg bw/d Devel- opmental toxicity: Cat 3, Xn, R 63	Hellwig, 1987

In a 2 generation rat drinking water study, MITC was given at 2, 10, 50-ppm corresponding to 0.13-5.63 mg/kg bw/d. Variations in weight gain were observed in both sexes at top dose which occasionally attained statistical significance. Gestation and lactation weight were not altered. Mating performance and fertility were not adversely affected. The number of pups born/female was marginally lower at 10 and 50 ppm without reaching statistical significance. Physical and functional development of pups was comparable amongst all groups. Slight delays in the onset of eye opening and pinna unfolding were observed at top dose but were considered incidental to treatment, as there were no delays in the completion of each parameter. Functional development of top dose pups was comparable to controls on days 1, 17 and 21.

In a developmental rat study, MITC was given by gavage at 0, 3, 10 or 30 mg/kg bw/d. At the end of the treatment, several dams at top dose had sticky and/or moist fur in the area of the snout before, and at the same location reddish but mainly dry fur. Body weight and body weight gain were significantly reduced at top dose and marginally at intermediate dose. Water consumption was increased in individual dams at 10 and 30 mg/kg bw/d. Reproduction data were not significantly affected in the groups. The number of foetuses weighing < 75% of the mean fetal weight/litter was increased at top dose. Placenta weight was significantly lowered at top dose. Sex distribution was comparable in the different test groups.

One anomaly (anophthalmia) was detected in one foetus/one litter at 10 mg/kg bw/d. No retardations were seen in any group. There were no statistically significant differences between the treated groups and the controls with regard to anomalies, variations and/or retardations.

In rabbits, MITC was given by gavage at 1, 3 or 10 mg/kg bw/d. No test article related signs or symptoms were observed in any female of the different groups. At top dose, a slightly higher reduction of mean body weight was considered to be compound-related. Food consumption was reduced at top dose from day 6-11.

No effects were seen on the mean number of implantations, pups or embryonic deaths. Body weight of fetuses were not affected. Sex ratio was similar in all groups. Investigations of the crania and body cavity and skeletal

of the fetuses did not show compound-related effects.

Table B.2.3.1-11: Summary of reproductive toxicity and teratogenicity of MITC

Type of test Test species	Test substance purity	Results			References
		NOAEL (mg/kg bw/day)	LOAEL (mg/kg bw/day)	Symptoms	
2-generation rat study, drinking water at nominal concentration of 2, 10 or 50 ppm	Batch n° 340178; purity?	NOAEL parental toxicity= 10 ppm =0.76-1.01 mg/kg bw/d) NOAEL reproduction toxicity > 50 ppm =3.6 mg/kg bw/d NOAEL offspring toxicity >50 ppm (3.6 mg/kg bw/d)	50 ppm (3.6 mg/kg bw/d) - -	↓ body weight gain - -	Barker (1987), Barker (1986) and Jackson (1988)
Developmental rat study, gavage at 0, 3, 10 or 30 mg/kg bw/d day 6-15 gestation	Batch n° ZH 6205 MK; 96.9%	NOAEL maternal toxicity= 3 mg/kg bw/d NOAEL developmental toxicity=10 mg/kg bw/d	30 mg/kg bw/d 10 mg/kg bw/d	↓ body weight gain, ↑ water consumption ↓ fetal weight	Hellwig and Hildebrand, 1987
Developmental rabbit study, gavage 0, 1, 3 or 10 mg/kg bw/d days 6-18	Batch n° ZNT 85/231-2; 98% w/w)	NOAEL parental toxicity= 3mg/kg bw/d NOAEL developmental tox=10 mg/kg bw/d	10 mg/kg bw/d -	↓body weight and body weight gain no effects	Becker et al, 1986

Summary of neurotoxicity studies

An acute neurotoxicity study was performed with metam sodium administered to rats at 50, 750 or 1500 mg/kg bw by gavage. In this study, a NOAEL systemic toxicity < 50 mg/kg bw/d was proposed and no neurotoxicity was seen in this study. NOAEL acute neurotoxicity > 1500 mg/kg bw/d. This study was conducted at very high dose levels and it is difficult to differentiate between direct and indirect effects on the nervous system. In any case, if metam should be considered as a neurotoxic substance, the effects reported in this study are observed at doses that are above the NOAEL for other toxic effects. Therefore, RMS concludes that the effects on the nervous system seen in this study are secondary to systemic toxicity.

In a repeat dose study, where metam sodium was administered in drinking water at doses going to 0.2 mg/ml (15-18 mg/kg bw/d), there were no signs of neurotoxicity.

Toxicity studies on metabolites

In soil, an average of 92% of metam sodium decomposes to MITC within a few hours and depending on soil moisture and soil decomposition, substantial amounts of MITC may remain in the soil for 12 days or more, in spite of the volatility of this compound. Photolysis of metam sodium in water and photolysis of MITC in air have been reported. Products in water include MITC and 1, 3-dimethylthiourea. Product in air includes methyl isocyanate (MIC) methyl isocyanide, sulfur dioxide, hydrogen sulfide, carbonyl sulfide, N-methylformamide and methylamine. Methylisocyanate is more toxic than MITC and it as well as some of these other compounds may contribute to some of the toxic effects of metam sodium.

Thus while metam sodium is itself non-volatile, its application results in significant production and emission of air contaminants. The half-life of MITC in air was reported as 29 to 39 hours in natural sunlight.

Therefore, following agricultural metam-sodium applications, inhalation exposure is essentially related to MITC, but might also include other degradation products such as CS₂, H₂S and MIC. There is uncertainty about how these breakdown products interact to produce the overall potential toxicity deriving from the use of metam-

sodium, but MITC, MIC and H₂S have all been associated with ocular and respiratory irritation. While there are no data to address mixed exposure effects, additive or synergistic effects of MITC, MIC and H₂S in respiratory and ocular tissues are plausible.

A quite complete dossier related to **MITC** is included in the DAR. For MIC, the company did not provide studies. Therefore, RMS used data reported in the open literature. ECB (Ispra) reported a rationale for classification of methylisocyanate as T; R24/R25 for dermal and oral toxicity, T⁺, R26 for inhalation and respiratory tract irritation (R37). MIC is a skin irritant (Xi, R38) and an eye irritant (R41). MIC is highly toxic for humans and an accidental release in Bhopal (India) caused thousands of deaths by acute respiratory failure. Respiratory toxicity was also seen in animal studies. MIC was classified by ECB as T⁺; R26, T; R24/25, Xn; R42/43, Xi; R37/38/41. H₂S is a respiratory tract irritant and symptoms commonly reported after accidental human exposure include dyspnea, sore throat, coughing, chest pain and signs of pulmonary obstruction.

Acute human exposure to CS₂ by inhalation leads to local irritation, pharyngitis and CNS toxicity.

Methylamine is known for its irritating properties to eyes; nose and throat upon brief exposure, and severe exposure may lead to pulmonary edema.

COS toxicity was investigated in laboratory animals and CNS lesions were reported.

The company addressed the possible presence of MITC, MIC, CS₂ and methylamine under field conditions at toxicologically meaningful concentrations after metam sodium applications. As reported under point B.6.15.2 in the study of Links, 2006, levels of CS₂, methylamine, and MIC at day 0-4 after application of metam sodium at realistic application conditions, were <0.4 mg/m³, 0.027 mg/m³, and <0.004 mg/m³, respectively. From this study, it was concluded that the potential exposure of the operator to MIC and the stationary measurements to MIC inside the tractor were both below the limit of detection. MIC, CS₂ and methylamine were not detected around the treated field. At detection limit, the upper bound estimate for results of MIC for all field samples would be 4-µg/m³. For CS₂ this would be 400-µg/m³ and for methylamine, this would be 27-µg/m³. Air concentrations of MITC ranged from the limit of detection (0.042 µg/m³) to a maximum concentration of 36-µg/m³ with a GM of 0.9 µg/m³ (n=96). The 95th percentile was 13.2 µg/m³. MITC concentrations in the tractor cabin were at the level of 0.070-0.076 mg/m³, during application reaching 0.107 mg/m³ outside the tractor.

These results show that under realistic application conditions of metam sodium, while MIC, CS₂ and methylamine were below the limit of detection, MITC was identified at significant levels, confirming the need to assess operator exposure to MITC but not to MIC or other metabolites. The toxicity of MITC was investigated by the company and a full dossier is included and reported in parallel to metam sodium.

Medical data:

The signs of toxicity are likely to be lachrimation, blepharospasm, conjunctivitis and chemical burns after contact with eyes, primary irritation, dermatitis, eczema, chemical burns after contact with skin, nausea, vomiting, burns, gastroenteritis, sleepiness, cardiac and respiratory disorders, shock, renal lesions after ingestion, and primary mucosal and upper respiratory tract irritation, throat pain, cough hoarseness after inhalation.

2.3.2 Acceptable daily intake (ADI)

Metam sodium/MITC is phytotoxic and damage to plants is noticeable rapidly making the plant/commodities not suitable for use. In order to avoid the risk of phytotoxicity, soil fumigation occurs usually 3-4 weeks prior to planting. Labels require a period of 3 weeks after metam sodium application to allow for dissipation of phytotoxic MITC before planting a crop.

Metam sodium is not stable when diluted and breaks down rapidly into MITC, the half-life of which in soil is short, ranging from several hours to seven days.

Metam sodium has been tested in rats, mice, dogs and rabbits by oral route or by inhalation. Depending on the species, target organ is respiratory tract, urinary bladder or liver.

After long-term exposure (104-weeks) to metam sodium in drinking water, the lowest NOAEL was reported in the rat at 1.5 mg/kg bw/d. In mice, a quite similar result was reported (NOAEL = 1.9 mg/kg bw/d).

However, a short-term drinking water study showed lower NOAELs in dogs, and in a 1-year dog study a NOAEL was proposed at 0.1 mg/kg bw/d.

Therefore, RMS considers that this dog study is the most appropriate for setting of an ADI for metam sodium. Applying a safety factor of 100 gives an ADI = 0.001 mg/kg bw/d.

$$\text{ADI metam sodium} = 0.001 \text{ mg/kg bw/d}$$

During the Peer-Review, the proposed ADI of Metam was confirmed.

For MITC, the lowest NOAEL = 0.4 mg/kg bw/d was reported in the 90-day dog drinking water study. (NOAEL revised upwards during the Peer-Review)

Applying a safety factor of 100 gives an ADI= 0.004 mg/kg bw/d.

$$\text{ADI}_{\text{MITC}} = 0.004 \text{ mg/kg bw/d}$$

The company had proposed to use the long-term drinking water study in mice with a NOAEL = 1.6 mg/kg bw/d (0.89 mg/kg MITC equivalent). Applying a safety factor of 100 gives an ADI= 0.02 mg/kg bw/d (0.009 mg/kg bw/d MITC equivalent).

2.3.3 Acute reference dose (ARfD)

Developmental toxicity was reported for metam sodium. In each of the reported studies, single cases of rare anomalies were reported at maternal toxic doses and detected in both rat and rabbit developmental studies. At maternal toxic doses, increased post implantation losses were reported.

RMS proposes to set an ARfD for metam sodium at 0.05 mg/kg bw/d, based on the NOAEL for developmental toxicity in rats at 5 mg/kg bw/d.

Initially, RMS proposed to set an ARfD for metam sodium at 0.05 mg/kg bw/d, based on the NOAEL for developmental toxicity in rats at 5 mg/kg bw/d.

During the Peer-Review, the proposed ARfD of Metam was revised upwards. The meeting agreed the ARfD was 0.1 mg/kg bw/day based on overall rat developmental study and supported by rabbit developmental study.

$$\text{ARfD}_{\text{metam sodium}} = 0.1 \text{ mg/kg bw/d}$$

The company made no proposal.

For MITC, an ARfD was initially proposed on the developmental toxicity NOAEL = 10 mg/kg bw/day reported in the rat study where pups showed a reduced body weight at 30 mg/kg bw/day.

However, during the Peer-Review, an ARfD of 0.03 mg/kg bw/day based on the NOAEL for rat maternal toxicity (at 3 mg/kg b.w./d in both the rat and the rabbit developmental study) with AF=100 was agreed upon.

$$\text{ARfD}_{\text{MITC}} = 0.03 \text{ mg/kg bw/d}$$

2.3.4 Acceptable operator exposure level (AOEL)

From the chemistry of metam sodium, occupational exposure is most likely to the volatile breakdown product, MITC, rather than to metam sodium, itself.

RMS proposes to set an AOEL systemic toxicity for metam sodium based on the 90-day drinking water rat study where a NOAEL= 0.5 mg/kg bw/d is proposed. This AOEL will be used for operator exposure assessment during mixing and loading operations. A correction for oral absorption is not required.

During the Peer-Review, the proposed AOEL of Metam was revised downwards. The AOEL originally proposed was 0.005 mg/kg bw/day, based on the 90-day rat drinking water study, with an SF of 100. It was agreed that the AOEL should be based on the one-year dog capsule feeding study at the same value as the ADI (0.001 mg/kg bw/day).

$$\text{AOEL}_{\text{metam sodium}} = 0.001 \text{ mg/kg bw/d}$$

In the initial DAR, the setting of an AOEL for operator exposure assessment on an oral study by gavage or drinking water was considered inappropriate for MITC, which is volatile, is the ultimate active substance, and is more toxic than the parent compound.

Inhalation toxicity of MITC was investigated after exposure of rats in a 4-week MITC inhalation study giving a NOAEL = 5 mg/m³ corresponding to 1.35 mg/kg bw/d.

Therefore, an AOEL for inhalation of MITC was initially proposed at 5 mg/m³ corresponding to 1.35 mg/kg bw/d.

While initially, the RMS proposed an AOEL of 0.0135 mg/kg bw for MITC, based on a rat 4 wk inhalation study, this proposal was criticised by some MS. It was noted that the overall database for MITC was based upon oral studies, although inhalation was the critical route of exposure. It was remarked that the 4 wk study on MITC was also supported by the 90 day study using Metam. In addition, it could be argued that 4 wks would reasonably cover the use pattern of the product (e.g. greenhouse application). However, taking into account the limited database for inhalation (only 4 wk study, and therefore of limited duration), it was considered by the meeting to use the NOAEL from 90 day oral dog study, as this duration could be considered more relevant for operator exposure (especially when the work of fumigation would be outsourced to contractors). In addition, the dog was considered the most sensitive species. On balance, during PRAPeR meeting, the experts agreed that the 90 day dog study on MITC should be used to set the AOEL, and it was considered that a 4-week would not be sufficient to cover the application window. This study was also used for the ADI. The agreed AOEL was 0.004 mg/kg bw/day for MITC.

AOEL MITC = 0.004 mg/kg bw/d.

Proposals from the company:

AOEL dermal (metam sodium) = 0.63 mg/person/day based on the 2 year carcinogenicity study in mice.

AOEL inhalation MITC = 1.7 mg/person/day based on the rat inhalation toxicity study.

2.3.5 Drinking water limit

The determination of a MAC value is not necessary, because according to Directive 91/414/EEC only the ADI and AOEL values have to be determined. In addition to this, the maximum admissible concentration of an active substance is 0.1 µg/L, as established by the Directive 89/778/EEC.

2.3.6 Impact on human or animal health arising from exposure to the metam sodium or to impurities contained in it

Operator, bystander, worker and resident exposure

Note for the revised DAR, prepared for the re-submission of the a.s. in August 2010.

The field and greenhouse trials were revisited, and operator, worker and bystander exposure to MITC re-assessed, based upon the conclusions of the EFSA and LoEP subsequent to the Peer-Review in 2008.

Input parameters were harmonised (70 kg b.w. for operators, and 60 kg b.w. for workers, bystanders and residents). The working duration was 7h/day for operators and 8h/day for workers. Bystanders were considered to be present in the neighbourhood of treated fields or greenhouses during one hour. Resident exposure was extrapolated for a 24h stay at more remote distances from the treated greenhouse (new trial).

The AOEL of MITC was 0.004 mg/kg b.w./d.

The exposure values based upon the agreed input parameters were compared with the revised AOEL, and the conclusions were amended accordingly.

For the sake of transparency, the agreed values were highlighted in yellow in the original text.

One new greenhouse study was added to the data package. Amendments and new data were highlighted in yellow. The new trial (reference IIIA 7.2.3 /03) was evaluated under **B.6.15.2.4 (Operator exposure towards MITC after application of Metam sodium in the greenhouse)**, "Second greenhouse trial (drip irrigation), evaluated during re-submission in August 2010"

All results (those agreed upon and concluded in the EFSA Report, and the new ones) are integrated in the final conclusions below.

Metam-sodium is a soil fumigant which is active against nematodes, soil-borne diseases, weed seeds, seedlings and soil pests. Metam-sodium is acting by decomposition to Methylisothiocyanate (MITC) and is used as a soluble concentrate (SL) containing 510 g/L (42.1 % w/w) Metam-sodium.

Metam-sodium is used to prepare soils for planting of crops like potatoes, cabbage, carrots, strawberries, melons, grapevine and orchards (see EU-GAP table).

Application of Metam-sodium is carried out by a soil-injection technique using tractor-mounted equipment as well as by a drip irrigation technique the latter of which does not require the presence of an operator except for coupling the drum to the drip irrigation installation. In addition, Metam-sodium is also applied for soil fumigation in greenhouses.

Metam-sodium is applied at a rate of up to 1200 L/ha corresponding to 612 kg Metam-sodium/ha and the product will be marketed in 60, 200 and 1,000 L containers or drums.

For the application of Metam-sodium for soil fumigation purposes the following application techniques are considered in this document:

- 1) Soil injection of the undiluted formulation followed by incorporation by rotavation and soil surface sealing with a roller (carrots, lamb's lettuce, potato, tomato) in field and in greenhouses.
- 2) Drip irrigation under plastic film on the planting row (cucumber, eggplant, pepper, tomato, strawberry) or on the planting row in glasshouse).

In order to clarify the different uses of Metam, two remarks are made on the EU-GAP table:

(i) the term "no dilution" was used in the sense that Metam is not diluted *prior* to application, contrary to what is common practice for most plant protection products. Metam is not to be loaded and mixed in a tank, so there is no "spray solution". In the case of drip irrigation with Metam the dilution with water takes place during the actual application, not in a tank but in the tubes of the irrigation system with instantaneous application.

(ii) It was of note that there was no exposure study in order to support the soil injection at 40 cm at the site of the de-rooted vine (0,2L/m²) in grapes. However, although the intended use in grapes is at the higher dose of 1020 kg a.s./ha, only an occasional treatment would be necessary (isolated cases of few trees in a row of vines), and the spot treatment at the foot of the de-rooted vine would most likely lead to a lower exposure of the operator than the treatment of a full field. The application rate on full field basis will be considerably lower than 1020 kg a.i./ha. Furthermore, the time between disinfection and the harvest of new grapes is considerably longer than in vegetable growing, therefore residue trials in this crop were considered less relevant. Taking this into account, the RMS considers this use in the EU-GAP table to be acceptable and covered by the risk assessments performed for the other intended uses. Refinements may however be considered at Member State level, if deemed necessary.

General summary and conclusions:

Operator, worker and bystander exposure to MITC after application of Metam

Measurements under realistic open field conditions, values as % of AOEL of MITC (0.004 mg/kg b.w./d) ; RPE (operator, worker) : combination filter A1P2, 2% penetration; figures including worst-case values

Operator, bw= 70kg, duration of the loading and application: 7 h/d

Worker, bw= 60kg, duration of the cultivation, seal breaking and/or plant hole drilling: 8 h/d

Bystander, bw= 60kg, presence in the neighbourhood of field or greenhouse at peak-level: 1 h/d

Operator exposure (personal measurements):

-Study 1*, soil injection:	450% of AOEL, w/o RPE	and 9.0% with RPE
-Study 2*, soil fumigation,	229% of AOEL, w/o RPE	and 4.6% with RPE
-Study 3*, soil injection,	239% of AOEL, w/o RPE	and 4.8% with RPE
-Study 4**, drip-irrigation;	145% of AOEL, w/o RPE	and 2.9% with RPE

[*: open field studies, **: newly submitted greenhouse/tunnel study]

Worker exposure ; 14-17 day after soil injection,

0-2 hr after breaking seal, personal measurements:

-Preparation of soil:	14-19% of AOEL w/o RPE	and 0.3-0.4% with RPE
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-Plastic film opening:	37% of AOEL w/o RPE	and 0.74% with RPE
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-Volatilisation from field, 18h post application, 1 m height

	27% of AOEL w/o RPE	and 0.54% with RPE
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-Hole drilling through plastic film, 18 days after greenhouse treatment (drip irrigation): personal measurement

	2.96% of AOEL w/o RPE	and 0.06% with RPE
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Bystander exposure (no RPE assumed):

-soil injection, distance of 100 m, during application:	18.7% of AOEL
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-soil injection, MITC in air 6 hour after application:	3.1% of AOEL
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-soil injection, 1.1-9 days after application, 1.5 m height:	7.3% of AOEL
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-drip irrigation in greenhouse, 10 h after application, at open side of greenhouse:	107-264% of AOEL
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drip irrigation in greenhouse, 10 h after application, 140-220m distance of greenhouse: 3.9% of AOEL

The exposure of a bystander, staying 1h in the neighbourhood of a freshly fumigated **field** is also below the AOEL, amounting to 19% of the AOEL in the worst case. However, at 10h post-application in a **greenhouse** (in fact an open tunnel), the ambient MITC level indicates that a bystander, staying 1 hour at the lee side of the open tunnel would be exposed at about 2.6× the AOEL. A less conservative approach, where average MITC levels were calculated from different sides of the greenhouse, or a time-weighted average for the period 2-14h post-treatment only at the open side of the tunnel, indicates that the exposure would be at the level of the AOEL. A resident, living at a distance of >140m from the treated greenhouse, would be exposed to about 4% of the AOEL, taking into account a presence during 24h when peak-levels of MITC were generated.

Overall, the application of Metam *undiluted* in **open field** by soil injection (including spot-application in grapes) is considered to be safe, if appropriate RPE is present.

The application in a **greenhouse** was not demonstrated to be safe in the case of soil injection.

However, it is proposed to handle the potential risk of the bystander by risk-mitigating measures (sufficient warning labels and installation of a safety perimeter around freshly treated *closed* greenhouses). It is stressed that the treatment should not be allowed while keeping the treated tunnels and greenhouses open. Greenhouses should be kept closed until 18d post-treatment.

A slight exceedance of the ADI was observed for the UK infants, toddlers and vegetarians (102-108 % of the ADI).

RMS considers that there is no chronic concern for the most sensitive categories of consumers based on the situation of no MITC residues that characterize the supervised residue trials.

There is no acute intake concerns for all the categories of the consumers.

2.4 Residues

2.4.1 Definition of the residues relevant to MRLs

-Plant products

The metabolism of Metam-sodium has been investigated in various crops (radishes, Chinese cabbage, tomatoes and turnips).

These studies were representative of the following categories of crops: root and tuber vegetables, leafy brassica and fruiting vegetables and therefore can be considered as sufficient to cover the supported uses on carrots, corn salad, cucumber, eggplant, pepper, potato, strawberry, tomato and grapes by soil injection or drip-irrigation of Metam-sodium on the planting row.

In radish roots and leaves, neither the parent compound nor its metabolite Methyl Isothiocyanate and the methylthiourea/ureas derivatives were detected in the different extracts. The TLC analysis of the organic extracts revealed broad zones of radioactivity spreading over the plates.

All the characterized compounds had a rather high polarity as concluded from their extractability into the aqueous soluble partitioned fractions and considering their chromatographic behaviour.

In Chinese cabbage leaves, partitioning of the extracted fractions revealed that the radioactivity was recovered mainly in the aqueous soluble phase.

The radioactive residues in Chinese cabbage leaves were found to have a highly polar character based on the extractability design and its behaviour on the TLC plates.

Neither the parent compound nor its metabolites Methyl Isothiocyanate or the methylureas/methylthioureas could be identified in the different extracts.

Ultrafiltration performed on the aqueous soluble fraction demonstrated that this fraction was related to very small molecules.

In tomatoes, the highly polar character of the radioactive residues in the extracted fractions was confirmed by their chromatographic behaviour.

Neither parent compound nor its metabolite MITC was present in detectable amounts.

No other metabolite could be detected since TLC analysis of the extracts demonstrated that sufficient isolation of the different fractions was impossible. In most cases, the radioactivity was spread widely over the plates.

As shown by ultrafiltration, a non-negligible amount of radioactivity exhibited a molecular weight less than 500 but further characterization was not possible as these polar radioactive residues could not be cleaved by enzymatic incubation (proteinase, β -glucosidase).

In turnip roots, TLC analysis of the hydrolysates extracts indicated a significant digestion of polar oligomers (radioactivity retained at the origin) and an increase in sugar and carbohydrate residues in the aqueous soluble fractions.

No Metam-sodium or its primary metabolite, MITC was found in either turnip root or top matrices.

No degradation of the parent compound into its substituted thioureas or methylated –ureas was observed.

The sequential hydrolysis of the post extraction solids with enzymes selective for cellulose, starch, protein and pectin and finally lignin extraction showed the distribution of the radioactive residues over a variety of natural products such as cellulose, hemicellulose, starch, proteins, pectin and lignin.

The radioactive residues of Metam-sodium were mainly characterized as natural products and the identification of glucose in the extractable residues suggested a complete incorporation of this compound into the carbon pool of the turnip crop.

The available metabolism studies showed that most of the radioactivity had been metabolised extensively and to a large extent incorporated into natural compounds such as sugars, starch, proteins, pectins, lignin and cellulose.

The residue definition for MRL enforcement purposes is proposed as MITC alone, as Metam-sodium is completely degraded in soil in its metabolite MITC, which shows biological activity.

-Livestock products

No metabolism and feeding studies in livestock were required and therefore no residue definition was proposed for animal matrices.

2.4.2 Residues relevant to consumer safety

The same residue definition in plant products as for monitoring applies for consumer exposure risk assessment.

2.4.3 Residues relevant to worker safety

See point 2.3.6.

2.4.4 Proposed EU MRLs and compliance with existing MRLs

Reference is made to Commission Regulation (EC) No.149/2008 amending Regulation (EC) No.396/2005 by establishing Annexes II, III and IV setting MRLs for products covered by Annex I thereto.

Expression of the residue	Crops	MRLs (mg/kg)
MITC	Carrots	0.01*
	Corn salad (lamb's lettuce)	0.01* (provisional) ⁽¹⁾
	Cucumber (G)	0.01*
	Eggplant (G)	0.01*
	Pepper (G)	0.01*
	Potato	0.01* (provisional) ⁽¹⁾
	Strawberry	0.01* (provisional) ⁽¹⁾
	Tomato (F/G)	0.01*
	Grapes	0.01* (provisional) ⁽¹⁾
⁽¹⁾ : Provisional MRL pending submission of additional residue trials.		

2.4.5 Proposed EU import tolerances and compliance with existing MRLs

None

2.4.6 Basis for differences, if any, in conclusions reached having regard to establish or proposal CAC MRLs

None

2.5 Fate and behaviour in the environment

2.5.1 Definition of the residues relevant to the environment

Soil

Due to a rapid degradation of Metam-sodium in soil, the predominant metabolite methyl isothiocyanate (MITC) rather than the parent Metam-sodium is considered as the only relevant residue for quantitation in soil.

MITC was detected in amounts of up to 90% of the applied parent in the aerobic soil metabolism study and acts as soil fumigant against a variety of soil borne pests.

The aim of the risk assessment for this active substance is the establishment of the duration of the toxic effects to the soil organisms and of the duration of their recovery/recolonisation period.

DMTU (impurity in the active substance) is transient in soil (geomean of 0.23 day). It is weakly sorbed to soil (average K_{Foc} of 22 mL/g; average $1/n$ of 0.76). The risk to groundwater has been assessed as negligible. The RMS considers that it is not necessary to include this compound in any residue definition for soil, water or air.

Residue definition for risk assessment (soil): Metam-sodium, MITC

Residue definition for monitoring (soil): MITC

Water surface and sediment

Due to a pronounced instability of Metam-sodium in water and sediment (DT_{50} whole system of 20 minutes), the predominant metabolite in water MITC rather than the parent Metam-sodium is considered as the only relevant residue in water and in sediment.

Other metabolites recovered in the water/sediment studies under aerobic and anaerobic conditions were lower than 5%AR after 8 hours.

Residue definition for risk assessment (surface water, sediment): MITC

Residue definition for monitoring (surface water, sediment): MITC

Ground water

Metam-sodium is rapidly degraded in the soil into MITC. The evaluation of possible groundwater contamination by the a.s. is not required.

Since the soil metabolite MITC was detected in soil in amounts greater than 5% of the applied parent, its relevance has to be checked according to the relevant guidance document (European Commission (2003): Guidance Document on the Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated Under Council Directive 91/414/EEC, Sanco/221/2000-rev.10-final):

MITC is the major metabolite that is biologically active. This metabolite is toxicologically and ecotoxicologically relevant. This compound is fully assessed in the DAR.

Residue definition for risk assessment: MITC

Residue definition for monitoring : MITC

Air

Degradation of Metam-sodium in soil or water results in the rapid formation of volatile breakdown MITC that can enter the air, while metam-sodium itself is not volatile and therefore not supposed to reach the air.

Residue definition for risk assessment: MITC

Residue definition for monitoring : MITC

2.5.2 Fate and behaviour in soil

Aerobic soil metabolism

The degradation and metabolism of [^{14}C]-Metam-sodium and its principal degradation product [^{14}C]-MITC have been evaluated in four soils under aerobic conditions at 20°C and 10°C. This study was designed to test the degradation of metam-sodium and MITC in soils by exclusion of dissipation through volatilization. The flasks were sealed during the incubation period, with aeration only at the end of each sampling interval.

The active substance metam-sodium and its major volatile metabolite MITC are rapidly degraded at 20°C, with a mean DT₅₀ of, respectively 10 minutes and 2.10 days. At 10°C, the degradation rates are 20 minutes and 8.31 days respectively for the a.s. and MITC. No other metabolite has been formed.

Mineralization reaches a maximum level 45.96-86.25% AR after incubation for 21 days at 20°C

Bound residue levels are in the range of 9.88-38.38% AR after incubation for 21 days at 20°C. Bound residue in two soil samples incubated for 21 days are containing 8.51-29.76 %AR as humin, 3.49-3.32% AR as fulvic acid and 1.09-0.15%AR as humic acid.

The geomean DT₅₀ of DMTU (impurity of the technical substance that has a maximum content of 3.5 g/L in metam-sodium) in soils is 0.23 days.

Anaerobic soil metabolism

Considering the supported uses of metam-sodium (Application into the soil by direct injection or through drip-irrigation system), it is not expected that metam-sodium or its volatile metabolite MITC would be exposed to anaerobic conditions. The efficacy of the compound is depending on volatilization of MITC in the soil pores under aerobic conditions.

Soil photolysis

As metam-sodium is incorporated in the soil with special equipment, it is basically not exposed to sunlight. Therefore it is not subject to photolysis. The volatile degradation product MITC dissipates from the soil and is therefore subject to the sunlight in the air phase.

As RMS, we consider that soil photolysis study is not required.

Field dissipation

The DT₅₀ lab determined at 20°C for both Metam-sodium and MITC is less than 60 days. However, several field studies were conducted, investigating the fate of MITC in the soil.

The field studies do not reflect the supported uses in Europe. The application was made by overhead-sprinkler system. The formulation was injected in the sprinkler irrigation pipeline while water was applied to the plot. Incorporation of the a.s. in soil was achieved by post-application spray irrigation in some experiments.

The method of application for the supported uses of metam-sodium in Europe is as follows:

- injection of the undiluted formulation in the soil or spray of the undiluted formulation onto soil, followed by incorporation by rotavation and soil surface sealing with a roller (carrots, lamb's lettuce, potato, tomato)
- injection of the undiluted formulation in the soil (grape replanting)
- drip irrigation under a plastic film on the planting row (strawberry)
- drip irrigation on the planting row in glasshouse (cucumber, eggplant, pepper, tomato)

As the active substance has not been incorporated deeply into the soil by rotavation in the field experiments, it can be expected that the volatilisation at soil surface is very important. Consequently, the dissipation rate of MITC is highly overestimated (Field dissipation of MITC in the range 0.54-3 days with a mean of 1.57 days). These results are not considered in the final risk assessment.

The additional field studies reported in the open literature are not adequate to derive regulatory endpoints.

The lab study of Hall (2004) is the most suitable study to determine DT₅₀ for PEC assessment.

The current regulatory simulation models available to predict concentrations in soil, water and air do not describe the key processes driving the dissipation of MITC well (especially volatile loss) and would return overly conservative Predicted Environmental Concentrations (PECs).

Soil residue testing - soil accumulation testing

Not required. Field DT90 of metam-sodium and MITC are < 1 year.

Soil adsorption of the active substance and metabolites

The Koc of metam-sodium is < 17.8 mL/g at pH 4 and 9

However, based on the rapid degradation of Metam-sodium to MITC, the relevance of its mobility is minor.

Mean Koc of MITC is 13.5 mL/g, mean 1/n is 0.83

The measured adsorption data for DMTU (impurity of the technical substance that has a maximum content of 3.5 g/L in metam-sodium) indicate that the substance is weakly sorbed to soil with an average K_{Foc} of 22 mL/g and an average 1/n of 0.76.

Column leaching studies

Not required. Adsorption/desorption studies are available for the the active substance and the major metabolite MITC.

Lysimeter study

Not required. The estimated PEC_{gw} for the active substance and metabolites were well below the 0.1 µg/l EU trigger value for a majority of FOCUS scenarios.

PEC soil

Metam-sodium is applied at the rates of 153-612 kg a.s./ha (broadcast application) or 1020 kg a.s./ha (localized application in grape)

The method of application for the supported uses of metam-sodium in Europe is as follows:

- injection of the undiluted formulation in the soil followed by incorporation by rotavation and soil surface sealing with a roller (carrots, lamb's lettuce, potato, tomato)
- injection of the undiluted formulation in the soil (grape replanting)
- drip irrigation under a plastic film on the planting row (strawberry)
- drip irrigation on the planting row in glasshouse (cucumber, eggplant, pepper, tomato)

The PEC calculations were performed for the worst case use in field tomato (higher dose rate of 612 kg a.s./ha, 15 cm incorporation).

The initial PEC soil were 272 mg a.s. /kg soil and 154 mg/kg soil respectively for metam-sodium (DT₅₀ of 0.0118 days) and MITC (DT₅₀ of 2.94 days, assuming complete degradation of the a.s. into MITC, molecular mass ratio DCVA/a.s. : 0.566/73.11/129.17).

2.5.3 Fate and behaviour in water*Hydrolysis*

Metam-sodium is readily hydrolysed (pH 5: DT₅₀ = 1.9 days; pH 7: DT₅₀ = 2.2 days; pH 9: DT₅₀ = 4.5 days).

Moreover, hydrolysis appears to be accelerated with decreasing pH. At low pH (pH 5), MITC and methylamine are the main degradation products. At higher pH (pH 7 and 9), mainly MITC (60% of AR at end of study at pH 7 (5d); 20% of AR at end of studies at pH 5 (1.8 d) and at pH 9 (5.4 d)); and MCDT (16% of AR at end of study at pH 9 (5.4 d)) are formed.

In a study acceptable as supplementary information, MITC is shown to degrade significantly by hydrolysis at every pH (DT₅₀ of ≈ 40, 50, 11 days at 25°C, respectively at pH 4, 7 and 9) and temperature (with the exception of pH 4 and 7 at 15°C).

Photolysis

In pH 7 buffered solution metam-sodium is very rapidly degraded by photolysis (DT₅₀ = 12 min (equivalent to 27.8 min of natural summer sunlight at latitude 38° N) into N-methylthioformamide (22% of AR after 25 min),

MITC (16% of AR after 25 min), methylamine (18% of AR after 25 min) and MCDT (14% of AR after 25 min).

Ready biodegradability

By default, metam is considered not readily biodegradable.

Water/sediment studies

In non-sterile aerobic water/ aerobic sediment system at 25°C in the dark, Metam-K metabolized with an estimated half-life of 19.72 minutes.

The major metabolite observed was MITC, which represented 74.4 % of the initial radioactivity at the 480 minutes sampling point. The fate of MITC in the aerobic water/sediment system was re-evaluated to obtain first order dissipation of DT_{50} values for MITC. These values include the volatilization of MITC from the system into the loss term. The half life of MITC in the system was found to be 158.75 min (2.6 hours).

No CO₂ determination has been performed (No NaOH trap present).

A second metabolite, identified as 1,3-Dimethylthiuramdisulfide (DMTD), reached a maximum of 29.0% of the initial radioactivity at 122 minutes, then declined to 13.6% at time 240 minutes and was not detected at 480 minutes.

The bound residue level decreased from a maximum level of 33%AR after 7 minutes to 14.4 %AR after 480 minutes (8 hours) .

The anaerobic aquatic metabolism was studied according to the same protocol in sterile and non-sterile systems. Metam-potassium degraded with an estimated half-life of 2.87 and 1.59 hours, respectively under non-sterile and sterile conditions.

The major metabolite observed was MITC, which represented 84.0% (non-sterile) and 65.0% (sterile) of the initial radioactivity by the end of the study. The fate of MITC in the anaerobic water/sediment systems was re-evaluated to obtain first order dissipation of DT_{50} values for MITC. These values include the volatilization of MITC from the system into the loss term. The half life of MITC in anaerobic non-sterile system was found to be 13.44 hours. In the sterile system, it was 10.60 hours.

Minor metabolites were formed during the course of this study at max level of 4.0% AR and decreased up to 0%AR after 3 days (under non-sterile anaerobic conditions).

The bound residue level reached a maximum level of 16.5% AR after 2 days (under non-sterile anaerobic conditions). No CO₂ determination has been performed (No NaOH trap present).

PECground water for metam-sodium and MITC

Simulations with MITC applied to carrots, corn salad, tomatoes and potatoes at rate of 1 x 86.6 – 346.4 kg MITC/ha corresponding to 153-612 kg a.s./ha, were conducted with the FOCUS-PELMO 3.3.2 and FOCUS-PEARL 3.3.3 and covered all relevant scenarios (Chateaudun, Hamburg, Jokioinen, Kremsmunster, Okehampton, Piacenza, Porto, Seville, Thiva).

Based on the very rapid degradation of Metam-sodium in soils, groundwater contamination with the parent compound can be excluded.

The PEC_{gw} should only be calculated for MITC

The FOCUS scenarios were appropriately chosen: representative crops are the field crops (no leaching for greenhouse crops; localized use, exceptional use in grapevine), application rate, one application/year.

The K_{foc}, Freundlich exponent were appropriately chosen.

As a general conclusion, it is expected that MITC would not exceed the 0.1 µg/L threshold under practical situations in several crop/pedoclimatic circumstances.

- A number of uses of metam-sodium occur under circumstances where downward movement of water is very unlikely. The applications to cucumber, pepper, aubergine and tomatoes in protected situations (glasshouse/polytunnel) are examples of such circumstances. In addition, application to strawberries outdoors involves covering the soil location with plastic film, which also prevents downward movement of water. The modelling undertaken in this exercise was based on the use of MITC as a soil fumigant.
- The uses on grapes are as a spot treatment and are very localised. Hence the overall application rate (for instance over an entire hectare) will be much lower than the application rate stated by m².
- The results of the simulations indicate that predicted environmental concentrations of MITC at 1 m soil depth could exceed 0.1 µg/L for some crop/scenario simulations. PECGW was simulated to be >0.1 µg/L for most winter carrot scenarios for both PELMO and PEARL. PECGW for carrots was lower for spring/summer applications. For FOCUS-cabbage, tomatoes and potatoes, PECGW for Porto, Sevilla and Thiva scenarios were all <0.1 µg/L. Simulations with FOCUS-cabbage were most likely to produce PECGW <0.1 µg/L. Consequently, in addition to glasshouse/polytunnel uses, safe use in 'open field' situations has also been demonstrated for several pedoclimatic scenarios.
- The PEC calculations have been performed under worst-case situation since the volatilization is not well simulated by the FOCUS modeling softwares. The soil is cultivated after a few days, before plantation, in order to enhance MITC volatilization.
- The specific mode of use of this a.s. also mitigates the possible groundwater contamination (in practice, application of metam-sodium is unlikely to occur annually)

PECgw were calculated for the impurity DMTU considering a 'worst case' application rate of 7 kg/ha. The results of the simulations indicate that predicted environmental concentrations of DMTU at 1 m soil depth would not exceed 0.1 µg/L for all crops and scenario simulations.

PECsurface water and sediment for metam-sodium and MITC

Simulations with MITC applied to carrots, corn salad, tomatoes and potatoes at rate of 1 x 86.6 – 346.4 kg MITC/ha corresponding to 153-612 kg a.s./ha, were conducted in accordance with the FOCUS Surface Water methodology at Steps 3/4 which has ten scenarios that together represent realistic worst-case combinations of soil, agriculture and weather across Europe (FOCUS, 2001). These simulations are used in conjunction with a suite of models to generate predicted environmental concentrations in surface water (PEC_{SW}) and sediment (PEC_{SED}). The models include SWASH v.2.1; Drift calculator v.1.1; MACRO v.4.4.2; PRZM_SW v.1.1.1 and TOXSWA v.2.2.1.

The input parameters that have been used in the FOCUS calculations have been appropriately chosen. PEC_{SW} and PEC_{SED} values for MITC have been calculated at Step 3 at appropriate application rates for the EU GAP. FOCUS Step 4 modelling has also been conducted to explore mitigation arising from the use of run-off reduction measures. The potential exposure at Step 4 was reduced for all PEC_{SW} values for run-off scenarios. Calculated PEC_{SW} values should be considered as unrealistically worst case, because FOCUS-MACRO and FOCUS-PRZM do not satisfactorily account for loss of volatile substances from the soil.

A number of uses of metam-sodium occur under circumstances where lateral movement of water is very unlikely. The applications to cucumber, pepper, aubergine and tomatoes in protected situations (glasshouse/polytunnel) are examples of such circumstances. In addition, application to strawberries outdoors involves covering the soil location with plastic film, which also prevents contact between lateral moving water and MITC in soil.

For the other uses, FOCUS surface water (SW) scenarios (FOCUS, 2001) provide a standard assessment tool. The use of MITC on carrots, corn salad, tomatoes and potatoes was simulated at application rates of 230.94 kg/ha, 173.21 kg/ha, 346.41 kg/ha and 86.60 kg/ha respectively using FOCUS surface water Steps 3 and

4. These PEC_{sw} have been taken as input for the TER aquatic organisms.

The assessment of risk to sediment organisms is not justified since

- The properties of MITC (low K_{oc}, high solubility in water) exclude exposure of the sediment organisms.
- low level of MITC observed transiently in the sediment phase of the w/s study (1.5-4.5 % AR in the sediment after 72 h)

The assessment of chronic risk to aquatic organisms is not justified since

- The DT50 MITC, whole water-sediment system is clearly below 2 days.
- The a.s. is applied once a year. Moreover, soil sterilants are generally not used every year.

Short-range transport

The input parameters that have been used in the EUSES calculations have been appropriately chosen. EUSES 2.1. predicts a worst case (19380 tonnes of metam-sodium, 100% emitted to air as MITC) EU-regional PEC_{SW} of 0.0153 µg/L following redistribution of MITC lost to air via volatilisation from treated soil which can be considered to assess the risk related to short range transport.

The risk to soil organisms related to short range transport (1.84 to 4.12 E-06 mg/kg soil) is covered by the risk assessment that has been performed for in-field exposure (max PEC = 153 mg MITC/kg soil)

The risk to aquatic organisms related to short range transport of MITC (0.0153 µg/L) is covered by the risk assessment that has been performed for edge-of-field exposure (max PEC_{sw} = 184 µg/L).

2.5.4 Fate and behaviour in air

Metam-sodium

Atkinson calculation of the oxidative photodegradation of Metam-sodium: the hydroxyl rate constant obtained was 64.3×10^{-12} cm³/molecule-sec and the half life was 1.997 hours (24h-day) (assuming a hydroxyl radical concentration of 1.5×10^6 OH/cm³). The a.s. is not persistent in atmosphere.

Metam-sodium is moderately volatile (vapour pressure of $5.75 \cdot 10^{-2}$ Pa at 25°C). It is very slightly volatile from water ($H = 1.28 \times 10^{-5}$ Pa.m³/mol at 25°C).

MITC

As revealed by the various soil metabolism study and by the water/sediment studies, MITC is the most significant volatile compound that can potentially reach the air. MITC is considered to be a highly volatile substance (vapour pressure of 1739 Pa at 20°C, interpolated from measurements at 15°C and 25°C). MITC is moderately volatile from water ($H = 14.2$ Pa.m³/mol at 20 °C)

The notifier submitted several field studies investigating the actual MITC concentrations in air. These studies were performed during the various steps of metam-sodium application (soil injection, seal breaking, soil injection in glasshouse) by professionals under the conditions of the practice (material, protective equipments, application period in autumn, realistic duration of the work). Data on the MITC concentrations in air at operator level (in the tractor) and at bystander level (at several meters of the field, outside the glasshouse) are available.

The rapporteur summarized the data in terms of MITC air concentrations expressed in mg/m³

All the studies indicated that the largest amounts of MITC are released to air at soil injection and for a few days after application (1-5 days). The levels of MITC released afterwards and at seal breaking are much lower.

The levels of MITC at several meters from the field are low (in comparison with the levels released at application site) and transient (no detectable level after a few days)

A high variability of the MITC concentrations is observed for the various experiments. This variability cannot

be explained in terms of application rate or material used.

Modelling simulations were provided by the notifier to evaluate the variability of MITC concentrations in air. The validity of these simulations is questionable.

The following MITC air concentrations are proposed for the operator/worker/ bystander exposure risk assessment.

Soil-injection using tractor mounted equipment (including tank filling)

- Exposure of the operator during soil-injection (including tank filling)

The level of 0.187 mg MITC/ m³ can be considered as a realistic worst case for operator exposure during soil injection. The max level is 0.592 mg MITC/m³ after minor incidents during application (contaminated gloves inside the cabin, contaminated soil on shoes)

- Exposure of the worker at seal removal (soil cultivation), cress test

The level of 0.0046 mg MITC/ m³ can be considered as a realistic worst case for worker exposure at seal removal and cress test.

- Exposure of the bystander during soil-injection

The level of 0.054 mg MITC/ m³ can be considered as a realistic worst case for bystander exposure during soil-injection of metam-sodium in field.

Glasshouse use (drip irrigation system)

- Exposure of the operator

The operator is not present in the glasshouse during application (closed system). Limited exposure can be expected during filling.

- Exposure of the worker at seal removal (soil cultivation), cress test

The level of 4.7 mg MITC/ m³ can be considered as a realistic worst case for worker exposure at seal removal and cress test.

- Exposure of the bystander

The level of 0.15-0.25 mg MITC/ m³, at 0-20 m distance, 0-4 days after treatment, can be considered as a realistic worst case for bystander exposure during the application of metam-sodium in glasshouse. Bystanders should not be allowed to stay near glasshouses (0-20 m) during treatments.

Exposure to CS₂, MIC, methylamine

Levels of CS₂, methylamine and MIC were respectively <0.4 mg/m³, <0.027 mg/m³, <0.004 mg/m³ (<LOD) at day 0-4 after soil injection. During this experiment, MITC has been recovered at level up to 0.036 mg/m³

Long-range transport (LRT)

It needs to be borne in mind that at this time there is no framework within Directive 91/414 to assess the risk arising from LRT, and particularly to the possibility of different sensitive species (FOCUS 2008).

The hazard potential to the atmosphere (long range transport) has been assessed according to the Focus guideline (2008). It depends strongly on the atmospheric residence time lifetime, which in turn depends on the rate by which removal processes (wet and dry deposition, chemical conversion) take place.

The estimation of the chemical conversion is based on the reassessment studies that have been submitted in the original dossier. MITC has been shown to have a DT₅₀ in air of a few days (DT₅₀ in troposphere (12 hr, days): 4.8-6.3 days), much less than 1 year. Even if the quality of studies and the accuracy of the results cannot be fully assessed by the RMS, similar estimations of degradation for other fumigants that have been performed by means of data proposed in the Guidance "Pesticides in air: considerations for Exposure assessment. SANCO/10553/2006 Rev 2 June 2008" indicate that the results are plausible (methylbromide, DT₅₀ OH radicals: 5.5 10⁸ days; 1,3-cis-dichloropropene, DT₅₀ OH radicals and ozone: 1.9 10⁶ days; chloropicrin, DT₅₀ photolysis: 0.28 days; methylisocyanate (degrade of MITC) DT₅₀ photolysis: 2.39 days)

The estimation of removal of air by deposition has been performed on the basis of the physicochemical proper-

ties that indicate that MITC is likely to be found in air, but with a high affinity for water. Therefore, it is likely to be partitioned predominately between the air and atmospheric water (including aerosols). This implies that MITC is susceptible to both wet and dry deposition and that it will be readily removed of the air column by precipitation.

Short degradation rates of MITC in soil (DT_{50} 2.1 days) and in water (hydrolytic DT_{50} at pH 7 and 25°C of 50 days; Lowrie, 2005) as well as its low bioaccumulation potential (MITC's relatively low LogP: 1.95, Flack, 1997) indicate that the risk related to residues re-deposited in remote environments is negligible. MITC does not contain halogen atoms and has not been considered by Montreal convention as a compound responsible of ozone layer depletion.

2.6 Effects on non-target species

Metam-sodium is a soil fumigant, formulated as an aqueous solution. Metam-sodium is rapidly degraded into Methylisothiocyanate (MITC), which is active on living organisms present in the soil at the time of the application.

The intended uses of metam-sodium are :

- carrot : 1 x 408 kg a.s./ha, field, soil injection + incorporation at 25 cm by rotavation
- corn salad : 1 x 306 kg a.s./ha, field, soil injection + incorporation at 15 cm by rotavation
- cucumber : 1 x 459 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- eggplant/aubergine : 1 x 612 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- pepper : 1 x 612 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- potato : 1 x 153 kg a.s./ha, field, soil injection + incorporation at 25 cm by rotavation
- strawberry : 1 x 612 kg a.s./ha, field, drip-irrigation under a plastic film on the planting row
- tomato : 1 x 612 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- tomato : 1 x 612 kg a.s./ha, field, soil injection at 5 cm + coverage by 10 cm of soil
- grape : 1 x 1020 kg a.s./ha, field, soil injection at 40 cm at the site of the de-rooted vine (0.2 L/m²)

The application of metam-sodium is on bare soil; the product is incorporated into the soil (soil injection or drip irrigation) and thereafter the soil is compressed with a roller. After a waiting period of 2 to 4 weeks, the soil is cultivated to allow the non-mineralised gasses to disperse. Since the product is phytotoxic, it is advisable to perform a germination test (Cress-test) on samples of soils collected from the treated field, before planting.

2.6.1 Effects on terrestrial vertebrates

The greenhouse uses of metam-sodium are excluded from the risk assessment since there will be no exposure to birds and mammals from closed crop systems.

The use of metam-sodium in grapes at vine planting is a very localized treatment and therefore the risk will be much lower and will be covered by the other field uses.

The field uses which distribute MITC widely throughout the soil, injection/rotavation, injection/coverage and drip irrigation are considered to present the greatest risk to birds and mammals, since the majority of the soil dwelling invertebrates will receive almost uniform exposure. These crops are carrot, corn salad and potato (injection/rotavation), tomato (injection/coverage) and strawberry (drip irrigation).

2.6.1.1 Effects on birds

TER calculations were performed for the acute and short-term risk assessment for birds based on the endpoints from studies performed with metam and converted into MITC, giving LD₅₀ (*Colinus virginianus*) = 119 mg MITC/kg b.w. and LC₅₀ (*Anas platyrhynchos*) > 183.4 mg MITC/kg b.w./day.

The acute risk assessment was based on first tier assumptions (PD, PT = 1) and initial measured residues resulting in TER of 6.23, 6.23, 9.37, 12.5 and 25.0 for insectivorous birds and TER of 6.80, 6.80, 10.2, 13.6 and 27.3 for vermivorous birds in strawberry, tomato, carrot, corn salad and potato, respectively.

The short-term risk assessment was based on first tier assumptions (PD, PT = 1) and arithmetic mean measured residues resulting in TER of 21.0, 21.0, 31.6, 42.1 and 84.3 for insectivorous birds and TER of 22.9, 22.9, 34.5, 45.9 and 92.0 for vermivorous birds in strawberry, tomato, carrot, corn salad and potato, respectively.

The risk is acceptable for the intended field uses in potato, corn salad and carrot (application rates 153, 306 and 408 kg a.s./ha). The risk is acceptable for the intended field use in strawberry (612 kg a.s./ha) due to the plastic film preventing exposure to birds. However, risk mitigation measures are needed for the intended field use in tomato (612 kg a.s./ha) since the acute TER value is below the trigger value and the fresh soil layer is not regarded sufficient to reduce the exposure to birds.

2.6.1.2 Effects on mammals

TER calculations were performed for the acute risk assessment for mammals, based on the worst case acute toxicity endpoint for MITC (from dossier dazomet), LD₅₀ (female mouse) = 100 mg MITC/kg b.w.

The acute risk assessment was based on initial measured residues and PD = 1, resulting in TER of 5.32, 5.32, 8.01, 10.6 and 21.3 for insectivorous mammals and TER of 4.49, 4.49, 6.75, 8.98 and 18.0 for vermivorous mammals in strawberry, tomato, carrot, corn salad and potato, respectively. Refinement in the diet of the woud

mouse is taken into consideration. For insectivorous mammals PD was set at 0.16 resulting in TER of 33, 33, 50, 67 and 133 for strawberry, tomato, carrot, corn salad and potato. For vermivorous mammals PD was set at 0.40 resulting in TER of 11, 11, 17, 22 and 45 for strawberry, tomato, carrot, corn salad and potato. The risk is acceptable for the intended field uses in potato and corn salad (application rates 153 and 306 kg a.s./ha) for insectivorous mammals based on first tier assumptions (PD = 1). The risk is acceptable for the intended field uses in carrot, strawberry and tomato (application rates 408 and 612 kg a.s./ha) for insectivorous mammals based on refinement (PD = 0.16). The risk is acceptable for the intended field use in potato (application rate 153 kg a.s./ha) for vermivorous mammals based on first tier assumptions (PD = 1). The risk is acceptable for the intended field uses in corn salad, carrot, strawberry and tomato (application rates 306, 408 and 612 kg a.s./ha) for vermivorous mammals based on refinement (PD = 0.40).

In conclusion, the risk of metam-sodium and its metabolite MITC to birds and mammals is acceptable for the intended uses.

2.6.2 Effects on aquatic species

The application of metam-sodium is on bare soil and the product is incorporated into the soil (soil injection or drip irrigation). Based on the application technique, drift of metam-sodium and its metabolite MITC to surface water can be excluded. Because of the rapid degradation of metam-sodium in soils (DT_{50} between 4 and 17 minutes), surface water contamination with the parent molecule can be excluded. Aquatic organisms may be exposed to the metabolite MITC as a result of drainage or run-off from treated fields.

The indoor uses pose no concern for surface water contamination (e.g. cucumber, eggplant/aubergine, pepper and tomato) whilst the outdoor uses on strawberries occur under a plastic film, thus also preventing connectivity between soil and run-off water. Therefore no MITC contamination of surface water bodies via run-off is possible for this use. The uses on grapes are as a spot treatment and are very localized. Hence the overall application rate (for instance over an entire hectare) will be much lower than the application rate stated by m^2 .

The Predicted Environmental Concentrations of MITC in surface water were calculated for the use in carrot (1 x 408 kg a.s./ha), in corn salad (1 x 306 kg a.s./ha), in tomato (1 x 612 kg a.s./ha) and in potato (1 x 153 kg a.s./ha). Based on the high application rate of MITC and its high toxicity to aquatic organisms, step 1-2 calculations are not sufficiently demonstrating safe uses and are therefore not reported. The run-off/drainage contributions of 2-5 % of the application rate that are assumed in step 1-2 calculations would lead to unrealistically high PEC_{SW} levels.

Step 3-4 calculations, using PRZM, MACRO and TOXSWA in combination with the FOCUS surface water scenarios were conducted.

Risk assessment for aquatic organisms:

The assessment of the chronic risk to aquatic organisms is not justified since the DT_{50} of MITC, whole water-sediment system is clearly below 2 days. The active substance is applied once a year. Moreover, soil sterilants are generally not used every year.

The assessment of the risk to sediment dwelling organisms is not justified since the properties of MITC (low K_{oc} , high solubility in water) exclude exposure of the sediment organisms. Moreover, a low level of MITC was observed transiently in the sediment phase of the w/s study (1.5-4.5 % AR in the sediment after 72 h).

The uses in greenhouse pose no risk to aquatic organisms.

FOCUS step 4 scenario, buffer zone of 20 m, carrot (1 x 408 kg a.s./ha) :

TER values for fish do not pass the trigger in 3 out of 5 scenarios (R1 p and R2 s acceptable)

TER values for aquatic invertebrates do not pass the trigger in 3 out of 5 scenarios (R1 p and R2 s acceptable)

The risk to algae and aquatic plants is acceptable for all scenarios

FOCUS step 4 scenario, buffer zone of 20 m, corn salad (1 x 306 kg a.s./ha) :

TER values for fish do not pass the trigger in 3 out of 7 scenarios (R1 p, R1 s (2nd crop), R3 s acceptable)

TER values for aquatic invertebrates do not pass the trigger in 3 out of 7 scenarios (R1 p, R1 s (2nd

crop), R3 s acceptable)

The risk to algae and aquatic plants is acceptable for all scenarios

FOCUS step 4 scenario, buffer zone of 20 m, tomatoes (1 x 612 kg a.s./ha) :

TER values for fish do not pass the trigger in 3 out of 3 scenarios

TER values for aquatic invertebrates do not pass the trigger in 3 out of 3 scenarios

The risk to algae and aquatic plants is acceptable for all scenarios

FOCUS step 4 scenario, buffer zone of 20 m, potatoes (1 x 153 kg a.s./ha) :

The risk to fish, aquatic invertebrates, algae and aquatic plants is acceptable for all scenarios

Some additional step 3 scenarios are also acceptable.

As already mentioned in the section on fate and behaviour, the PEC_{sw} values should be used with precaution. The FOCUS sw models were not developed with soil fumigants in mind. The models do not properly consider the volatilisation of MITC and therefore highly overestimate the actual surface water contamination.

In conclusion, the risk of metam-sodium and its metabolite MITC to aquatic organisms is acceptable for the intended uses with a buffer zone of 20 m.

2.6.3 Effects on bees and other arthropods

2.6.3.1 Effects on bees

There is no direct spraying on plant material. The germination test proves that there is no concern of residues of metam-sodium or MITC in the planted crops. Therefore, bees are not at risk in-field and off-field since they are not exposed to contaminated crops or weeds. Bees are not exposed to the uses in greenhouse.

In conclusion, the risk of metam-sodium and its metabolite MITC to bees is acceptable for the intended uses.

2.6.3.2 Effects on other arthropods

There is no direct spraying on plant material. The germination test proves that there is no concern of residues of metam-sodium or MITC in the planted crops. Therefore, leaf-dwelling arthropods are not at risk in-field and off-field since they are not exposed to contaminated crops or weeds. Non-target arthropods are not exposed to the uses in greenhouse.

The effects of the treatment with the formulated Metam-Sodium were tested on the soil-dwelling arthropod *Aleochara bilineata*. A bioassay was performed with treated soil after 55 days of aging under field conditions. No biologically relevant effects were observed for the reproduction at the application rate of 1 x 1200 L Metam-Sodium/ha (608.4 kg a.s./ha). This aged residue study demonstrates that *Aleochara bilineata* is able to recolonize the field after 55 days of aging.

However, the risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field. An extended laboratory study is only able to assess the potential for recolonisation, but not actual recovery. Therefore, a semi-field or field study should demonstrate that the field can be recolonized with non-target arthropods from the border stripes (off-field). In this new study, several species should be tested (*Aleochara bilineata*, *Pardosa*, *Folsomia candida*, *Hypoaspis aculeifer*, ...).

A field trial (Aldershof S., 2010) was performed to determine the effects of metam-sodium on the non-target arthropod fauna of arable land in SW-France after one application in spring. The field study is well performed (different taxa were sampled with soil and pitfall sampling) and good reported (evaluations by different statistical methods).

Metam-sodium application at the highest rate of 612 kg a.s./ha has initial adverse effects on soil arthropods living in the soil and at the soil surface. The field study demonstrates that actual recovery in the field will occur for the most important taxa within one year:

- For the soil samples 0% taxa showed a recovery > 1 year. The arthropod taxa that would be expected to be most at risk from a soil injected treatment such as metam-sodium would be the small and relatively immobile soil dwelling taxa such as Collembola, soil mites, larvae of soil dwelling beetles (e.g. Aleo-

charinae and some Carabidae). All of these groups showed clear recovery within one year of application of metam-sodium (see also B.9.7).

- For the pitfall samples only 2% taxa showed a recovery > 1 year. From Table B.9.5.3-4 it appears that of all the sampled taxa the only taxon that did not show full recovery within one year was Heteroptera. Also from Figure B.9.5.3-3A (PRC 1+2) it is clear that Heteroptera contributed largely to the delayed response pattern. Heteroptera are primarily foliage dwelling arthropods and therefore not strongly associated with bare soil, which is the GAP for the application of metam. From Figure B.9.5.3-8 it is clear that any effects of metam-sodium on Heteroptera did not begin to occur until 4 months after treatment. Such a long delay to onset of effects is due to an indirect effect, either the decline in numbers of a suitable prey (for example aphids) on the carrot plants or decline in quality of a host plant (for phytophagous Heteroptera). The numbers of Heteroptera in metam-sodium treated plots were not statistically different from controls in samples taken the year after treatment. Despite being reported as not having shown recovery, the data shows that no difference was observed in absolute numbers just before and one year after treatment.

For the most important soil inhabiting and soil surface dwelling species the recovery occurs within one year. For 2% of pitfall sampling taxa recovery is still ongoing in the next spring. In conclusion, the risk of metam-sodium and its metabolite MITC to non-target arthropods is sufficiently addressed for the field uses at the EU level. RMS proposes that potential risk mitigation measures are taken into consideration at the Member State level.

2.6.4 Effects on earthworms and other soil macro-organisms

2.6.4.1 Effects on earthworms

Earthworms are not exposed to the uses in greenhouse.

As a general soil fumigant, it is expected that metam-sodium will have initial effects on the entire soil fauna and flora, including earthworm populations. Therefore, the risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field.

An earthworm field study (Lühns U., 2002) was conducted from May 31, 2001 until May 22, 2002.

The assessment of the effects of metam-sodium and its metabolite MITC should be done in comparison with the agricultural control only (same soil cultivation).

One year after treatment of 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha), the earthworm abundance was 103.5 % and 85.2 % respectively of the agricultural control.

The earthworm biomass was 123.7 % and 85.8 % one year after application of 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha) respectively.

Amongst the collected earthworms, the most abundant species was *Aporrectodea caliginosa*. 4^{1/2} months after treatment with 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha), the abundance of *Aporrectodea caliginosa* was comparable to that in the agricultural control.

The abundance of juvenile earthworms one year after application of 300 L Metam-Sodium/ha (equivalent to 152.1 kg a.s./ha) was comparable to the agricultural control, whereas at 1200 L Metam-Sodium/ha (equivalent to 608.4 kg a.s./ha) it was still statistically significantly lower.

It was concluded that one year after application of 152.1 kg a.s./ha, the earthworm population in the field has recovered.

One year after application of 608.4 kg a.s./ha, there is a clear indication of an almost completed process of recovery. Since there was a reduced plant cover (lower food source) at 608.4 kg a.s./ha, this represents a worst case situation.

The notifier provided information on the migration distances of earthworm species, indicating that the recovery observed in the test plots is representative for the field situation.

In conclusion, the risk of metam-sodium and its metabolite MITC to earthworms is acceptable for the field use at the lower application rate of 153 kg a.s./ha and is sufficiently addressed for the higher application rate of 612 kg a.s./ha at the EU level (an almost completed process of recovery was demonstrated over a period of one year). RMS proposes that potential risk mitigation measures are taken into consideration at the Member State level for the higher application rates, allowing the earthworms to recover in the field.

2.6.4.2 Effects on other soil macro-organisms

Non-target soil macro-organisms are not exposed to the uses in greenhouse.

As a general soil fumigant, it is expected that metam-sodium will have initial effects on the entire soil fauna and flora, including Collembola populations. Therefore, the risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field. An extended laboratory study is only able to assess the potential for recolonisation, but not the actual recovery. Therefore, a semi-field or field study should demonstrate that the field can be recolonised with Collembola from the border stripes (off-field) or underlying soil layers (in-field). This new field study can be integrated with the requested semi-field or field study for the non-target arthropods.

There is no evidence from any of the density graphs in the field study of Aldershof (2010) that long-term effects on soil dwelling macro-invertebrates occurred due to metam-sodium treatment. All affected soil dwelling invertebrates had fully recovered in abundance within the same season and no adverse effects extended into the year after treatment.

In conclusion, the risk of metam-sodium and its metabolite MITC to non-target soil macro-organisms is acceptable for the intended field uses since recovery within 1 year after application was demonstrated.

2.6.5 Effects on soil micro-organisms

Non-target soil micro-organisms are not exposed to the uses in greenhouse.

As a general soil fumigant, it is expected that metam-sodium will have initial effects on the entire soil fauna and flora, including non-target soil micro-organisms. Therefore, the risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field.

A soil microflora laboratory test (Reis K.H., 2002) was conducted with soil samples from the earthworm field study with application rates of 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha). The effects of metam-sodium and its metabolite MITC on nitrogen and carbon transformation were transient and the processes were not drastically impaired.

In conclusion, the risk of metam-sodium and its metabolite MITC to non-target soil micro-organisms is acceptable for the intended uses.

2.6.6 Effects on other non-target organisms (flora and fauna)

The application of metam-sodium is on bare soil; the product is incorporated into the soil (soil injection or drip irrigation) and thereafter the soil is compressed with a roller. The mode of application excludes the off-field exposure.

In conclusion, the risk of metam-sodium and its metabolite MITC to non-target terrestrial plants is acceptable for the intended uses.

2.6.7 Effects on biological methods of sewage treatment

EC_{50} (activated sludge, 3 hours) = 4.36 mg metam-sodium/L

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Added in August 2010:

The following list of end points is an amended version of the peer-reviewed list of end points (version dated November 2008) that was included in the EFSA conclusion dated 26 November 2008 (EFSA Scientific Report (2008) No 203). Changes made as a result of the assessment of new data provided in the resubmission dossier (2010), are highlighted in yellow.

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡

Metam
(The given data belong to the variant metam-sodium, unless specified otherwise)

Function (e.g. fungicide)

Nematicide, fungicide, herbicide, insecticide

Rapporteur Member State

Belgium

Co-rapporteur Member State

Not applicable

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡

N-methyldithiocarbamic acid
Variant: sodium N-methyldithiocarbamate

Chemical name (CA) ‡

methylcarbomodithioic acid
Variant : Methylcarbomodithioic acid sodium salt

CIPAC No ‡

20
Variant : 20.011

CAS No ‡

144-54-7
Variant : 137-42-8

EC No (EINECS or ELINCS) ‡

Metam-sodium: 205-293-0

FAO Specification (including year of publication) ‡

20.1Na/13/S/15, published in AGP:CP/82 (1979):
“The metam-sodium content shall be declared (g/L at 20°C or % w/w). When the combined carbon disulphide is determined and expressed as metam-sodium the content obtained shall not differ from that declared by more than ± 5% of the declared content.”

Minimum purity of the active substance as manufactured ‡

Technical concentrates (TK):
Metam-sodium TK: min. 400 g/kg – max. 442 g/kg
Metam-potassium TK: min. 520 g/kg – max. 560 g/kg
Dry weight basis (calculated):
Metam-sodium: min. 983 g/kg
Metam-potassium: min. 990 g/kg

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured

Methylisothiocyanate (MITC)
 - max. 0.22 g/kg on dry weight basis (metam-sodium);
 - max. 0.42 g/kg on dry weight basis (metam-potassium)

N,N'-dimethylthiourea (DMTU)
 - max. 7.22 g/kg on a dry weight basis (metam-sodium)
 - max. 6 g/kg on a dry weight basis (metam-potassium)

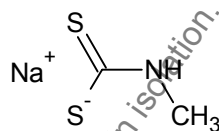
Molecular formula ‡

C₂H₅NS₂
 Variant : C₂H₄NNaS₂

Molecular mass ‡

107.2 u
 Variant: 129.2 u

Structural formula ‡



‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	86.5 – 90.5 °C (99.9%)																
Boiling point (state purity) ‡	Not applicable																
Temperature of decomposition (state purity)	150 °C (97%)																
Appearance (state purity) ‡	(97.0%): white crystalline powder; (510 g/L aqueous solution): yellow clear solution																
Vapour pressure (state temperature, state purity) ‡	$5.75 \cdot 10^{-2}$ Pa at 25°C (99.9%)																
Henry's law constant ‡	8.34×10^{-6} Pa.m ³ .mol ⁻¹																
Solubility in water (state temperature, state purity and pH) ‡	578.29 g/L at 20°C (distilled water; pH increases to 9.2 - 9.3) (99.9%) 734 g/L at 20°C (pH 9 buffer; pH increases to 10.1) (99.2%) Water solubility is not significantly affected by pH																
Solubility in organic solvents ‡ (state temperature, state purity)	<table> <tr> <th colspan="2">Solubility at 20°C in g/L (99.9%)</th></tr> <tr> <th></th><th>solubility at 20°C (g/L)</th></tr> <tr> <td>n-heptane</td><td>< 0.2126</td></tr> <tr> <td>Xylene</td><td>< 0.2611</td></tr> <tr> <td>1,2-dichloroethane</td><td>< 0.2620</td></tr> <tr> <td>ethyl acetate</td><td>< 0.2032</td></tr> <tr> <td>acetone</td><td>< 0.2188</td></tr> <tr> <td>methanol</td><td>33 – 40</td></tr> </table>	Solubility at 20°C in g/L (99.9%)			solubility at 20°C (g/L)	n-heptane	< 0.2126	Xylene	< 0.2611	1,2-dichloroethane	< 0.2620	ethyl acetate	< 0.2032	acetone	< 0.2188	methanol	33 – 40
Solubility at 20°C in g/L (99.9%)																	
	solubility at 20°C (g/L)																
n-heptane	< 0.2126																
Xylene	< 0.2611																
1,2-dichloroethane	< 0.2620																
ethyl acetate	< 0.2032																
acetone	< 0.2188																
methanol	33 – 40																
Surface tension ‡ (state concentration and temperature, state purity)	72.0 mN/m at 21°C (1 g/L) (97.0%)																
Partition co-efficient ‡ (state temperature, pH and purity)	log P _{O/W} ≤ - 2.91 at 20 °C (pH 6.9) (99.9%) No significant pH-effect expected (cfr. dissociation constants)																
Dissociation constant (state purity) ‡	pK _{aI} = 2.99; pK _{aII} = 11.06 (99.2%)																

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

UV/VIS absorption (max.) incl. ϵ ‡
(state purity, pH)

	$\lambda_{\max}$ (nm)	ϵ (L.mol ⁻¹ .cm ⁻¹)
Neutral (distilled water)	205.0	7502.8
	248.0	7942.3
	280.0	9924.0
	at λ 290 nm	> 10
Alkaline (0.1 M NaOH)	248.0	8042.5
	280.0	9796.8
	at λ 290 nm	> 10
Acidic (0.1M HCl)	Metam-sodium hydrolysed too fast to measure accurately	

Flammability ‡ (state purity)

Not auto-flammable (510 g/L aqueous solution, i.e. TK);
Flash point: > 97°C (510 g/L aqueous solution, i.e. TK)

Explosive properties ‡ (state purity)

Not explosive (TK; statement)

Oxidising properties ‡ (state purity)

Not oxidising (TK; statement)

Physical and chemical properties of the relevant metabolite methylisothiocyanate (MITC)

Appearance (state purity) ‡

Colourless crystalline solid (97.0%)

Vapour pressure (state temperature, state purity) ‡

1739 Pa (20°C, 99.4%)

Henry's law constant ‡

$H = 14.2 \text{ Pa.m}^3.\text{mol}^{-1}$

Solubility in water (state temperature, state purity and pH) ‡

8.94 g/L at 20°C (97.0%, pH 7.5)

Partition co-efficient ‡
(state temperature, pH and purity)

$\log P_{ow}$ at 20°C: 1.05 (pH 7.5, 97.0%)

UV/VIS absorption (max.) incl. ϵ ‡
(state purity, pH)

97.0% pure:

	$\lambda_{\max}$ (nm)	ϵ (L.mol ⁻¹ .cm ⁻¹)
Neutral (distilled water)	235	635
	283	65
	321	17
Alkaline (0.1 M NaOH)	276	46
	320	5
	at λ 290 nm	Not reported, but > 10 based on spectrum
Acidic (0.1M HCl)	235	635
	283	23
	324	6
	at λ 290 nm	Not reported, but > 10 based on spectrum

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

List of end points

EPCO Manual E4 - rev. 4 (September 2005)

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Summary of representative uses evaluated (metam-sodium)

Crop and/or situation (a)	Member State or Country	Product name	F G or I	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max		
Carrot	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Soil injection + incorporation at 25 cm by rotavation	April-June	1	n.a.	n.a.	No dilution	408	n.a.	(One application every two years in carrot)
Carrot	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Soil injection + incorporation at 25 cm by rotavation	Oct-Dec	1	n.a.	n.a.	No dilution	408	n.a.	(One application every two years in carrot)
Corn salad (=lamb’s lettuce)	FR, ES, BE, DE, IT	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Soil injection + incorporation at 15 cm by rotavation	April-Aug	1	n.a.	n.a.	No dilution	306	n.a.	
Cucumber	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	G	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Drip-irrigation under a plastic film on the planting row	June-Aug	1	n.a.	n.a.	No dilution 45000-180000	459	n.a.	see note ** below table

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

List of end points

EPCO Manual E4 - rev. 4 (September 2005)

Rapporteur Member State

Month and year

Active Substance (Name)

Belgium	November 2008 Revision August 2010	Metam
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Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/ha min max	water l/ha min max	kg as/ha min max		
Eggplant / aubergine	CY, ES, FR, EL, IT, MT, NL, PT	*	G	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Drip-irrigation under a plastic film on the planting row	June-Aug	1	n.a.	n.a.	No dilution 60000-240000	612	n.a.	see note ** below table
Pepper	BE, CY, ES, FR, EL, HU, IT, MT, NL, PL, PT, UK	*	G	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Drip-irrigation under a plastic film on the planting row	June-Aug	1	n.a.	n.a.	No dilution 60000-240000	612	n.a.	see note ** below table
Potato	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Soil injection + incorporation at 25 cm by rotavation	Sept-Nov	1	n.a.	No dilution		153	n.a.	
Strawberry	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Drip irrigation under a plastic film on the planting row	Jul-Oct	1	n.a.	n.a.	No dilution 60000-240000	612	n.a.	see note ** below table

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

List of end points

EPCO Manual E4 - rev. 4 (September 2005)

Rapporteur Member State

Month and year

Active Substance (Name)

Belgium	November 2008 Revision August 2010	Metam
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Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

Crop and/or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks: (m)
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/ha min max	water l/ha min max	kg as/ha min max		
Tomato	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	G	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Drip irrigation under a plastic film on the planting row	Feb-Aug	1	n.a.	n.a.	No dilution 60000-240000	612	n.a.	see note ** below table
Tomato	DE, BE, CY, ES, FR, MT, EL, PL, HU, IE, IT, NL, PT, UK	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Soil injection at 5 cm + coverage by 40 cm of soil	March	1	n.a.	n.a.	No dilution	612	n.a.	
Grape	FR, IT, DE, ES, EL, HU, PT	*	F	Nematodes Soil fungi Weeds Insects	SL	510 g/l	Soil injection at 40 cm at the site of the de-rooted vine (0.2 L/m ²)	Autumn. Before replanting	1	n.a.	n.a.	No dilution	1020	n.a.	Spot treatment see note *** below table

*: The preparation is identical to the technical active substance. Different tradenames are used in different EU member states: Solasan, Terrasan, Monam, Nemasol, Traitam Sol, Metam sodio, etc.

** Note: Diluted with water directly in the drip irrigation lines at concentration 0.5 - 2.0 % v/v

*** Note: Although the intended use in grapes is at the higher dose of 1020 kg a.s./ha, only an occasional treatment would be necessary (isolated cases of few trees in a row of vines), and the spot treatment at the foot of the de-rooted vine would most likely lead to a lower exposure of the operator than the treatment of a full field. The application rate on full field basis will be considerably lower than 1020 kg a.i./ha. Furthermore, the time between disinfection and the harvest of new grapes is considerably longer than in vegetable growing, therefore residue trials in this crop were considered less relevant. Taking this into account, the RMS considers this use in the EU-GAP table to be acceptable and covered by the risk assessments performed for the other intended uses. Refinements may however be considered at Member State level, if deemed necessary.

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

List of end points

EPCO Manual E4 - rev. 4 (September 2005)

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s). (a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure) (b) Outdoor or field use (F), greenhouse application (G) or indoor application (I) (c) e.g. biting and suckling insects, soil born insects, foliar fungi, weeds (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR) (e) GCPF Codes - GIFAP Technical Monograph No 2, 1989 (f) All abbreviations used must be explained (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated	(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). (j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application (k) Indicate the minimum and maximum number of application possible under practical conditions of use (l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha) (m) PHI - minimum pre-harvest interval
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‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Methods of Analysis**Methods of Analysis****Analytical methods for the active substance (Annex IIA, point 4.1)**

Technical as (analytical technique)	CS ₂ -evolution method (CIPAC method 20/13/M/1.3)
Impurities in technical as (analytical technique)	HPLC-UV, titration, ion chromatography, MITC and DMTU: HPLC-UV
Plant protection product (analytical technique)	a.s.: CS ₂ -evolution method (CIPAC method 20/13/M/1.3); MITC and DMTU: HPLC-UV

Analytical methods for residues (Annex IIA, point 4.2)**Residue definitions for monitoring purposes**

Food of plant origin	MITC (provisional)
Food of animal origin	None
Soil	MITC
Water surface	MITC
drinking/ground	MITC and DMTU (provisional)
Air	MITC

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-MS (ILV available): Food commodities of plant origin with high water content and with high acid content: LOQ = 0.01 mg/kg (MITC)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not required, as no MRL's are proposed.
Soil (analytical technique and LOQ)	GC-NPD (conf. technique: column of different polarity): LOQ = 0.02 mg/kg (MITC)
Water (analytical technique and LOQ)	GC-NPD (conf. technique: column of different polarity): LOQ = 0.1 µg/L (MITC) Open for ground water for the compound DMTU
Air (analytical technique and LOQ)	GC-NPD (conf. technique: column of different polarity): LOQ = 0.5 µg/m ³ (MITC)

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Methods of Analysis

Body fluids and tissues (analytical technique and LOQ)

HPLC-MS (conf. technique: HPLC-MS-MS):
blood plasma, urine: LOQ = 0.05 mg/L (N-acetyl-S-[(methylamino)carbothioyl]cysteine, i.e. appropriate target analyte from a toxicological point of view)

GC-NPD (conf. technique: column of different polarity):
liver: LOQ = 0.1 mg/kg (MITC, i.e. appropriate target analyte from a toxicological point of view)

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

Active substance

RMS/peer review proposal

R31

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Mammalian toxicology**Impact on Human and Animal Health****Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1) metam and MITC**

Rate and extent of oral absorption ‡	85 % (based on urinary (50%) and expired air (35%) excretion within 48 h)
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	Slight potential for accumulation in thyroid
Rate and extent of excretion ‡	Rapid and extensive (app. 85 %) within 48 h, mainly via urine (50 %) within 24 h, 4 % via faeces, 35 % via expired air
Metabolism in animals ‡	Extensive degradation of metam into MITC which is further conjugated with GSH or decomposes into MIC, COS and CO ₂ . Another important metabolic pathway is formation of CS ₂ which is related to acidic conditions of stomach
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites: Methylisothiocyanate (MITC), methylisocyanate (MIC), COS, CS ₂
Toxicologically relevant compounds ‡ (environment)	Methylisothiocyanate (MITC), methylisocyanate (MIC), COS, CS ₂

Acute toxicity (Annex IIA, point 5.2) metam sodium

Rat LD ₅₀ oral ‡	896 mg/kg bw	R22
Rat LD ₅₀ dermal ‡	2000 mg/kg bw	-
Rat LC ₅₀ inhalation ‡	2.54 mg/L air /4h (whole body)	R20
Skin irritation ‡	Corrosive	R34
Eye irritation ‡	Non-irritant	-
Skin sensitisation ‡	Sensitising (M & K)	R43

Acute toxicity (Annex IIA, point 5.2) MITC

Rat LD ₅₀ oral ‡	147 mg/kg bw	R25
Rat LD ₅₀ dermal ‡	1290 mg/kg bw	R21
Rat LC ₅₀ inhalation ‡	0.54 mg/L air /4h (whole body)	R23 R37
Skin irritation ‡	Corrosive	R34
Eye irritation ‡	No study required	-
Skin sensitisation ‡	Sensitising (M & K)	R43

Short term toxicity (Annex IIA, point 5.3) metam sodium

Target / critical effect ‡	Nasal cavity (rat), urinary bladder(mice), liver(dog)	
Relevant oral NOAEL ‡	1-year, dog 0.1 mg/kg bw/day 90-day rat: 0.5 mg/kg bw/day 90-day mice: 0.8 mg/kg bw/day	R48/22
Relevant dermal NOAEL ‡	21-day, rabbit: 31.2 mg/kg bw/day	
Relevant inhalation NOAEL ‡	90-day rat: 6.5 mg/m ³ corresponding to 1.75 mg/kg bw/d	

Short term toxicity (Annex IIA, point 5.3) MITC

Target / critical effect ‡	Nasal cavity (rat), liver (dog)	
Relevant oral NOAEL ‡	90-day, dog 0.04 mg/kg bw/day	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Mammalian toxicology

Relevant dermal NOAEL ‡	No data - not required	
Relevant inhalation NOAEL ‡	28-day rat : 5 mg/m ³ (1.35 mg/kg bw/d)	

Genotoxicity ‡ (Annex IIA, point 5.4)

Metam and MITC are unlikely to be genotoxic	
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Long term toxicity and carcinogenicity (Annex IIA, point 5.5) Metam sodium

Target/critical effect ‡	Nasal cavity (rat) urinary bladder (mice)	
Relevant NOAEL ‡	1.5 mg/kg bw/day; 2-year, rat 1.9 mg/kg bw/day; 24-month, mouse	
Carcinogenicity ‡	Angiosarcomas in mice	R40

Long term toxicity and carcinogenicity (Annex IIA, point 5.5) MITC

Target/critical effect ‡	Changes in some WBC parameters	
Relevant NOAEL ‡	0.44 mg/kg bw/day; 2-year, rat 3.3 mg/kg bw/day; 24-month, mouse	
Carcinogenicity ‡	MITC is unlikely to pose a risk to humans	

Reproductive toxicity (Annex IIA, point 5.6) Metam sodium**Reproduction toxicity**

Reproduction target / critical effect ‡	Decreased pup and litter weight at the parental toxic dose in the rat	
Relevant parental NOAEL ‡	0.03 mg/L (4 mg/kg bw/day)	
Relevant reproductive NOAEL ‡	>0.1 mg/L (12 mg/kg bw/day)	
Relevant offspring NOAEL ‡	0.03mg/L (4 mg/kg bw/day)	

Developmental toxicity

Developmental target / critical effect ‡	Increased incidence of variations and retardations at maternally toxic dose in rats; decreased number live foetuses and increased incidence of dead implants at maternal toxic doses in rabbits	R63 (R61 ?)
Relevant maternal NOAEL ‡	Rat: 5 mg/kg bw/day Rabbit: 5 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 5 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

Reproductive toxicity (Annex IIA, point 5.6) MITC**Reproduction toxicity**

Reproduction target / critical effect ‡	Reproduction parameters not significantly altered	
Relevant parental NOAEL ‡	0.7 mg/kg bw/day	
Relevant reproductive NOAEL ‡	>3.6 mg/kg bw/day	
Relevant offspring NOAEL ‡	>3.6 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Decreased fetal weight at maternal toxic doses in rabbits	
Relevant maternal NOAEL ‡	Rat: 3 mg/kg bw/day Rabbit: 3 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 10 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Mammalian toxicology**Neurotoxicity (Annex IIA, point 5.7) metam sodium**

Acute neurotoxicity ‡	NOAEL > 1500 mg/kg bw	
Repeated neurotoxicity ‡	NOAEL = 14.7 mg/kg bw/d	
Delayed neurotoxicity ‡	No data-not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No studies performed
Studies performed on metabolites or impurities ‡	No further studies performed

Medical data ‡ (Annex IIA, point 5.9) metam sodium

no medical surveillance data for manufacturing plant personnel was found for metam sodium

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡ metam sodium	0.001 mg/kg bw/day	dog, 1-year gavage study	100
ADI MITC	0.004	dog, 90-d drinking water study	100
AOEL ‡ metam sodium	0.001 mg/kg bw/day	dog, 1-year gavage	100
AOEL MITC	0.004 mg/kg bw	dog, 90-d drinking water study	100
ARfD ‡ metam sodium	0.1 mg/kg bw	rat, overall developmental toxicity	100
ARfD MITC	0.03 mg/kg bw/day	rat, developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50% ECMonam)	Concentrate: 1 %; 12% : for the dilution ‡ Rat <i>in vivo</i> and comparative <i>in vitro</i> (human/rat skin)
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Exposure scenarios (Annex IIIA, point 7.2)

Operator exposure to metam sodium	Not relevant: metam sodium decomposes very rapidly into MITC.
Operator exposure to MITC	Measurements under realistic open field conditions; values as % of AOEL of MITC (0.004 mg/kg b.w./d) ; RPE (operator, worker): combination filter A1P2, 2% penetration; figures including worst-case values Operator, bw= 70kg, duration of the loading and application: 7 h/d Worker, bw= 60kg, duration of the cultivation, seal breaking and/or plant hole drilling: 8 h/d

‡ End point identified by the EU-Commission as relevant for Member States when applying the Uniform Principles

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Mammalian toxicology

Workers exposure to metam sodium

Workers exposure to MITC

Bystanders exposure to metam sodium

Bystanders exposure to MITC

Resident exposure to MITC

Bystander, bw= 60kg, presence in the neighbourhood of field or greenhouse at peak-level: 1 h/d

Operator exposure (personal measurements);

-Study 1*, soil injection: 450% of AOEL, w/o RPE
9.0% with RPE

-Study 2*, soil fumigation, 229% of AOEL, w/o RPE
4.6% with RPE

-Study 3*, soil injection, 239% of AOEL, w/o RPE
4.8% with RPE

-Study 4**, drip-irrigation: 145% of AOEL, w/o RPE
2.9% with RPE

[*: open field studies **: newly submitted greenhouse/tunnel study]

Not relevant: metam sodium decomposes very rapidly into MITC.

Worker exposure ; 14-17 day after soil injection, 0-2 hr after breaking seal, personal measurements:

-Preparation of soil: 14-19% of AOEL w/o RPE
0.3-0.4% with RPE

-Plastic film opening: 37% of AOEL w/o RPE
0.74% with RPE

-Volatilisation from field, 18h post application, 1 m height

27% of AOEL w/o RPE
0.54% with RPE

-Hole drilling through plastic film, 18 days after greenhouse treatment (drip irrigation); personal measurement

2.96% of AOEL w/o RPE
0.06% with RPE

Not relevant: metam sodium decomposes very rapidly into MITC.

Bystander exposure (no RPE assumed):

-soil injection, distance of 100 m, during application: 18.7% of AOEL

-soil injection, MITC in air 6 hour after application: 3.1% of AOEL

- soil injection, 1.1-9 days after application, 1.5 m height: 7.3% of AOEL

-drip irrigation in greenhouse, 10 h after application, at open side of greenhouse: 107-264% of AOEL

Resident exposure (no RPE assumed):

drip irrigation in greenhouse, 10 h after application, 140-220m distance of greenhouse: 3.9% of AOEL

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Mammalian toxicology**Classification and proposed labeling with regard to toxicological data (Annex IIA, point 10)**

Substance classified (metam sodium)

RMS/peer review proposal
Repr. Cat 3; R63 (R61?): Carc. Cat 3; R 40: Xn, R48/22: Xn; R20/22: C; R34: R43

Substance classified (MITC)

RMS/peer review proposal
C ; R34 : T; R23/25: Xn ; R21 : R43

Rapporteur Member State	Month and year	Active Substance (Name)
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Residues**Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)**

Plant groups covered

OPEN

-Root and Tuber vegetables (radish & turnip),

-Leafy Brassica (Chinese cabbage),

-Fruiting vegetables (Tomato).

Rotational crops

OPEN

Rotational crops studies are not required considering the DT50/DT90 values respectively for Metam-sodium and MITC.

Moreover, given the use pattern of Metam as a soil fumigant before planting, the primary crops metabolism data address the metabolism of Metam in rotational crops.

Metabolism in rotational crops similar to metabolism in primary crops?

OPEN

N/A

Processed commodities

OPEN

Not required.

Residue pattern in processed commodities similar to residue pattern in raw commodities?

Not relevant.

N/A

Plant residue definition for monitoring

MITC (provisional)

Plant residue definition for risk assessment

MITC (provisional)

Conversion factor (monitoring to risk assessment)

None.

N/A

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered

OPEN

Not required

Time needed to reach a plateau concentration in milk and eggs

-

Animal residue definition for monitoring

N/A

Animal residue definition for risk assessment

N/A

Conversion factor (monitoring to risk assessment)

N/A

Metabolism in rat and ruminant similar (yes/no)

N/A

Fat soluble residue: (yes/no)

No (Log Po/w: -2.9 at 20 °C).

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Residues**Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)**

OPEN subject to the primary crop metabolism being concluded on.

Not relevant

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

OPEN

Not required.

In the individual residue trials performed in the US, the storage stability conditions and intervals of storage (i.e., harvest to extraction interval, extraction to analysis interval) ranged between 30 and 40 days.

This frozen storage period is also valid for the additional supervised residue trials submitted in the framework of the resubmission.

Residues from livestock feeding studies (Annex IIA, point 6.4 Annex IIIA, point 8.3)

Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)

Potential for accumulation (yes/no):

Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)

Ruminant:	Poultry:	Pig:
Conditions of requirement of feeding studies		
N/A	N/A	N/A
No	No	No
N/A	N/A	N/A
Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant)		
Residue levels in matrices : Mean (max) mg/kg		
Muscle	-	-
Liver	-	-
Kidney	-	-
Fat	-	-
Milk	-	-
Eggs	-	-

List of end points

EPCO Manual E4 - rev. 4 (September 2005)

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Residues

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
OPEN Lettuce	Indoor	MITC: <0.01 mg/kg	Further residue trials should be provided to confirm the no residue situation both for MITC and DMTU.	0.01* mg/kg (provisional) ⁽¹⁾	0.01	
Pepper	Indoor	MITC: <0.01-<0.01-<0.01 mg/kg DMTU: na-<0.01-<0.01 mg/kg		0.01* mg/kg	0.01	
Tomato	Indoor	MITC: <0.01-<0.01-<0.01-<0.01- <0.01 mg/kg DMTU: na-<0.01-<0.01-<0.01- <0.01 mg/kg		0.01* mg/kg	0.01	
Carrot	Outdoor	MITC: 4 x <0.01mg/kg DMTU: 4 x <0.01mg/kg		0.01* mg/kg	0.01	
Cucumber	Indoor	MITC: 2x <0.01mg/kg DMTU: 2x <0.01mg/kg		0.01* mg/kg	0.01	
Eggplant	Indoor	MITC: 2x <0.01mg/kg DMTU: 2x <0.01mg/kg		0.01* mg/kg	0.01	
Strawberry		No residue trial provided		0.01* mg/kg (provisional) ⁽¹⁾	-	
Potato		No residue trial provided		0.01* mg/kg	-	

List of end points

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Residues

				(provisional) ⁽¹⁾		
Grapes		No residue trial provided		0.01* mg/kg (provisional) ⁽¹⁾	■	
A sufficient number of acceptable residue trials using the validated BASF analytical method 234/2 have to be provided in order to confirm the situation of no residue for all the intended uses. ⁽¹⁾ : Although no residue trial was provided for these crops, a no-residue situation is expected according to the Good Agricultural Practice of Metam.						

- (a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
- (b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
- (c) Highest residue

Rapporteur Member State	Month and year	Active Substance (Name)
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Residues

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.004 mg/kg b.w./day for MITC.		
TMDI (% ADI) according to WHO European diet	OPEN		
	N/A		
TMDI (% ADI) according to national (to be specified) diets	OPEN		
	N/A		
TMDI (% ADI) according to EFSA PRIMo Model rev.2A	TMDI: 2.5 % ADI (PT general population)		
IEDI (WHO European Diet) (% ADI)	OPEN		
	N/A		
NEDI (specify diet) (% ADI)	OPEN		
	N/A		
Factors included in IEDI and NEDI	OPEN		
	N/A		
ARfD	0.03 mg/kg bw/day (based on a rat developmental study)		
IENTI (% ARfD)	OPEN		
	5.1 %	Potatoes	
	2.2 %	Table grapes	
	2.1 %	Carrots	
	2.1 %	Peppers	
	1.9 %	Cucumbers	
NESTI (% ARfD) according to national (to be specified) large portion consumption data	OPEN		
	N/A		
Factors included in IESTI and NESTI	OPEN		
	N/A		
The risk assessment calculation cannot be finalised pending the results of the new residue database for each supported crop.			

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
OPEN				
Not required				

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Residues

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Expression of the residue	Crops	MRLs (mg/kg)
MITC	Carrots (F)	0.01*
	Corn salad (lamb's lettuce) (F)	0.01* (provisional) ⁽¹⁾
	Cucumber (G)	0.01*
	Eggplant (G)	0.01*
	Pepper (G)	0.01*
	Potato	0.01* (provisional) ⁽¹⁾
	Strawberry	0.01* (provisional) ⁽¹⁾
	Tomato (F/G)	0.01*
	Grapes	0.01* (provisional) ⁽¹⁾
OPEN. No proposal. Further residue trials are required for all the supported uses.		
⁽¹⁾ : Provisional MRL pending submission of residue trials.		

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Fate and behaviour in the environment**Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)**

Mineralization after 100 days ‡

(MITC as test substance)
45.96-86.25 % after 21 d (study termination), [¹⁴C-thiocarbonyl]-label (n = 4). Amount found in the NaOH trap.

Non-extractable residues after 100 days ‡

(MITC as test substance)
9.88-38.38% after 21 d (study termination), [¹⁴C-thiocarbonyl]-label (n = 4)

Metabolites requiring further consideration ‡
- name and/or code, % of applied (range and maximum)

(metam-sodium as test substance)
Methyl isothiocyanate (MITC) : 82.9 % at 1-2 d (n= 1)
Recovered as volatile

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days

No acceptable data available. Not required for the representative uses.

Non-extractable residues after 100 days

No acceptable data available. Not required for the representative uses.

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)

No acceptable data available. Not required for the representative uses.

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)

No acceptable data available. Not required for the representative uses.

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Fate and behaviour in the environment

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X ¹	pH (water)	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (minutes)	DT ₅₀ (d) 20 °C pF2/10kPa	St. (s)	Method of calculation
Sandy loam	-	5.4	20°C, 50% MWHC	17/57	-	0.87	Linear regression, first order
Sandy loam	-	5.7	20°C, 50% MWHC	4/13	-	1.00	
Silt loam	-	7.1	20°C, 50% MWHC	11/36	-	0.86	
Clay loam	-	7.7	20°C, 50% MWHC	9/30	-	0.99	
Sandy loam	-	5.4	10°C, 50% MWHC	22/72	-	0.70	
Geometric mean				10.8			

MITC	Aerobic conditions							
Soil type	X ¹	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _{dp} /k _f	DT ₅₀ (d) 20 °C pF2/10kPa	(χ ² error)	Method of calculation
Sandy loam	-	5.2	20°C, 50% MWHC	2.78/9.23	-	3.24/10.78	3.5	SFO
Sandy loam	-	4.5	20°C, 50% MWHC	2.94/9.77	-	2.64/8.76	8.3	
Silt loam	-	6.1	20°C, 50% MWHC	0.97/3.21	-	1.08/3.60	5.4	
Clay loam	-	7.6	20°C, 50% MWHC	1.91/6.35	-	2.12/7.03	2.0	
Sandy loam	-	5.2	10°C, 50% MWHC	8.31/27.61	-			
Geometric mean				2.63 d		2.10/6.99		

Impurity DMTU	Aerobic conditions							
Soil type	X ¹	pH	t. °C / % MWHC	DT ₅₀ / DT ₉₀ (d)	f. f. k _{dp} /k _f	DT ₅₀ (d) 20 °C pF2/10kPa	(χ ² error)	Method of calculation
Silt loam	-	5.74	20°C/ 50% MWHC	0.15/0.49	-	0.080/0.265	8.5	SFO
Loam	-	7.27	20°C/ 50% MWHC	0.35/1.18	-	0.190/0.632	5.2	
Sandy loam	-	6.40	20°C/ 50% MWHC	0.30/0.99	-	0.171/0.568	8.2	
clay	-	7.20	20°C/ 50% MWHC	0.17/0.57	-	0.082/0.273	3.8	
Geometric mean				0.23/0.76		0.121/0.401		

¹ X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

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Fate and behaviour in the environment

Field studies ‡

Parent	Aerobic conditions
The field studies do not reflect the mode of application relevant for the uses supported in Europe (Application into the soil by direct injection or through drip-irrigation system). The application was made by overhead-sprinkler system. The formulation was injected in the sprinkler irrigation pipeline while water was applied to the plot. Incorporation of the a.s. in soil was achieved by post-application spray irrigation in some experiments.	
Data gap identified to consider data available in the public scientific literature and to other regulatory authorities. The additional field studies reported in the open literature have been re-evaluated and are adequate to derive regulatory endpoints.	

pH dependence ‡

(yes / no) (if yes type of dependence)

-
Not required

Soil accumulation and plateau concentration ‡

Laboratory studies ‡

Parent, MITC	Anaerobic conditions
Not required	

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡
HPLC determination: K _{oc} < 17.8 mL/g at pH 4 and 9

Metabolite MITC ‡							
Soil Type	OC %	Soil pH	K _d (mL/g)	K _{oc} (mL/g)	K _f (mL/g)	K _{foc} (mL/g)	1/n
Loamy sand	1.02	5.55	1	1	0.21	20.2	0.845
Clay loam	4.03	7.25	1	1	0.42	10.5	0.819
Loamy sand	2.84	5.41	1	1	0.43	15.3	0.825
Loam	3.29	4.78	1	1	0.42	12.7	0.905
Clay	2.74	6.86	1	1	0.25	9.0	0.755
Arithmetic mean						13.5	0.830
pH dependence (yes or no)			no				

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Fate and behaviour in the environment

Impurity DMTU ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	I/n
Clay	1.75	7.20	1	1	0.175	10	0.75
Loamy sand	2.16	5.40	1	1	0.152	7	0.73
Silty clay	3.93	7.36	1	1	0.290	7	0.82
Sandy loam	0.98	6.40	1	1	0.100	10	0.75
Arithmetic mean						9	0.76
pH dependence (yes or no)			no				

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡

Not required

Aged residues leaching ‡

Not required

Lysimeter/ field leaching studies ‡

Not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

DT₅₀ (metam-sodium): 0.0118 days (17 minutes)

Method of calculation

Kinetics: 1st order

Representative worst case from laboratory study.

Application data

Crop: field tomato

Depth of soil layer: 15 cm

Soil bulk density: 1.5 g/cm³

% plant interception: 0%

Number of applications: 1

Interval (d): -

Application rate(s): 612 kg as/ha

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Fate and behaviour in the environment

PEC _(s) (mg/kg)	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	272	-	-	-
Short term 24h	<0.0001	4.630	-	-
2d	<0.0001	2.315	-	-
4d	<0.0001	1.158	-	-
Long term 7d	<0.0001	0.661	-	-
28d	<0.0001	0.165	-	-
50d	<0.0001	0.092	-	-
100d	<0.0001	0.046	-	-

MITC

Method of calculation

Molecular weight relative to the parent: 0.566 = 73.11/129.17
DT₅₀ (d): 2.94 days
Kinetics: first order kinetics
Field or Lab: representative worst case from lab study.

Application data

Crop: field tomato
0 % plant interception:
15 cm soil incorporation
Number of applications: 1
Interval (d): -
Application rate assumed: 346 kg MITC/ha (assumed MITC is formed at a maximum of 100 % of the applied dose)

PEC _(s) (mg/kg)	Single application	Single application	Multiple application	Multiple application
	Actual	Time weighted average	Actual	Time weighted average
Initial	153.778	-	-	-

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡

pH 5: DT50 a.s. : 1.9 d at 25 °C (1st order, r²=0.98)
MITC: 20 % AR (1.8 d)

pH 7: DT50 a.s. : 2.2 d at 25 °C (1st order, r²=0.92)
MITC: 60 % AR (5 d)

pH 9: DT50 a.s. : 4.5 d at 25 °C (1st order, r²=0.98)
MITC: 20 % AR (5.4 d)

pH 5: DT50 MITC : ~ 40 d at 25 °C (1st order)

pH 7: DT50 MITC : 50 d at 25 °C (1st order)

pH 9: DT50 MITC : 11 d at 25 °C (1st order)

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Fate and behaviour in the environment

MITC	Distribution 3.2-8.5% AR as in water at study termination (8-72 hours) 3.2-7.2% AR in sediment at study termination (8-72 hours) 58.2-79.4% AR as volatile at study termination (8-72 hours)									
Water / sediment system	pH water phase	pH sed	t. °C	DT ₅₀ -DT ₉₀ whole sys.	St. (r ²)	DT ₅₀ -DT ₉₀ Water *	r ²	DT ₅₀ -DT ₉₀ sed	St. (r ²)	Method of calculation
Non-sterile aerobic	7.4	6.7	25	-	0.906	2.65/8.79 h	0.906	-	-	Linear 1st ord.
Sterile anaerobic	7.4	6.7	25	-	0.973	10.60/35.22h	0.973	-	-	Non-lin 1 st ord.
Non-sterile anaerobic	7.4	6.7	25	-	0.995	13.44/44.65h	0.995	-	-	Non-lin 1 st ord.
Geometric mean				-		Not relevant				
Mineralization and non extractable residues										
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).		Non-extractable residues in sed. max x % after n d		Non-extractable residues in sed at end of the study)			
Non sterile aerobic	7.4	6.7	Not measured		33% after 7 min		14.4% after 8 hours			
sterile anaerobic	7.4	6.7	Not measured		21.9% after 8 hours		21.1% after 72 hours			
Non sterile anaerobic	7.4	6.7	Not measured		16.5% after 48 hours		13.3% after 72 hours			

* DT50 water includes dissipation due to volatilisation

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent

Parameters used in FOCUS_{sw} step 1 and 2Parameters used in FOCUS_{sw} step 3 (if performed)

Application rate

Not required, since metam-sodium itself is subject to rapid degradation (laboratory DT₅₀'s ranged from 4 - 23 minutes) and is not expected to reach surface water

Not required

Not required

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Fate and behaviour in the environment

Metabolite MITC

Parameters used in FOCUSsw step 3

SWASH v.2.1; Drift calculator v.1.1; MACRO v.4.2;
PRZM_SW v.1.1.1 and TOXSWA v.2.2.1

Molecular Mass (g mol⁻¹):73.12
 Vapour Pressure (Pa):1739
 Aqueous Solubility (mg/L):8940
 Soil Adsorption Coefficient (K_{om}) (ml/g):13.5
 Freundlich Exponent (1/n):0.83
 DT₅₀ (days): 2.10
 Plant Uptake Coefficient: 0
 Dissipation rate in sediment: 1000 d (default)
 Dissipation rate in water: 1000 d (default)

Metabolite kinetically generated in simulation :no

Parameters used in FOCUSsw step 4

Application rate

Carrot (root vegetables)
 Application rate: 230.94 kg MITC/ha. (*)
 No. of applications: 1/year
 Time of application (month or season): see below
 Incorporation (cm): 25 cm for PRZM (CAM4),
 default for MACRO

Corn salad (leafy vegetables)
 Application rate: 173.21 kg MITC/ha. (*)
 No. of applications: 1/year
 Time of application (month or season):
 see below
 Incorporation (cm): 15 cm for PRZM (CAM4), default
 for MACRO

Tomatoes (fruiting vegetables)
 Application rate: 346.41 kg MITC/ha. (*)
 No. of applications: 1/year
 Time of application (month or season): see below
 Incorporation (cm): 15 cm for PRZM (CAM5), default
 for MACRO

Potatoes
 Application rate: 86.60 kg MITC/ha. (*)
 No. of applications: 1/year
 Time of application (month or season): see below
 Incorporation (cm): 25 cm for PRZM (CAM4),
 default for MACRO

* : The dose rate of MITC is based on 100% conversion
 from metam-sodium and a molecular weight conversion
 of 73.11/129.19.

Main routes of entry

Run-off, drainage

Summary of emergence and harvest dates, application windows and application dates for FOCUS-root vegetables,
 FOCUS-leafy vegetables, FOCUS-fruiting vegetables and FOCUS-potatoes (FOCUS, 2002)

Scenario	Emergence date	Harvest date	Possible window of application	Application date generated by PAT *
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Fate and behaviour in the environment

Carrots (Root vegetables)				
D3	25-Apr	15-Aug	30 Sep-31 Oct	29-Sep-1992
D6	25-Feb	13-May	30 Sep-31 Oct	06-Oct-1986
R1	20-Apr	10-Aug	30 Sep-31 Oct	06-Oct-1978
R2 (1 st crop)	28-Feb	31-May	30 Sep-31 Oct	09-Oct-1989
R2 (2 nd crop)	22-Jul	15-Oct	Not simulated*	
R3	26-Feb	13-May	30 Sep-31 Oct	22-Oct-1975
R4	26-Feb	13-May	30 Sep-31 Oct	30-Sep-1985
Corn salad (Leafy Vegetables)				
D3	25-Apr	20-Jul	01 Apr-01 May	04-Apr-1992
D3	05-Aug	20-Oct	01 Jun-01 Jul	14-Jun-1992
D4	10-May	26-Sep	01 Apr-01 May	18-Apr-1985
D6	15-Aug	30-Nov	01 Jun-01 Jul	01-Jun-1986
R1	20-Apr	15-Jul	01 Apr-01 May	26-Apr-1984
R1	31-Jul	15-Oct	01 Jun-01 Jul	01-Jun-1978
R2	28-Feb	01-Jul	Not simulated**	
R2	31-Jul	15-Nov	01 Jun-01 Jul	04-Jun-1989
R3	01-Mar	01-Jun	Not simulated**	
R3	15-Jun	15-Sep	01 Jun-01 Jul	02-Jun-1975
R4	01-Mar	01-Jun	Not simulated**	
R4	15-Jun	15-Sep	01 Jun-01 Jul	01-Jun-1985
Tomatoes [Fruiting vegetables (March application)]				
D6	10-Apr	10-Aug	01 Mar-31 Mar	05-Mar-1986
R2	15-Mar	31-Aug	01 Mar-31 Mar	01-Mar-1977
R3	10-May	25-Aug	01 Mar-31 Mar	01-Mar-1980
R4	20-Apr	15-Jul	01 Mar-31 Mar	05-Mar-1984
Tomatoes [Fruiting vegetables (April application)]				
D6	10-Apr	10-Aug	31 Mar-30 Apr	03-Apr-1986
R2	15-Mar	31-Aug	31 Mar-30 Apr	22-Apr-1977
R3	10-May	25-Aug	31 Mar-30 Apr	04-Apr-1980

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R4	20-Apr	15-Jul	31 Mar-30 Apr	08-Apr-1984
Potatoes				
D3	10-May	15-Sep	16 Sep-16 Oct	26-Sep-1992
D4	22-May	23-Sep	24 Sep-24-Oct	28-Sep-1985
D6 (1 st crop)	10-Apr	15-Jul	01 Sep-01 Oct	04-Sep-1986
D6 (2 nd crop)	05-Aug	25-Nov	26 Nov-26 Dec	06-Dec-1986
R1	05-May	08-Sept	09 Sep-09 Oct	17-Sep-1978
R2	15-Mar	15-Jun	01 Sep-01 Oct	29-Sep-1989
R3	10-Apr	01-Sep	02 Sep-02 Oct	23-Sep-1975

*PAT – Pesticide Application Timer: included in FOCUS surface water models

*application would have been at same time as R1 first crop, and would have generated same answer

**application prior to planting would be in February which is outside GAP window

Step 3 PEC_{SW} and PEC_{SED} for MITC following application to carrots (FOCUS-root vegetables)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
D3	Ditch	0.2740	0.3760	0.2730	0.2730	0.2700	0.2670	0.2560	0.2450	0.2370
D6	Ditch	1.6640	0.1540	0.8840	0.6670	0.4540	0.3020	0.1730	0.1180	0.0891
R1	Pond	0.2840	0.0461	0.2190	0.1710	0.1110	0.0685	0.0411	0.0281	0.0211
R1	Stream	43.2370	2.4000	10.3130	5.1600	2.5810	1.4750	1.0580	0.7060	0.5290
R2	Stream	5.2130	0.5920	2.8640	1.8200	0.9360	0.5380	0.2700	0.1800	0.1350
R3	Stream	115.4920	7.9930	43.1230	21.5770	10.7920	6.1680	3.1000	2.0670	1.5500
R4	Stream	49.7660	5.8790	39.0220	21.1170	10.5870	6.0500	3.0250	2.0170	1.5130

Step 3 PEC_{SW} and PEC_{SED} for MITC following application to corn salad (FOCUS-leafy vegetables)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
D3	Ditch	0.0002	0.0006	0.0002	0.0002	0.0001	0.0001	0.0001	0.0001	0.0001
D3	Ditch	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
D4	Pond	0.0129	0.0142	0.0128	0.0126	0.0120	0.0108	0.0100	0.0078	0.0063
D4	Stream	0.4280	0.3190	0.4240	0.4180	0.3980	0.3590	0.3230	0.2630	0.2180
D6	Ditch	0.0000	0.0000	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R1	Pond	0.1230	0.0187	0.0935	0.0712	0.0447	0.0269	0.0168	0.0137	0.0103
R1	Stream	40.7640	3.2110	15.7520	7.8800	3.9410	2.2520	1.1850	0.7910	0.5930
R1	Pond	0.4290	0.0603	0.3270	0.2410	0.1420	0.0867	0.0452	0.0301	0.0226
R1	Stream	2.6630	0.3520	1.8580	0.9300	0.4650	0.3030	0.1530	0.1020	0.0767
R2	Stream	78.4160	6.5440	34.0310	17.0210	8.5120	4.8650	2.6250	1.7500	1.3120
R3	Stream	10.7750	1.4630	9.2480	4.7150	2.3590	1.3480	0.6740	0.4500	0.3370
R4	Stream	28.6220	3.2870	19.8350	9.9230	4.9630	3.0680	1.5400	1.0270	0.7700

N/A The simulated period was too short for calculation of PEC_{SW}

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Step 3 PEC_{SW} and PEC_{SED} for MITC following application to tomatoes (FOCUS-fruiting vegetables)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
D6	Ditch	0.8410	0.4650	0.8210	0.7530	0.5820	0.4240	0.3360	0.3030	0.2900
R2	Stream	25.0930	2.7080	14.6930	8.4610	4.2740	2.4540	1.2270	0.8180	0.6140
R3	Stream	184.6650	15.8750	94.9340	47.5660	23.7960	13.6020	7.2900	4.8650	3.6490
R4	Stream	114.8120	6.5240	33.0880	17.8840	8.9440	5.1120	2.5860	1.7300	1.2970

Step 3 PEC_{SW} and PEC_{SED} for MITC following application to potatoes (FOCUS-potatoes)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
D3	Ditch	0.0319	0.0728	0.0318	0.0318	0.0317	0.0316	0.0314	0.0309	0.0304
D4	Pond	0.5980	0.2530	0.5930	0.5780	0.5520	0.4950	0.3680	0.2940	0.2350
D4	Stream	3.3540	1.3000	2.8920	2.6940	2.6090	2.3530	1.7350	1.3910	1.1310
D6 (1 st crop)	Ditch	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
D6 (2 nd crop)	Ditch	9.0840	2.8030	8.3550	7.6220	6.8140	5.6700	3.7440	2.7030	2.1650
R1	Pond	0.0858	0.0126	0.0605	0.0436	0.0272	0.0181	0.0094	0.0063	0.0047
R1	Stream	13.0580	1.0790	4.3770	3.1090	2.5550	0.9120	0.4560	0.3040	0.2290
R2	Stream	0.1190	0.0170	0.0659	0.0444	0.0231	0.0133	0.0067	0.0044	0.0033
R3	Stream	0.3280	0.0397	0.1650	0.0904	0.0452	0.0262	0.0131	0.0087	0.0066

Step 4 PEC_{SW} and PEC_{SED} for MITC in all run-off scenarios with 97.5% run-off reduction following application to carrots (FOCUS-root vegetables)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
R1	Pond	0.0071	0.0015	0.0055	0.0043	0.0028	0.0017	0.0010	0.0007	0.0005
R1	Stream	1.1090	0.0752	0.2590	0.1300	0.0648	0.0371	0.0286	0.0190	0.0143
R2	Stream	0.1620	0.0229	0.0897	0.0570	0.0293	0.0169	0.0085	0.0056	0.0042
R3	Stream	3.1860	0.2650	1.1650	0.5830	0.2920	0.1670	0.0838	0.0559	0.0419
R4	Stream	1.5490	0.2240	0.5210	0.6600	0.3310	0.1890	0.0947	0.0631	0.0473

Step 4 PEC_{SW} and PEC_{SED} for MITC in all run-off scenarios with 97.5% run-off reduction following application to corn salad (FOCUS-leafy vegetables)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
R1	Pond	0.0031	0.0006	0.0023	0.0018	0.0011	0.0007	0.0004	0.0003	0.0003
R1	Stream	1.0340	0.1010	0.3970	0.1990	0.0995	0.0568	0.0302	0.0202	0.0151
R1	Pond	0.0116	0.0020	0.0083	0.0061	0.0036	0.0022	0.0012	0.0008	0.0006
R1	Stream	0.0831	0.0137	0.0585	0.0293	0.0146	0.0095	0.0048	0.0032	0.0024
R2	Stream	2.4020	0.2420	1.0400	0.5200	0.2600	0.1490	0.0804	0.0536	0.0402
R3	Stream	0.3360	0.0566	0.2900	0.1480	0.0743	0.0424	0.0212	0.0142	0.0106
R4	Stream	0.8930	0.1260	0.6240	0.3120	0.1560	0.0966	0.0485	0.0323	0.0242

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Fate and behaviour in the environment

Step 4 PEC_{SW} and PEC_{SED} for MITC in all run-off scenarios with 97.5% run-off reduction following application to tomatoes (FOCUS-fruitlegging vegetables)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
R2	Stream	0.7820	0.1040	0.4600	0.2650	0.1340	0.0767	0.0384	0.0256	0.0192
R3	Stream	5.7780	0.5970	3.0450	1.5260	0.7640	0.4370	0.2330	0.1560	0.1170
R4	Stream	3.5220	0.2440	1.0130	0.5420	0.2710	0.1550	0.0783	0.0524	0.0393

Step 4 PEC_{SW} and PEC_{SED} for MITC in all run-off scenarios with 97.5% run-off reduction following application to potatoes (FOCUS-potatoes)

Scenario	Waterbody	Max PEC _{SW} (µg/L)	Max PEC _{SED} (µg/kg)	1 day TWAEC _{SW} (µg/L)	2 day TWAEC _{SW} (µg/L)	4 day TWAEC _{SW} (µg/L)	7 day TWAEC _{SW} (µg/L)	14 day TWAEC _{SW} (µg/L)	21 day TWAEC _{SW} (µg/L)	28 day TWAEC _{SW} (µg/L)
R1	Pond	0.0022	0.0004	0.0015	0.0011	0.0007	0.0005	0.0002	0.0002	0.0001
R1	Stream	0.3890	0.0391	0.1290	0.0876	0.0438	0.0258	0.0129	0.0086	0.0065
R2	Stream	0.0037	0.0007	0.0020	0.0014	0.0007	0.0004	0.0002	0.0001	0.0001
R3	Stream	0.0101	0.0015	0.0051	0.0028	0.0014	0.0008	0.0004	0.0003	0.0002

A number of uses of metam-sodium occur under circumstances where lateral movement of water is very unlikely. The applications to cucumber, pepper, aubergine and tomatoes in protected situations (glass-house/polytunnel) are examples of such circumstances. In addition, application to strawberries outdoors involves covering the soil location with plastic film, which also prevents contact between lateral moving water and MITC in soil.

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Fate and behaviour in the environment**PEC (ground water) (Annex IIIA, point 9.2.1)**

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)

<u>Metam-sodium</u> Not required , since the a.s. itself is subject to rapid degradation (laboratory DT₅₀'s ranged from 4- 23 minutes) and is not expected to reach groundwater <u>MITC</u> For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PEARL 3.3.3, PELMO 3.3.2 Scenarios : Chateaudun, Hamburg, Jokioinen, Kremsmunster, Porto, Sevilla, Thiva, Piacenza Crop: carrot, cabbage (surrogate for corn salad), tomato Molecular Mass (g mol⁻¹): 73.12 Vapour Pressure (Pa): 1739 at 20°C Aqueous Solubility (mg/L):8940 at 20°C Soil Adsorption Coefficient (mean K_{oc}) (ml/g): 13.5 (Kom = 7.83) Freundlich Exponent (1/n_f): 0.83 Arithmetic mean DT_{50 laboratory} (days): 2.10 at 20°C and pF2 Plant Uptake Coefficient: 0 <u>Impurity DMTU</u> For FOCUS gw modelling, values used – Modelling using FOCUS model(s), with appropriate FOCUSgw scenarios, according to FOCUS guidance. Model(s) used: PEARL 3.3.3, PELMO 3.3.2 Scenarios : Chateaudun, Hamburg, Jokioinen, Kremsmunster, Porto, Sevilla, Thiva, Piacenza Crop: carrot, cabbage (surrogate for corn salad), tomato Molecular Mass (g mol⁻¹): 104.18 Vapour Pressure (Pa): 832.95 at 20°C Aqueous Solubility (mg/L):581980 at 20°C Soil Adsorption Coefficient (mean K_{oc}) (ml/g): 9(Kom = 5) Freundlich Exponent (1/n_f): 0.76 Arithmetic mean DT_{50 laboratory} (days): 0.121 at 20°C and pF2 Plant Uptake Coefficient: 0	<u>MITC:</u> <u>Carrot</u> Application rate: 230.94 kg MITC/ha. No. of applications: 1/year Time of application (month or season): see below Incorporation (cm): 25
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Application rate

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Cabbage (surrogate for corn salad)
 Application rate: 173.21 kg MITC/ha.
 No. of applications: 1/year
 Time of application (month or season): see below
 Incorporation (cm): 15

Tomato
 Application rate: 346.41 kg MITC/ha.
 No. of applications: 1/year
 Time of application (month or season):
 Incorporation (cm): 15

Potato
 Application rate: 86.60 kg MITC/ha.
 No. of applications: 1/year
 Time of application (month or season): see below
 Incorporation (cm): 25

Impurity DMTU:
Carrot, Cabbage (surrogate for corn salad), tomatoes:
 Application rate: 7 kg DMTU/ha. (extreme worst case)
 No. of applications: 1/year
 Time of application (month or season): see below
 Incorporation (cm): 25, 15, 25 cm, respectively for carrot, cabbage and tomatoes

Location	Emergence/Transplanting	Harvest	Application date
Carrots			
Châteaudun	10-Mar	31-May	01-Oct
	10-Jul	20-Sep	
Hamburg	10-Mar	31-May	01-Oct
	10-Jul	20-Sep	
Kremsmünster	10-Mar	31-May	01-Oct
	10-Jul	20-Sep	
Porto	28-Feb	31-May	16-Oct
	22-Jul	15-Oct	
Thiva	15-Mar	22-May	01-Oct
	15-Jun	10-Sep	
Corn salad			
Châteaudun	20-Apr	15-Jul	21-Jul
	31-Jul	15-Oct	
Hamburg	20-Apr	15-Jul	21-Jul
	31-Jul	15-Oct	
Jokioinen	20-May	20-Sep	10-May
Kremsmünster	20-Apr	15-Jul	21-Jul
	31-Jul	15-Oct	
Porto	28-Feb	01-Jul	21-Jul
	31-Jul	15-Nov	

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Sevilla	01-Mar	01-Jun	05-Jun
	15-Jun	15-Sep	
Thiva	15-Aug	30-Nov	05-Aug
Tomatoes			
Châteaudun	10-May	25-Aug	10-Mar
Piacenza	10-May	25-Aug	10-Mar
Porto	15-Mar	31-Aug	10-Mar
Sevilla	15-Apr	01-Jul	10-Mar
Thiva	10-Apr	10-Sep	10-Mar

Additional simulations run for alternate date; **for efficacy considerations, autumn application not possible in Jokioinen

Calculated 80th percentile annual average worst-case predicted environmental concentration at 1 m soil depth (µg/L) using the FOCUS-PELMO 3.3.2 groundwater scenarios - MITC

Scenario	80 th Percentile Annual Average PEC _{GW} (µg/L)					
	FOCUS-carrots		FOCUS-cabbage	FOCUS-tomatoes		FOCUS-potatoes
	Winter	Spring		10 March	20 April	
Châteaudun	1.398	0.000	0.000	0.000	0.000	0.001
Hamburg	118.665	0.104	0.334	N/A	N/A	10.308
Jokioinen	N/A	0.000	0.000	N/A	N/A	197.734
Kremsmünster	20.888	0.000	0.000	N/A	N/A	0.540
Okehampton	N/A	N/A	N/A	N/A	N/A	1.208
Piacenza	N/A	N/A	N/A	2.040	0.039	0.645
Porto	0.367	0.000	0.000	0.000	*	0.000
Sevilla	N/A	N/A	0.000	0.000	*	0.000
Thiva	0.160	0.000	0.000	0.000	*	0.000
Thiva (1 year in 2)	0.050	*	*	*	*	*

N/A: Scenario not applicable to FOCUS crop

*Scenario not required

Calculated 80th percentile annual average worst-case predicted environmental concentration at 1 m soil depth (µg/L) using the FOCUS-PEARL 3.3.3 groundwater scenarios - MITC

Scenario	80 th Percentile Annual Average PEC _{GW} (µg/L)					
	FOCUS-carrots		FOCUS-cabbage	FOCUS-tomatoes		FOCUS-potatoes
	Winter	Spring		10 March	20 April	
Châteaudun	11.961	1.552	0.002	0.376	0.018	0.066
Hamburg	254.373	2.954	0.276	N/A	N/A	6.456
Jokioinen	N/A	0.378	0.003	N/A	N/A	49.264
Kremsmünster	43.011	0.301	0.061	N/A	N/A	0.827
Okehampton	N/A	N/A	N/A	N/A	N/A	1.947
Piacenza	N/A	N/A	N/A	48.561	1.262	0.591

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Porto	7.038	0.000	0.000	0.001	*	0.000
Sevilla	N/A	N/A	0.013	0.002	*	0.000
Thiva	0.111	0.023	0.000	0.000	*	0.000
Thiva (1 year in 2)	0.060	*	*	*	*	*

N/A: Scenario not applicable to FOCUS crop

*Scenario not required

Calculated 80th percentile annual average worst-case predicted environmental concentration at 1 m soil depth (µg/L) using the FOCUS-PELMO 3.3.2 groundwater scenarios- DMTU

Scenario	80 th Percentile Annual Average PEC _{GW} (µg/L)		
	FOCUS-carrots	FOCUS-cabbage	FOCUS-tomatoes
Châteaudun	0.000	0.000	0.000
Hamburg	0.000	0.000	N/A
Jokioinen	N/A	0.000	N/A
Kremsmünster	0.000	0.000	N/A
Okehampton	N/A	N/A	N/A
Piacenza	N/A	N/A	0.000
Porto	0.000	0.000	0.000
Sevilla	N/A	0.000	0.000
Thiva	0.000	0.000	0.000

N/A: Scenario not applicable to FOCUS crop

Calculated 80th percentile annual average worst-case predicted environmental concentration at 1 m soil depth (µg/L) using the FOCUS-PEARL 3.3.3 groundwater scenarios - DMTU

Scenario	80 th Percentile Annual Average PEC _{GW} (µg/L)		
	FOCUS-carrots	FOCUS-cabbage	FOCUS-tomatoes
Châteaudun	0.000	0.000	0.000
Hamburg	0.000	0.000	N/A
Jokioinen	0.000	0.000	N/A
Kremsmünster	0.000	0.000	N/A
Okehampton	N/A	N/A	N/A
Piacenza	N/A	N/A	0.000
Porto	0.000	0.000	0.000
Sevilla	N/A	0.000	0.000
Thiva	0.000	0.000	0.000

N/A: Scenario not applicable to FOCUS crop

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Fate and behaviour in the environment

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)

MITC - short range transport
Model(s) used: EUSES 2.1
 Scenarios : area of 200 km by 200 km with 20 million inhabitants for regional calculations. It is assumed that 10% of the EU production and use of the product takes place within this area i.e. 10% of the estimated emission is used as input for the region.
 Molecular mass (g/mol):73.12
 Melting point (°C):34
 Boiling point (°C):118
 Vapour pressure at 20°C (Pa):1739
 Water solubility at 20°C (mg/L):8940
 Log P at 20°C:1.05
 K_{OC} (ml/g):13.5
 DT₅₀ water (d): 50
 DT₅₀ soil (d): 2.1
 DT₅₀ air (d): 8.9
 Tonnage per year: 10970
 Fraction of EU volume for region (%): 10
 Industry category: Agricultural chemicals
 Use category: Plant protection products, agricultural
 Fraction of tonnage released to air: 1

Regional PECs for MITC in different environmental compartments

Compartment	PEC	Unit
Surface water	0.0153	µg/L
Air	6.63E-05	µg/L
Agricultural soil	1.84E-03	µg/kg _{swt}
Pore water of agricultural soil	5.15E-03	µg/L
Natural soil	4.12E-03	µg/kg _{swt}
Industrial soil	4.12E-03	µg/kg _{swt}
Sediment	0.015	µg/kg _{swt}

PEC_(gw) From lysimeter / field studies

Parent	1 st year	2 nd year	3 rd year
Annual average (µg/L)	Not available	Not available	Not available
MITC	1 st year	2 nd year	3 rd year
Annual average (µg/L)	Not available	Not available	Not available

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Fate and behaviour in the environment

	Process	Rate Constant	DT ₅₀ in troposphere (12 hr, days)
1	Direct photodegradation	$1.8 \times 10^{-6}/\text{sec}$	8.9
2	Reaction with hydroxyl radicals	$7.65 \times 10^{-7}/\text{sec}$	22.0
3	Reaction with O(³ P) species	$7.5 \times 10^{-7}/\text{sec}$	21.4
4	Direct photodegradation and Reaction with hydroxyl radicals	$2.565 \times 10^{-6}/\text{sec}$	6.3
5	Direct photodegradation and Reaction with hydroxyl radicals and Reaction with O(³ P) species	$3.315 \times 10^{-6}/\text{sec}$	4.8

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡

	MITC Process	Rate Constant	DT ₅₀ in troposphere (12 hr, days)
1	Direct photodegradation	$1.8 \times 10^{-6}/\text{sec}$	8.9
2	Reaction with hydroxyl radicals	$7.65 \times 10^{-7}/\text{sec}$	22.0
3	Reaction with O(³ P) species	$7.5 \times 10^{-7}/\text{sec}$	21.4
4	Direct photodegradation and Reaction with hydroxyl radicals	$2.565 \times 10^{-6}/\text{sec}$	6.3
5	Direct photodegradation and Reaction with hydroxyl radicals and Reaction with O(³ P) species	$3.315 \times 10^{-6}/\text{sec}$	4.8

Quantum yield of direct phototransformation

Photochemical oxidative degradation in air ‡

Volatilisation ‡

Metabolites

Not required

DT₅₀ of metam 1.997 hours based on 24h-day derived by the Atkinson model (version v1.90). OH concentration assumed = 1.5×10^6 OH/cm³

DT₅₀ of MITC = 78.6 days based on 12 h-day derived by the Atkinson model (version v1.92). OH concentration assumed = 1.5×10^6 OH/cm³

from plant surfaces (BBA guideline): not available

from soil surfaces (BBA guideline): not available

MITC

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Fate and behaviour in the environment**PEC (air)**

Method of calculation

Based on monitoring results

PEC_(a)

Maximum concentration

MITC air concentrations are proposed for the operator/worker/ bystander exposure risk assessment. These concentrations have not been peer reviewed by fate and behavior experts.

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).

Soil: metam-sodium, MITC
Surface Water: MITC
Sediment: MITC
Ground water: MITC
Air: MITC

Residue definition for monitoring

Soil: MITC
Surface Water: MITC
Sediment: MITC
Ground water: MITC
Air: MITC

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)

Not required

Surface water (indicate location and type of study)

Not required

Ground water (indicate location and type of study)

The Netherlands, around 1990-1995.
In shallow groundwater, 2-3 samples out of 126 were in the range 0.1-2.5 µg MITC/L. All other samples were below 0.1 µg MITC/L.
In the deeper groundwater, MITC was one of the compounds that was analyzed by drinking water companies in the period 1992-1995, but not detected

Germany, in 1985-1986.
MITC was analyzed in the program, but not found in any of the sampling points.

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Fate and behaviour in the environment

Air (indicate location and type of study)

See table below

Operation	Study location	Metam-sodium Application rate	MITC concentration in air at operator level	MITC concentration in air at bystander level
During soil-injection using tractor mounted equipment	15 fields, The Netherlands	153 kg a.s./ha	Inside the tractor: 0.012-0.169 mg MITC/m ³ levels after 2 minor incidents: contaminated gloves inside the cabin, contaminated soil on shoes: 0.189-0.592 mg MITC/m ³	outside the tractor: ND-0.054 mg MITC/m ³
During soil-injection using tractor mounted equipment (including tank filling)	11 fields, The Netherlands	214 to 357 kg a.s./ha	Inside the tractor: 0.006-0.187 mg MITC/m ³	-
4-78 hours after soil-injection using tractor mounted equipment	2 fields, Wisconsin	166 kg a.s./ha.	-	Above the treated fields (samplings at 10-200 cm height, 4 to 78 hours after treatment): 0.0002-0.0074 mg MITC/m ³
1-5 days after soil-injection	2 fields, The Netherlands	153 kg a.s./ha.	-	at a distance of 0 to 214 m of the field : max level of 0.003 mg MITC/m ³ at day 1-5 after application
During soil cultivation, 14-17 days after fumigation (seal breaking)	3 fields, The Netherlands	153 kg a.s./ha	Inside the tractor: ND-0.0046 mg MITC/m ³	-
During soil cultivation, 3-4.5 weeks after fumigation (seal breaking)			Inside the tractor: ND	-
During soil-injection using self-propelled equipment	1 glasshouse, The Netherlands	994 kg a.s./ha	Inside the glasshouse (no operator present): maximum level of 65 mg MITC/m ³ , 6 hours after treatment; Around 40 mg MITC/m ³ , 0-3 days after treatment around 4.7 mg/m ³ at day 5	Outside the glasshouse (0-20 m distance): 0.15-0.25 mg MITC/m ³ , 0-4 days after treatment; constant level of around 0.01 mg/m ³ for 4-8 days after application.

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Fate and behaviour in the environment

Operation	Study location	Metam-sodium Application rate	MITC concentration in air at operator level	MITC concentration in air at bystander level
During soil-injection using self-propelled equipment	1 field, Germany	153 kg a.s./ha	Inside the tractor: 0.070-0.076 mg MITC/m ³	at a distance of 0 to 100 m of the field: highest residues levels found downwind of the field ; Levels of <0.00004 (<LOD) to 0.036 mg MITC/m ³ at day 0-4 after application Levels of CS ₂ <0.4 mg/m ³ (<LOD) at day 0-4 after application, for all samplings Levels of methylamine <0.027 mg/m ³ (<LOD) at day 0-4 after application, for all samplings Levels of MIC <0.004 mg/m ³ (<LOD) at day 0-4 after application, for all samplings

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

R53 (by default, No acceptable study)

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Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg b.w./day)	End point (mg/kg feed)
Birds ‡				
<i>Colinus virginianus</i>	metam-sodium	Acute	LD ₅₀ = 211 ¹	-
<i>Colinus virginianus</i>	metam-sodium	Short-term	LC ₅₀ > 448	> 5000
<i>Anas platyrhynchos</i>	metam-sodium	Short-term	LC ₅₀ > 324 ²	> 5000
Mammals ‡				
rat	metam-sodium	Acute	LD ₅₀ = 896	-
	MITC	Acute	LD ₅₀ = 147 ³	-
rat	metam-sodium	Long-term	NOAEL = 1.5	-
	MITC	Long-term	NOAEL = 0.44	-
Additional higher tier studies ‡				
Not required.				

¹ corresponding to LD₅₀ = 119 mg MITC/kg b.w.

² corresponding to LC₅₀ > 183.4 mg MITC/kg b.w./day

³ for the risk assessment the worst case acute toxicity endpoint for MITC (from dossier dazomet), LD₅₀ (female mouse) = 100 mg MITC/kg b.w. was used

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Metam-sodium is a soil fumigant, formulated as an aqueous solution. Metam-sodium is rapidly degraded into Methylisothiocyanate (MITC), which is active on living organisms present in the soil at the time of the application.

The intended uses of metam-sodium are :

- carrot : 1 x 408 kg a.s./ha, field, soil injection + incorporation at 25 cm by rotavation
- corn salad : 1 x 306 kg a.s./ha, field, soil injection + incorporation at 15 cm by rotavation
- cucumber : 1 x 459 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- eggplant/aubergine : 1 x 612 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- pepper : 1 x 612 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- potato : 1 x 153 kg a.s./ha, field, soil injection + incorporation at 25 cm by rotavation
- strawberry : 1 x 612 kg a.s./ha, field, drip-irrigation under a plastic film on the planting row
- tomato : 1 x 612 kg a.s./ha, greenhouse, drip-irrigation under a plastic film on the planting row
- tomato : 1 x 612 kg a.s./ha, field, soil injection at 5 cm + coverage by 10 cm of soil
- grape : 1 x 1020 kg a.s./ha, field, soil injection at 40 cm at the site of the de-rooted vine (0.2 L/m²)

The application of metam-sodium is on bare soil; the product is incorporated into the soil (soil injection or drip irrigation) and thereafter the soil is compressed with a roller. After a waiting period of 2 to 4 weeks, the soil is cultivated to allow the non-mineralised gasses to disperse. Since the product is phytotoxic, it is advisable to perform a germination test (Cress-test) on samples of soils collected from the treated field, before planting.

Member States experts at PRAPeR 53 discussed the risk assessment for the birds and mammals exposed to metam-sodium and to the main metabolite (MITC). Experts suggest that the most probable contaminated food items for birds and mammals would be the soil invertebrates (included earthworms). The experts agreed that an acute risk assessment for insectivorous birds and mammals should be provided, even if the soil invertebrates were expected to be killed. A data gap was identified for the applicant to conduct an acute risk assessment to

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Ecotoxicology

assess the effects of metam-sodium and its metabolite MITC to terrestrial vertebrates feeding on soil invertebrates.

Member States experts agreed that acute risk assessment was necessary for the metabolite MITC for mammals. Experts agreed that lowest endpoint could be used in the risk assessment in accordance with previous assessment of active substance with common metabolite, unless scientific reasons suggest not to do it. Otherwise RMS should provide a risk assessment for the metabolite MITC using the lower endpoint of 100 mg/kg b.w. obtained from a mouse oral toxicity study in the dazomet DAR.

New data gap was identified by EFSA for the submission of a new risk assessment for MITC to mammals based on the agreed endpoint of 100 mg/kg b.w.

Acute risk assessment for **insectivorous birds** eating contaminated soil invertebrates on bare soil for the use in field crops (based on endpoint $LD_{50} = 119$ mg MITC/kg b.w.)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.20	0.046	19.1	6.23	10
tomato	346 (612)	1.20	0.046	19.1	6.23	10
carrot	230 (408)	1.20	0.046	12.7	9.37	10
corn salad	173 (306)	1.20	0.046	9.55	12.5	10
potato	86.3 (153)	1.20	0.046	4.76	25.0	10

* metam-sodium application rate in brackets

Short-term risk assessment for insectivorous birds eating contaminated soil invertebrates on bare soil for the use in field crops (based on endpoint $LC_{50} > 183.4$ mg MITC/kg b.w./day)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.20	0.021	8.72	21.0	10
tomato	346 (612)	1.20	0.021	8.72	21.0	10
carrot	230 (408)	1.20	0.021	5.80	31.6	10
corn salad	173 (306)	1.20	0.021	4.36	42.1	10
potato	86.3 (153)	1.20	0.021	2.17	84.3	10

* metam-sodium application rate in brackets

Acute risk assessment for **vermivorous birds** eating contaminated earthworms on bare soil for the use in field crops (based on endpoint $LD_{50} = 119$ mg MITC/kg bw)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.1	0.046	17.5	6.80	10
tomato	346 (612)	1.1	0.046	17.5	6.80	10
carrot	230 (408)	1.1	0.046	11.6	10.2	10
corn salad	173 (306)	1.1	0.046	8.75	13.6	10
potato	86.3 (153)	1.1	0.046	4.37	27.3	10

* metam-sodium application rate in brackets

Short-term risk assessment for vermivorous birds eating contaminated earthworms on bare soil for the use in field crops (based on endpoint $LC_{50} > 183.4$ mg MITC/kg b.w./day)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.1	0.021	7.99	22.9	10
tomato	346 (612)	1.1	0.021	7.99	22.9	10
carrot	230 (408)	1.1	0.021	5.31	34.5	10
corn salad	173 (306)	1.1	0.021	4.00	45.9	10

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Ecotoxicology

potato	86.3 (153)	1.1	0.021	1.99	92.0	10
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* metam-sodium application rate in brackets

Acute risk assessment for insectivorous mammals eating contaminated soil invertebrates on bare soil for the use in field crops (based on endpoint LD₅₀ = 100 mg MITC/kg bw)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.18	0.046	18.8	5.32	10
tomato	346 (612)	1.18	0.046	18.8	5.32	10
carrot	230 (408)	1.18	0.046	12.5	8.01	10
corn salad	173 (306)	1.18	0.046	9.39	10.6	10
potato	86.3 (153)	1.18	0.046	4.68	21.3	10

* metam-sodium application rate in brackets

Acute risk assessment for insectivorous mammals eating contaminated soil invertebrates on bare soil for the use in field crops (based on endpoint LD₅₀ = 100 mg MITC/kg bw and PD = 0.16)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	PD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.18	0.046	0.16	3.00	33	10
tomato	346 (612)	1.18	0.046	0.16	3.00	33	10
carrot	230 (408)	1.18	0.046	0.16	2.00	50	10
corn salad	173 (306)	1.18	0.046	0.16	1.50	67	10
potato	86.3 (153)	1.18	0.046	0.16	0.75	133	10

* metam-sodium application rate in brackets

Acute risk assessment for vermivorous mammals eating contaminated earthworms on bare soil for the use in field crops (based on endpoint LD₅₀ = 100 mg MITC/kg bw)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.4	0.046	22.3	4.49	10
tomato	346 (612)	1.4	0.046	22.3	4.49	10
carrot	230 (408)	1.4	0.046	14.8	6.75	10
corn salad	173 (306)	1.4	0.046	11.1	8.98	10
potato	86.3 (153)	1.4	0.046	5.56	18.0	10

* metam-sodium application rate in brackets

Acute risk assessment for vermivorous mammals eating contaminated earthworms on bare soil for the use in field crops (based on endpoint LD₅₀ = 100 mg MITC/kg bw and PD = 0.40)

Field uses of metam-sodium	MITC rate assuming complete conversion from metam-sodium* (kg/ha)	FIR/bw	RUD	PD	ETE	TER	Annex VI Trigger value
strawberry	346 (612)	1.4	0.046	0.40	8.91	11	10
tomato	346 (612)	1.4	0.046	0.40	8.91	11	10
carrot	230 (408)	1.4	0.046	0.40	5.92	17	10
corn salad	173 (306)	1.4	0.046	0.40	4.46	22	10
potato	86.3 (153)	1.4	0.046	0.40	2.22	45	10

* metam-sodium application rate in brackets

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Ecotoxicology

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity ¹ (mg/L)
Laboratory tests ‡				
Fish				
<i>Lepomis macrochirus</i>	metam-sodium	96 h (static)	Mortality, LC ₅₀	> 0.175 mg a.s./L (measured at 96 h)
<i>Oncorhynchus mykiss</i>	Vapam	96 h (static)	Mortality, LC ₅₀	0.24 mg form/L (0.078 mg a.s./L) (nom)
<i>Lepomis macrochirus</i>	Vapam	96 h (static)	Mortality, LC ₅₀	1.19 mg form/L (0.389 mg a.s./L) (nom)
<i>Cyprinodon variegatus</i>	Vapam	96 h (static)	Mortality, LC ₅₀	1.3 mg form/L (0.425 mg a.s./L) (nom)
Striped <i>Majatis</i>	Vapam	96 h (static)	Mortality, LC ₅₀	1.5 mg form/L (0.491 mg a.s./L) (nom)
<i>Oncorhynchus mykiss</i>	MITC	96 h (semi-static)	Mortality, LC ₅₀	0.0531 mg/L (mm)
<i>Oncorhynchus mykiss</i>	MITC	96 h (flow-through)	Mortality, LC ₅₀	0.094 mg/L (mm)
<i>Lepomis macrochirus</i>	MITC	96 h (flow-through)	Mortality, LC ₅₀	0.142 mg/L (mm)
<i>Oncorhynchus mykiss</i>	MITC	28 d (flow-through)	Growth NOEC	0.004 mg/L (mm)
Aquatic invertebrate				
<i>Daphnia magna</i>	Metam-Fluid 510 g/L	48 h (static)	Mortality, EC ₅₀	2.34 mg form/L (0.99 mg a.s./L) (nom)
<i>Daphnia magna</i>	MITC	48 h (semi-static)	Mortality, EC ₅₀	0.076 mg/L (mm)
<i>Daphnia magna</i>	MITC	21 d (semi-static)	Reproduction, NOEC	0.00625 mg/L (nom)
Sediment dwelling organisms				
Not required. The assessment of the risk to sediment dwelling organisms is not justified since the properties of MITC (low K _{oc} , high solubility in water) exclude exposure of the sediment organisms. Moreover, a low level of MITC was observed transiently in the sediment phase of the w/s study (1.5-4.5 % AR in the sediment after 72 h).				

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Group	Test substance	Time-scale (Test type)	End point	Toxicity ¹ (mg/L)
Algae				
<i>Pseudokirchneriella subcapitata</i>	Metam-Sodium 510 g/L	96 h (static)	Biomass: E _b C ₅₀ (72 h) Growth rate: E _r C ₅₀ (72 h)	0.556 mg a.s./L 1.08 mg a.s./L (initially measured)
<i>Pseudokirchneriella subcapitata</i>	MITC	72 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	0.28 mg/L 0.58 mg/L (initially measured)
<i>Anabaena flos-aquae</i>	MITC	72 h (static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	2.12 mg/L 3.72 mg/L (initially measured)
Higher plant				
<i>Lemna gibba</i>	MITC	7 d (semi-static)	Biomass: E _b C ₅₀ Growth rate: E _r C ₅₀	0.59 mg/L 1.18 mg/L (mean measured initial)
Microcosm or mesocosm tests				
Not required. An acceptable risk of metam-sodium and its metabolite MITC has been proven for the intended uses with a buffer zone of 20 m.				

¹ indicate whether based on nominal (nom) or mean measured concentrations (mm). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

The indoor uses pose no concern for surface water contamination. (e.g. cucumber, eggplant/aubergine, pepper and tomato) whilst the outdoor uses on strawberries occur under a plastic film, thus also preventing connectivity between soil and run-off water. Therefore no MITC contamination of surface water bodies via run-off is possible for this use. The uses on grapes are as a spot treatment and are very localized. Hence the overall application rate (for instance over an entire hectare) will be much lower than the application rate stated by m².

The assessment of the chronic risk to aquatic organisms is not justified since the DT₅₀ of MITC, whole water-sediment system is clearly below 2 days. The active substance is applied once a year. Moreover, soil sterilants are generally not used every year.

As already mentioned in the section on fate and behaviour, the PEC_{sw} values should be used with precaution. The FOCUS sw models were not developed with soil fumigants in mind. The models do not properly consider the volatilisation of MITC and therefore highly overestimate the actual surface water contamination.

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Ecotoxicology

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in carrot (1 x 408 kg a.s./ha) based on FOCUS step 3, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{SW} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	D 3	ditch	<i>Oncorhynchus mykiss</i>	96 h	0.0531	1 m	0.2740	194	100
	D 6	ditch				1 m	1.6640	31.9	100
	R 1	pond				1 m	0.2840	187	100
	R 1	stream				1 m	43.2370	1.23	100
	R 2	stream (1 st crop)				1 m	5.2130	10.2	100
	R 3	stream				1 m	115.4920	0.46	100
	R 4	stream				1 m	49.7660	1.07	100
MITC	D 3	ditch	<i>Daphnia magna</i>	48 h	0.076	1 m	0.2740	277	100
	D 6	ditch				1 m	1.6640	45.7	100
	R 1	pond				1 m	0.2840	268	100
	R 1	stream				1 m	43.2370	1.76	100
	R 2	stream (1 st crop)				1 m	5.2130	14.6	100
	R 3	stream				1 m	115.4920	0.66	100
	R 4	stream				1 m	49.7660	1.53	100
MITC	D 3	ditch	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	1 m	0.2740	1022	10
	D 6	ditch				1 m	1.6640	168	10
	R 1	pond				1 m	0.2840	986	10
	R 1	stream				1 m	43.2370	6.48	10
	R 2	stream (1 st crop)				1 m	5.2130	53.7	10
	R 3	stream				1 m	115.4920	2.42	10
	R 4	stream				1 m	49.7660	5.63	10
MITC	D 3	ditch	<i>Lemna gibba</i>	7 d	0.59	1 m	0.2740	2153	10
	D 6	ditch				1 m	1.6640	355	10
	R 1	pond				1 m	0.2840	2077	10
	R 1	stream				1 m	43.2370	13.6	10
	R 2	stream (1 st crop)				1 m	5.2130	113	10
	R 3	stream				1 m	115.4920	5.11	10

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Ecotoxicology

	R 4	stream				1 m	49.7660	11.9	10
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Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in corn salad (1 x 306 kg a.s./ha) based on FOCUS step 3, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	D 3	ditch (1 st crop)	<i>Oncorhynchus mykiss</i>	96 h	0.0531	1 m	0.0002	>10000	100
	D 3	ditch (2 nd crop)				1 m	0.0000	>10000	100
	D 4	pond				1 m	0.0129	4116	100
	D 4	stream				1 m	0.4280	124	100
	D 6	ditch				1 m	0.0000	>10000	100
	R 1	pond (1 st crop)				1 m	0.1230	432	100
	R 1	stream (1 st crop)				1 m	40.7640	1.30	100
	R 1	pond (2 nd crop)				1 m	0.4290	124	100
	R 1	stream (2 nd crop)				1 m	2.6630	19.9	100
	R 2	stream (2 nd crop)				1 m	78.4160	0.68	100
	R 3	stream (2 nd crop)				1 m	10.7750	4.93	100
	R 4	stream (2 nd crop)				1 m	28.6220	1.86	100
MITC	D 3	ditch (1 st crop)	<i>Daphnia magna</i>	48 h	0.076	1 m	0.0002	>10000	100
	D 3	ditch (2 nd crop)				1 m	0.0000	>10000	100

Rapporteur Member State	Month and year	Active Substance (Name)
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Ecotoxicology

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
	D 4	pond				1 m	0.0129	5891	100
	D 4	stream				1 m	0.4280	178	100
	D 6	ditch				1 m	0.0000	>10000	100
	R 1	pond (1 st crop)				1 m	0.1230	618	100
	R 1	stream (1 st crop)				1 m	40.7640	1.86	100
	R 1	pond (2 nd crop)				1 m	0.4290	177	100
	R 1	stream (2 nd crop)				1 m	2.6630	28.5	100
	R 2	stream (2 nd crop)				1 m	78.4160	0.97	100
	R 3	stream (2 nd crop)				1 m	10.7750	7.05	100
	R 4	stream (2 nd crop)				1 m	28.6220	2.66	100
MITC	D 3	ditch (1 st crop)	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	1 m	0.0002	>10000	10
	D 3	ditch (2 nd crop)				1 m	0.0000	>10000	10
	D 4	pond				1 m	0.0129	>10000	10
	D 4	stream				1 m	0.4280	654	10
	D 6	ditch				1 m	0.0000	>10000	10
	R 1	pond (1 st crop)				1 m	0.1230	2276	10
	R 1	stream (1 st crop)				1 m	40.7640	6.87	10

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Ecotoxicology

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
	R 1	pond (2 nd crop)				1 m	0.4290	653	10
	R 1	stream (2 nd crop)				1 m	2.6630	105	10
	R 2	stream (2 nd crop)				1 m	78.4160	3.57	10
	R 3	stream (2 nd crop)				1 m	10.7750	26.0	10
	R 4	stream (2 nd crop)				1 m	28.6220	9.78	10
MITC	D 3	ditch (1 st crop)	<i>Lemna gibba</i>	7 d	0.59	1 m	0.0002	>10000	10
	D 3	ditch (2 nd crop)				1 m	0.0000	>10000	10
	D 4	pond				1 m	0.0129	>10000	10
	D 4	stream				1 m	0.4280	1379	10
	D 6	ditch				1 m	0.0000	>10000	10
	R 1	pond (1 st crop)				1 m	0.1230	4797	10
	R 1	stream (1 st crop)				1 m	40.7640	14.5	10
	R 2	pond (2 nd crop)				1 m	0.4290	1375	10
	R 1	stream (2 nd crop)				1 m	2.6630	222	10
	R 2	stream (2 nd crop)				1 m	78.4160	7.52	10

Rapporteur Member State	Month and year	Active Substance (Name)
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Ecotoxicology

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{SW} , initial (µg a.s./L)	TER	Annex VI Trigger value
	R 3	stream (2 nd crop)				1 m	10.7750	54.8	10
	R 4	stream (2 nd crop)				1 m	28.6220	20.6	10

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in tomato (1 x 612 kg a.s./ha) based on FOCUS step 3, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{SW} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	D 6	ditch	<i>Oncorhynchus mykiss</i>	96 h	0.0531	1 m	0.8410	63.1	100
	R 2	stream				1 m	25.0930	2.12	100
	R 3	stream				1 m	184.6650	0.29	100
	R 4	stream				1 m	114.8120	0.46	100
MITC	D 6	ditch	<i>Daphnia magna</i>	48 h	0.076	1 m	0.8410	90.4	100
	R 2	stream				1 m	25.0930	3.03	100
	R 3	stream				1 m	184.6650	0.41	100
	R 4	stream				1 m	114.8120	0.66	100
MITC	D 6	ditch	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	1 m	0.8410	333	10
	R 2	stream				1 m	25.0930	11.2	10
	R 3	stream				1 m	184.6650	1.52	10
	R 4	stream				1 m	114.8120	2.44	10
MITC	D 6	ditch	<i>Lemna gibba</i>	7 d	0.59	1 m	0.8410	702	10
	R 2	stream				1 m	25.0930	23.5	10
	R 3	stream				1 m	184.6650	3.19	10
	R 4	stream				1 m	114.8120	5.14	10

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in potato (1 x 153 kg a.s./ha) based on FOCUS step 3, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{SW} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	D 3	ditch	<i>Oncorhynchus mykiss</i>	96 h	0.0531	1 m	0.0319	1665	100
	D 4	pond				1 m	0.5980	88.8	100

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Ecotoxicology

	D 4	stream				1 m	3.3540	15.8	100
	D 6	ditch (1 st crop)				1 m	0.0000	>10000	100
	D 6	ditch (2 nd crop)				1 m	9.0840	5.85	100
	R 1	pond				1 m	0.0858	619	100
	R 1	stream				1 m	13.0580	4.07	100
	R 2	stream				1 m	0.1190	446	100
	R 3	stream				1 m	0.3280	162	100
MITC	D 3	ditch	<i>Daphnia magna</i>	48 h	0.076	1 m	0.0319	2382	100
	D 4	pond				1 m	0.5980	127	100
	D 4	stream				1 m	3.3540	22.7	100
	D 6	ditch (1 st crop)				1 m	0.0000	>10000	100
	D 6	ditch (2 nd crop)				1 m	9.0840	8.37	100
	R 1	pond				1 m	0.0858	886	100
	R 1	stream				1 m	13.0580	5.82	100
	R 2	stream				1 m	0.1190	639	100
	R 3	stream				1 m	0.3280	232	100
MITC	D 3	ditch	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	1 m	0.0319	8777	10
	D 4	pond				1 m	0.5980	468	10
	D 4	stream				1 m	3.3540	83.5	10
	D 6	ditch (1 st crop)				1 m	0.0000	>10000	10
	D 6	ditch (2 nd crop)				1 m	9.0840	30.8	10
	R 1	pond				1 m	0.0858	3263	10
	R 1	stream				1 m	13.0580	21.4	10
	R 2	stream				1 m	0.1190	2353	10
	R 3	stream				1 m	0.3280	854	10
MITC	D 3	ditch	<i>Lemna gibba</i>	7 d	0.59	1 m	0.0319	>10000	10
	D 4	pond				1 m	0.5980	987	10
	D 4	stream				1 m	3.3540	176	10
	D 6	ditch (1 st crop)				1 m	0.0000	>10000	10
	D 6	ditch (2 nd crop)				1 m	9.0840	64.9	10

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	R 1	pond				1 m	0.0858	6876	10
	R 1	stream				1 m	13.0580	45.2	10
	R 2	stream				1 m	0.1190	4958	10
	R 3	stream				1 m	0.3280	1799	10

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in carrot (1 x 408 kg a.s./ha) based on FOCUS step 4, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	R 1	pond	<i>Oncorhynchus mykiss</i>	96 h	0.0531	20 m	0.0071	7479	100
	R 1	stream				20 m	1.1090	47.9	100
	R 2	stream				20 m	0.1620	328	100
	R 3	stream				20 m	3.1860	16.7	100
	R 4	stream				20 m	1.5490	34.3	100
MITC	R 1	pond	<i>Daphnia magna</i>	48 h	0.076	20 m	0.0071	>10000	100
	R 1	stream				20 m	1.1090	68.5	100
	R 2	stream				20 m	0.1620	469	100
	R 3	stream				20 m	3.1860	23.9	100
	R 4	stream				20 m	1.5490	49.1	100
MITC	R 1	pond	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	20 m	0.0071	>10000	10
	R 1	stream				20 m	1.1090	252	10
	R 2	stream				20 m	0.1620	1728	10
	R 3	stream				20 m	3.1860	87.9	10
	R 4	stream				20 m	1.5490	181	10
MITC	R 1	pond	<i>Lemna gibba</i>	7 d	0.59	20 m	0.0071	>10000	10
	R 1	stream				20 m	1.1090	532	10
	R 2	stream				20 m	0.1620	3642	10
	R 3	stream				20 m	3.1860	185	10
	R 4	stream				20 m	1.5490	381	10

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in corn salad (1 x 306 kg a.s./ha) based on FOCUS step 4, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	R 1	pond (1 st crop)	<i>Oncorhynchus mykiss</i>	96 h	0.0531	20 m	0.0031	>10000	100

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Ecotoxicology

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
	R 1	stream (1 st crop)				20 m	1.0340	51.4	100
	R 1	pond (2 nd crop)				20 m	0.0110	4827	100
	R 1	stream (2 nd crop)				20 m	0.0831	639	100
	R 2	stream (2 nd crop)				20 m	2.4020	22.1	100
	R 3	stream (2 nd crop)				20 m	0.3360	158	100
	R 4	stream (2 nd crop)				20 m	0.8930	59.5	100
MITC	R 1	pond (1 st crop)	<i>Daphnia magna</i>	48 h	0.076	20 m	0.0031	>10000	100
	R 1	stream (1 st crop)				20 m	1.0340	73.5	100
	R 1	pond (2 nd crop)				20 m	0.0110	6909	100
	R 1	stream (2 nd crop)				20 m	0.0831	915	100
	R 2	stream (2 nd crop)				20 m	2.4020	31.6	100
	R 3	stream (2 nd crop)				20 m	0.3360	226	100
	R 4	stream (2 nd crop)				20 m	0.8930	85.1	100
MITC	R 1	pond (1 st crop)	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	20 m	0.0031	>10000	10
	R 1	stream (1 st crop)				20 m	1.0340	271	10
	R 1	pond (2 nd crop)				20 m	0.0110	>10000	10

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Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
	R 1	stream (2 nd crop)				20 m	0.0831	3369	10
	R 2	stream (2 nd crop)				20 m	2.4020	117	10
	R 3	stream (2 nd crop)				20 m	0.3360	833	10
	R 4	stream (2 nd crop)				20 m	0.8930	314	10
MITC	R 1	pond (1 st crop)	<i>Lemna gibba</i>	7 d	0.59	20 m	0.0031	>10000	10
	R 1	stream (1st crop)				20 m	1.0340	571	10
	R 1	pond (2 nd crop)				20 m	0.0110	>10000	10
	R 1	stream (2 nd crop)				20 m	0.0831	7100	10
	R 2	stream (2 nd crop)				20 m	2.4020	246	10
	R 3	stream (2 nd crop)				20 m	0.3360	1756	10
	R 4	stream (2 nd crop)				20 m	0.8930	661	10

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in tomato (1 x 612 kg a.s./ha) based on FOCUS step 4, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer-zone	PEC _{sw} , initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	R 2	stream	<i>Oncorhynchus mykiss</i>	96 h	0.0531	20 m	0.7820	67.9	100
	R 3	stream				20 m	5.7780	9.19	100
	R 4	stream				20 m	3.5220	15.1	100
MITC	R 2	stream	<i>Daphnia magna</i>	48 h	0.076	20 m	0.7820	97.2	100
	R 3	stream				20 m	5.7780	13.2	100
	R 4	stream				20 m	3.5220	21.6	100

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Ecotoxicology

MITC	R 2	stream	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	20 m	0.7820	358	10
	R 3	stream				20 m	5.7780	48.5	10
	R 4	stream				20 m	3.5220	79.5	10
MITC	R 2	stream	<i>Lemna gibba</i>	7 d	0.59	20 m	0.7820	754	10
	R 3	stream				20 m	5.7780	102	10
	R 4	stream				20 m	3.5220	168	10

Toxicity Exposure Ratio's (TER's) for aquatic organisms exposed to the metabolite MITC for the intended use in potato (1 x 153 kg a.s./ha) based on FOCUS step 4, laboratory soil degradation data

Test substance	Scenario	Water body type	Test species	Time-scale	Endpoint (mg a.s./L)	Buffer zone	PEC _{sw} initial (µg a.s./L)	TER	Annex VI Trigger value
MITC	R 1	pond	<i>Oncorhynchus mykiss</i>	96 h	0.0531	20 m	0.0022	>10000	100
	R 1	stream				20 m	0.3890	137	100
	R 2	stream				20 m	0.0037	>10000	100
	R 3	stream				20 m	0.0101	5257	100
MITC	R 1	pond	<i>Daphnia magna</i>	48 h	0.076	20 m	0.0022	>10000	100
	R 1	stream				20 m	0.3890	195	100
	R 2	stream				20 m	0.0037	>10000	100
	R 3	stream				20 m	0.0101	7525	100
MITC	R 1	pond	<i>Pseudokirchneriella subcapitata</i>	72 h	0.28	20 m	0.0022	>10000	10
	R 1	stream				20 m	0.3890	720	10
	R 2	stream				20 m	0.0037	>10000	10
	R 3	stream				20 m	0.0101	>10000	10
MITC	R 1	pond	<i>Lemna gibba</i>	7 d	0.59	20 m	0.0022	>10000	10
	R 1	stream				20 m	0.3890	1517	10
	R 2	stream				20 m	0.0037	>10000	10
	R 3	stream				20 m	0.0101	>10000	10

Bioconcentration

	metam-sodium	MITC	Metabolite2	Metabolite3
logP _{ow}	- 2.91	1.05	-	-
Bioconcentration factor (BCF) ¹ ‡	Not required.			
Annex VI Trigger for the bioconcentration factor	-	-	-	-

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Bioconcentration				
Clearance time (days) (CT ₅₀)	-	-	-	-
(CT ₉₀)	-	-	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	-	-	-	-

¹ only required if log P_{O/W} > 3.* based on total ¹⁴C or on specific compounds**Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)****Hazard quotients for honey bees (Annex IIIA, point 10.4)**

The application of metam-sodium is on bare soil; the product is incorporated into the soil (soil injection or drip irrigation) and thereafter the soil is compressed with a roller. After a waiting period of 2 to 4 weeks, the soil is cultivated to allow the non-mineralised gasses to disperse. Since the product is phytotoxic, it is advisable to perform a germination test (Cress-test) on samples of soils collected from the treated field, before planting.

There is no direct spraying on plant material. The germination test proves that there is no concern of residues of metam-sodium or MITC in the planted crops. Therefore, bees are not at risk in-field and off-field since they are not exposed to contaminated crops or weeds. Bees are not exposed to the uses in greenhouse.

In conclusion, the risk of metam-sodium and its metabolite MITC to bees is acceptable for the intended uses.

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Not required.

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (kg a.s./ha) ^{1,2}	End point	% effect ³	Trigger value
<i>Aleochara bilineata</i>	adults	Metam-Sodium 507 g a.s./L, aged field soil, 28 d	608.4 kg a.s./ha, aged for 55 days	Reproduction	14.6 %	50 %

¹ indicate whether initial or aged residues² for preparations indicate whether dose is expressed in units of a.s. or preparation³ indicate if positive percentages relate to adverse effects or not

effect on reproduction : negative values : adverse effects; positive values : no adverse effects

Field or semi-field tests

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Required.

The risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field. An extended laboratory study is only able to assess the potential for recolonisation, but not actual recovery. Therefore, a semi-field or field study should demonstrate that the field can be recolonised with non-target arthropods from the border stripes (off-field). In this new study, several species should be tested (*Aleochara bilineata*, *Pardosa*, *Folsomia candida*, *Hypoaspis aculeifer*, ...).

A field trial (Aldershof S., 2010) was performed to determine the effects of metam-sodium on the non-target arthropod fauna of arable land in SW-France after one application in spring. The field study is well performed (different taxa were sampled with soil and pitfall sampling) and good reported reevaluations by different statistical methods).

Metam-sodium application at the highest rate of 612 kg a.s./ha has initial adverse effects on soil arthropods living in the soil and at the soil surface. The field study demonstrates that actual recovery in the field will occur for the most important taxa within one year:

- For the soil samples 0% taxa showed a recovery > 1 year. The arthropod taxa that would be expected to be most at risk from a soil injected treatment such as metam-sodium would be the small and relatively immobile soil dwelling taxa such as Collembola, soil mites, larvae of soil dwelling beetles (e.g. Aleocharinae and some Carabidae). All of these groups showed clear recovery within one year of application of metam-sodium (see also B.9.7).
- For the pitfall samples only 2% taxa showed a recovery > 1 year. From Table B.9.5.3-4 it appears that of all the sampled taxa the only taxon that did not show full recovery within one year was Heteroptera. Also from Figure B.9.5.3-3A (PRC 1+2) it is clear that Heteroptera contributed largely to the delayed response pattern. Heteroptera are primarily foliage dwelling arthropods and therefore not strongly associated with bare soil, which is the GAP for the application of metam. From Figure B.9.5.3-8 it is clear that any effects of metam-sodium on Heteroptera did not begin to occur until 4 months after treatment. Such a long delay to onset of effects is due to an indirect effect, either the decline in numbers of a suitable prey (for example aphids) on the carrot plants or decline in quality of a host plant (for phytophagous Heteroptera). The numbers of Heteroptera in metam-sodium treated plots were not statistically different from controls in samples taken the year after treatment. Despite being reported as not having shown recovery, the data shows that no difference was observed in absolute numbers just before and one year after treatment.

For the most important soil inhabiting and soil surface dwelling species the recovery occurs within one year. For 2% of pitfall sampling taxa recovery is still ongoing in the next spring. In conclusion, the risk of metam-sodium and its metabolite MITC to non-target arthropods is sufficiently addressed for the field uses at the EU level. RMS proposes that potential risk mitigation measures are taken into consideration at the Member State level.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point ¹
Earthworms			
An earthworm field study (Lührs U., 2002) was performed with the formulation Metam-Sodium 507 g a.s./L.			
Other soil macro-organisms			

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Test organism	Test substance	Time scale	End point ¹
Required. The risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field. An extended laboratory study is only able to assess the potential for recolonisation, but not the actual recovery. Therefore, a semi-field or field study should demonstrate that the field can be recolonised with Collembola from the border stripes (off-field) or underlying soil layers (in-field). This new field study can be integrated with the requested semi-field or field study for the non-target arthropods. There is no evidence from any of the density graphs in the field study of Aldershot (2010) that long-term effects on soil dwelling macro-invertebrates occurred due to metam-sodium treatment. All affected soil dwelling invertebrates had fully recovered in abundance within the same season and no adverse effects extended into the year after treatment. The risk of metam-sodium and its metabolite MITC to non-target soil macro-organisms is acceptable for the intended field uses since recovery within 1 year after application was demonstrated.			
Soil micro-organisms			
A soil microflora laboratory test (Reis K.H., 2002) was conducted with soil samples from the earthworm field study with application rates of 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha). The effects of metam-sodium and its metabolite MITC on nitrogen and carbon transformation were transient and the processes were not drastically impaired.			
Field studies ²			

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Ecotoxicology

Test organism	Test substance	Time scale	End point ¹
An earthworm field study (Lühns U., 2002) was conducted from May 31, 2001 until May 22, 2002. The assessment of the effects of metam-sodium and its metabolite MITC should be done in comparison with the agricultural control only (same soil cultivation). One year after treatment of 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha), the earthworm abundance was 103.5 % and 85.2 % respectively of the agricultural control. The earthworm biomass was 123.7 % and 85.8 % one year after application of 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha) respectively. Amongst the collected earthworms, the most abundant species was <i>Aporrectodea caliginosa</i>. 4^{1/2} months after treatment with 300 and 1200 L Metam-Sodium/ha (equivalent to 152.1 and 608.4 kg a.s./ha), the abundance of <i>Aporrectodea caliginosa</i> was comparable to that in the agricultural control. The abundance of juvenile earthworms one year after application of 300 L Metam-Sodium/ha (equivalent to 152.1 kg a.s./ha) was comparable to the agricultural control, whereas at 1200 L Metam-Sodium/ha (equivalent to 608.4 kg a.s./ha) it was still statistically significantly lower. In conclusion, one year after application of 152.1 kg a.s./ha, the earthworm population in the field has recovered. One year after application of 608.4 kg a.s./ha, there is a clear indication of an almost completed process of recovery. Since there was a reduced plant cover (lower food source) at 608.4 kg a.s./ha, this represents a worst case situation. EFSA: The experts agreed that after the application of the 608.4 kg a.s./ha, there was no clear indications of the full recovery of earthworms after one year, therefore, some uncertainties of recovery in the field area still remained. A data gap was identified to the applicant to address concerns rest on the recovery/recolonisation of earthworms. The notifier provided information on the migration distances of earthworm species, indicating that the recovery observed in the test plots is representative for the field situation. In conclusion, the risk of metam-sodium and its metabolite MITC to earthworms is acceptable for the field use at the lower application rate of 153 kg a.s./ha and is sufficiently addressed for the higher application rate of 612 kg a.s./ha at the EU level (an almost completed process of recovery was demonstrated over a period of one year). RMS proposes that potential risk mitigation measures are taken into consideration at the Member State level for the higher application rates, allowing the earthworms to recover in the field.			

¹ indicate where end point has been corrected due to log Pow >2.0 (e.g. LC_{50corr})

² litter bag, field arthropod studies not included at 8.3.2/10.5 above, and earthworm field studies

Toxicity/exposure ratios for soil organisms

The application of metam-sodium is on bare soil; the product is incorporated into the soil (soil injection or drip irrigation) and thereafter the soil is compressed with a roller. After a waiting period of 2 to 4 weeks, the soil is cultivated to allow the non-mineralised gasses to disperse. Since the product is phytotoxic, it is advisable to perform a germination test (Cress-test) on samples of soils collected from the treated field, before planting.

The experts agreed that after the application of the 608.4 kg a.s./ha, there was no clear indications of the full recovery of earthworms after one year, therefore, some uncertainties of recovery in the field area still remained. A data gap was identified to the applicant to address concerns rest on the recovery/recolonisation of earthworms. Risk to metam and its metabolite should be addressed in terms of recovery in the field. RMS suggests that a semi-field or field study should demonstrate the recolonisation of the fields.

The expert at the PRAPeR 53 agreed to propose a data gap for the applicant to provide a semi-field or field study to address the recovery potential of soil non-target macro-organisms.

EFSA noted while drafting the conclusion that there was some concern about the risk of metam-sodium to earthworm in the glasshouse uses. EFSA considers, for permanent glasshouse the risk was considered low but for temporary glasshouse tunnels that included natural soil (non-artificial substrate) member states might wish to ask for further data to clarification the risk to earthworms.

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Ecotoxicology

Soil organisms (non-target arthropods, earthworms, soil macro-organisms and soil micro-organisms) are not exposed to the uses in greenhouse.

The updated risk assessment for non-target arthropods, earthworms and soil macro-organisms is presented above.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

The application of metam-sodium is on bare soil; the product is incorporated into the soil (soil injection or drip irrigation) and thereafter the soil is compressed with a roller. The mode of application excludes the off-field exposure.

In conclusion, the risk of metam-sodium and its metabolite MITC to non-target terrestrial plants is acceptable for the intended uses.

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	Endpoint
Activated sludge	EC ₅₀ (3 hours) = 4.36 mg a.s./L

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	metam-sodium, MITC
water	MITC
sediment	MITC
groundwater	MITC

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

Active substance

Metabolite

Preparation

RMS/peer review proposal

metam-sodium : N, R50

MITC : N, R50

RMS/peer review proposal

Not required. The formulated product is equivalent to the active substance.

Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	November 2008 Revision August 2010	Metam

Ecotoxicology

Code/Trivial name	Chemical name	Structural formula
Metam-sodium	sodium N-methyldithiocarbamate	$\text{H}_3\text{C}-\text{NH}-\text{C}(\text{S})_2\text{S}^- \text{Na}^+$
MITC	Methylisothiocyanate	$\text{H}_3\text{C}-\text{N}=\text{C}=\text{S}$
MIC	Methylisocyanate	$\text{H}_3\text{C}-\text{N}=\text{C}=\text{O}$
DMTU	N,N'-dimethylthiourea (or 1,3-dimethylthiourea)	$\text{H}_3\text{C}-\text{NH}-\text{C}(=\text{S})-\text{NH}-\text{CH}_3$
DMU	N,N'-dimethylurea	$\text{H}_3\text{C}-\text{NH}-\text{C}(=\text{O})-\text{NH}-\text{CH}_3$
	N-methylthioformamide	$\text{H}_3\text{C}-\text{NH}-\text{C}(=\text{S})-\text{H}$
MCDT	sodium methylcarbamo(dithioperoxo)thioate	$\text{H}_3\text{C}-\text{NH}-\text{C}(=\text{S})-\text{S}-\text{S}^- \text{Na}^+$
	Carbon disulphide	$\text{S}=\text{C}=\text{S}$
	methylamine	$\text{H}_3\text{C}-\text{NH}_2$

LEVEL 3

Metam

Proposed decision with respect to the application for inclusion of the active substance in Annex I

WARNING: This document forms part of an EC evaluation data package and should not be read in isolation. Registration must not be granted on the basis of this document.

3.1 Background to the proposed decision

The information provided by the notifier was sufficient to evaluate the a.s according to Directive 91/414/EEC. The evaluation of the data and the risk assessment that were performed showed that the use of metam-sodium according to GAP does not cause unacceptable risk to human beings and to the environment.

3.2 Proposed decision concerning inclusion in Annex I

It is proposed to include metam-sodium (incl. salts metam-sodium and metam-potassium) in Annex I. However, it is noted that the majority of data provided in the dossier evaluated by the RMS belongs to the variant metam-sodium.

3.3 Rationale for the postponement of the decision to include the active substance in Annex I, or for the conditions and restrictions to be associated with a proposed inclusion in Annex I, as appropriate

None.

LEVEL 4

Metam

Further information to permit a decision to be made, or to support a review of the conditions and restrictions associated with the proposed inclusion in the Annex I

4.1 Identity of the active substance

None (for main notifier Taminco)

4.2 Physical and chemical properties of the active substance

A GLP storage stability study with the analysis of the technical concentrates for relevant impurities before and after storage (cf. data gap identified in EFSA conclusion of 26 November 2008) is ongoing.

4.3 Data on application and further information

None

4.4 Classification, packaging and labelling

None

4.5 Methods of analysis

None

4.6 Toxicology and metabolism

None

4.7 Residue data

None

4.8 Environmental fate and behaviour

None

4.9 Ecotoxicology

None