CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance metam[1]

European Food Safety Authority[2]

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SUMMARY

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,[3] as amended by Commission Regulation (EC) No 1095/2007.[4] This Regulation requires the European Food Safety Authority (EFSA) to organise upon request of the European Commission a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within six months a conclusion on the risk assessment to the European Commission.

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 set out in the EFSA Conclusion issued on 26 November 2008 (EFSA, 2008).

Following the Council Decision of 13 July 2009 (2009/562/EC)[5] concerning the non-inclusion of metam in Annex I to Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Taminco N.V. made a resubmission application for the inclusion of metam in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (SANCO/206/2008; European Commission, 2009) as follows:

- the risk to consumers given the data gaps identified in the residue section and the possible impact of the relevant impurity DMTU; as a consequence, the consumers risk assessment could not be finalised;

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[1] On request from the European Commission, Question No EFSA-Q-2010-01465, issued on 8 August 2011.
[2] Correspondence: pesticides.peerreview@efsa.europa.eu
[3] OJ No L 224, 21.08.2002, p. 25, as amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)
[4] OJ L 246, 21.9.2007, p. 19
[5] OJ L 196, 28.7.2009, p. 22

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- the fate and behaviour in soil and water due to inadequate information on the major metabolite MITC and impurity DMTU. As a consequence, the risk to groundwater could not be finalised;

- MITC is volatile and long-range transport and potential effects on the atmosphere need to be further addressed;

- The risk assessment of acute effects of metam and its metabolite MITC to terrestrial vertebrates feeding on soil invertebrates;

- Further information is required to address the recovery potential of the non-target arthropods, earthworms and non-target soil macro-organisms.

And concerns were identified with regard to

- the potential for contamination of groundwater by the major metabolite MITC in some scenarios;

- the risk assessment for operators and workers in greenhouses;

- risk to aquatic organisms.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Belgium, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (Belgium, 2010). The Additional Report was received by the EFSA on 31 August 2010.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 14 September 2010. The EFSA collated and forwarded all comments received to the European Commission on 28 October 2010.

In accordance with Article 20, following consideration of the Additional Report and the comments received, the European Commission requested the EFSA to conduct a focussed peer review in the areas of environmental fate and behaviour and ecotoxicology, and deliver its conclusions on metam.

The conclusion from the original review was reached on the basis of the evaluation of the representative uses as a nematicide, fungicide, herbicide and insecticide by soil fumigation prior to the planting of carrot, lamb's lettuce, cucumber, aubergine, pepper, potato, strawberry, tomato and grapes. The conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the same representative uses. Full details of the representative uses can be found in Appendix A.

The representative formulated product for the evaluation was "Metam sodium 510 g/L", a soluble concentrate (SL), registered under different trade names in Europe.

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method such as the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Storage stability data where the relevant impurities are analysed for was identified as a data gap. Spectra are available for the relevant impurity MITC[6] and also for the relevant impurity DMTU[7].

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[6] MITC: methyl isothiocyanate
[7] DMTU: *N,N'*-dimethylthiourea

As for mammalian toxicology, metam-sodium is harmful by oral ingestion and inhalation (R22 and R20 proposed). In irritation tests, metam-sodium was not irritant to eyes but was corrosive to skin, therefore R34 (“Causes burns”) was proposed. Metam-sodium is a skin sensitiser (R43 “May cause sensitisation by skin contact” proposed). The relevant short-term No Observed Adverse Effect Levels (NOAELs) are 0.1, 0.5 and 0.8 mg/kg bw/day in dogs, rats and mice, respectively. In particular, the occurrence of severe hepatotoxicity in dogs was considered to support the proposal of R48/22 (“Danger of serious damage to health by prolonged exposure if swallowed”) to the European Chemicals Agency (EChA). Metam did not show any genotoxic potential, but caused angiosarcomas in mice, therefore R40 (“Limited evidence of a carcinogenic effect”) was proposed. The relevant long-term NOAEL was 1.5 mg/kg bw/day based on reduced bodyweight gain, specific lesion within the nasal passages, and changes in some haematology and spleen (haemosiderin depots) parameters in rats. In multigeneration tests, the relevant parental, reproductive and offspring NOAELs were 4, 12 and 4 mg/kg bw/day, respectively. Tested in developmental toxicity studies, metam-sodium caused an increased incidence of variations and retardations at maternally toxic dose in rats and decreased number of live foetuses, and increased number of dead implants in rabbits, with relevant maternal and developmental NOAEL in rats of 5 mg/kg bw/day and of 5 and 10 mg/kg bw/day, respectively, in rabbits. The malformations occurred at low incidences (sometimes in singularity), but in a consistent manner, at the top-doses, in the presence of quite severe maternal toxicity. Effects were clearly treatment related and associated with maternal toxicity: the classification as R63 (“Possible risk of harm to the unborn child”) was proposed for consideration to the EChA. The Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 0.001 mg/kg bw/day, based on the 1-year dog study NOAEL with a Safety Factor (SF) 100; the Acute Reference Dose (ARfD) is 0.1 mg/kg bw based on an overall rat developmental toxicity NOAEL and supported by rabbit developmental study (SF 100).

MITC is toxic via ingestion (R25 proposed) and via inhalation (R23 proposed). It is harmful in contact with skin (R21 proposed). In skin irritation tests it was corrosive (R34 proposed). It was also irritative to the respiratory system (R37 proposed). It is a skin sensitiser (R43 proposed).

The relevant NOAEL for short-term exposure to MITC is 0.4 mg/kg bw/day, based on body weight decrease, haematological findings and blood chemistry at 2 mg/kg bw/day (in the 90d dog study). MITC did not show any genotoxic, carcinogenic, reproductive or developmental toxicity potential. The relevant NOAEL for long-term toxicity is 0.44 mg/kg bw/day based on haematological changes in rats; the relevant parental NOAEL is 0.7 mg/kg bw/day, the reproductive and offspring NOAEL is >3.6 mg/kg bw/day. The relevant maternal and developmental toxicity NOAELs in rats are 3 and 10 mg/kg bw/day. The ADI and AOEL are 0.004 mg/kg bw/day based on the 1 year and 90-day studies in dog, respectively; the ARfD is 0.03 mg/kg bw based on a NOAEL for rat maternal toxicity with SF 100. The operator exposure in open field is below the AOEL with the use of Respiratory Protective Equipment (RPE); the bystander exposure for applications in the open field is below the AOEL and worker exposure for applications in the open field is below the AOEL without the use of Personal Protective Equipment (PPE).The operator exposure for drip irrigation in greenhouses is 2.9% of the AOEL with the use of RPE. The worker exposure is below the AOEL even without RPE 18 days after application. Bystander exposure exceeds the AOEL 10 hours after application within 12 metres of the greenhouse. The PRAPeR meeting of experts considered the impurity DMTU as relevant.

Metabolism studies were supplied but no metabolites were identified. It was noted that the majority of the metabolism studies were under dosed. The meeting of experts considered the under dosing and lack of identification and it was concluded that as long as fate and behaviour had not identified any significant metabolites in soil then the metabolism data could be accepted. In the resubmission, the evaluation performed in the area of fate and behaviour confirmed that no other significant metabolites (other than MITC) are present and therefore the metabolism data are acceptable. In the resubmission the residue trials data set was completed and it can be concluded that the uses do not lead to residues >0.01 mg/kg. It can be concluded that there is no need for processing studies, rotational crop studies or livestock studies. The risk assessment can be finalised and MRLs are proposed for all representative crops at 0.01* mg/kg.

Degradation of metam and its known active metabolite MITC in soil was investigated in four soils under dark aerobic conditions at 20 °C. The experts in the meeting were not confident that these experiments provided a realistic representation of the fate and behaviour of metam and MITC in soil mainly due to the mode of application used in the study with respect to the application in field where volatilisation is minimized by compacting soil or with plastic films. However, the meeting noted that a number of scientific studies investigating the persistence of metam and MITC are available in the public domain and to regulatory authorities. Consequently, in the original review a data gap was identified to address the range of half-lives available for metam and MITC and whether they are applicable to the metam EU risk assessment. In the resubmission dossier the applicant presented a number of studies from the scientific literature. Available scientific literature allows a relationship between the concentration of MITC in soil and its rate of degradation to be established. MITC degrades slowly at higher concentration rates. Whereas the GLP study available in the original dossier (Hall, 2004; summarized in the DAR of Belgium, 2010) was considered scientifically acceptable, it was performed with a MITC concentration in the low range of the ones that would result from the representative uses proposed for metam. It was agreed that only the use in potato (153 kg metam /ha) could be considered covered by the end points derived from this study. A new data gap was identified to address those situations where the soil concentrations of the metabolite MITC due to the use of metam are expected to be significantly higher than the concentration used in the available GLP study.

Taking into consideration the application rates of metam other than for the use on grape (306 – 612 kg / ha), during the peer review it was considered that impurities need to be addressed for the potential environmental and ground water contamination. The notifier submitted an overview of the main impurities present in the technical material that was summarized by the RMS in the addendum (Belgium, 2008). The meeting of experts in toxicology agreed that the impurity DMTU should be regarded as toxicologically relevant and therefore a data gap was identified in the original review for a ground water exposure assessment. The route and rate of degradation of the relevant impurity DMTU in four soils under aerobic conditions was investigated in one study submitted with the resubmission dossier. DMTU may be considered to have very low persistence in soil.

PEC soil for metam and MITC were calculated for the worst case use other than grape, in field tomato (612 kg a.s. / ha) assuming 15 cm incorporation. Time dependent PEC soil need to be updated once the data gaps identified for persistence in soil are solved. Initial PECs in soil may be used for the EU risk assessment.

Mobility of metam was investigated by the HPLC method. According this experiment metam may be considered to be very highly mobile in soil. In the original review a batch adsorption / desorption study was available for MITC in four soils. This compound was very high mobile in these soils (K_{foc} = 27 mL / g). The meeting of experts concluded that adsorption in the study may have been overestimated due to the fact that experimental K_{oc} values are simultaneously affected by degradation and volatilisation during the experiment. A new study is available in the resubmission dossier that investigates adsorption / desorption of MITC in five soils. The very high mobility of MITC is confirmed by these experiments (K_{FOC} = 9 – 20.2 mL / g).

In the original review a new data gap was identified by EFSA to address the mobility of the impurity DMTU in soil in order to obtain adequate input parameters for ground water modelling. According to the new study available in the resubmission dossier it may be expected that DMTU will exhibit very high mobility in soil (K_{FOC} = 7 – 10 mL / g).

Hydrolysis of metam is relatively fast at any pH. Hydrolysis of MITC at 25 °C occurs with half-lives of ≈ 40 d (pH 4), 50 d (pH 7) and 11 d (pH 9). Major hydrolysis products of MITC were DMU, DMTU and MDTA (metam). The fact that one of the major metabolites of MITC is metam indicates that in water metam and MITC are in equilibrium.

Aqueous photolysis of metam under simulated sunlight is very fast (DT_{50} = 12 min; equivalent to 27.8 min at 38 °N). No acceptable ready biodegradation study is available and therefore the substance is considered to be not readily biodegradable.

In the aerobic water /sediment experiment (25 °C) metam degrades rapidly in the whole system ($DT_{50whole\ system}$ = 0.32 h). The meeting agreed that the information provided by the notifier did not allow any quantitative estimation of the effect of temperature on the volatilisation. Consequently, in the original review the meeting of experts identified a data gap to address the effect of temperature on the dissipation of MITC from water by volatilisation. In the resubmission dossier a theoretical calculation on the dependence of volatilisation on the temperature is presented. According to this calculation volatilisation rates are about half at 12 °C than at 25 °C but it is still expected that $DissT_{50}$ would be shorter than 1 d. No new water sediment study at lower temperature was provided in the resubmission. The data from the anaerobic water sediment study were considered not relevant for the representative uses and it was not found scientifically justified to average dissipation rates from aerobic and anaerobic experiments

Due to the data gaps identified on the derivation of various key modelling input parameters and to the fact that FOCUS SW modelling does not consider volatilisation-deposition route of entry in surface water, the available PEC_{SW} were not considered appropriate for the EU risk assessment. The meeting of experts in the original review identified 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. In the resubmission new calculations of PEC SW for the active metabolite MITC have been provided. FOCUS SW Step 3 calculations presented in this reassessment may be used as a worst case in the aquatic risk assessment; however, FOCUS SW Step 4 calculations provided do not follow FOCUS Landscape recommendations. Additionally the applicant has provided an estimation of the PEC SW resulting from volatilisation deposition of MITC. Without further mitigation, the exposure of the aquatic environment resulting from this route can be considered covered by the assessment performed for the edge-of-field exposure.

The meeting of experts identified the need to recalculate MITC PEC_{GW} values with adequate input parameters (when available) using FOCUS GW or a higher tier approach if appropriate. In the resubmission dossier new PEC GW calculations were provided for MITC. However, the persistence end point available for this substance was considered by the peer review to represent only situations where the substance is applied at lower application rates such as the representative use in potato (153 kg metam /ha; equivalent to 86.6 kg MITC/ha). Potential groundwater contamination was assessed for the use in potato assuming rotation and applications once every third year. With these restrictions the limit of 0.1 μg / L is exceeded in 5 of the 9 scenarios simulated. Additionally the 10 μg / L are exceeded in two of the scenarios with a calculated maximum of 197.73 μg MITC / L in Jokioinen (PELMO 3.2.2 calculation).

In the original review, a new data gap was identified by EFSA to address the potential ground water contamination of impurity DMTU. In the resubmission dossier, potential groundwater contamination by the impurity DMTU has been addressed. DMTU did not exceed the trigger of 0.1 μg / L for any of the scenarios and uses simulated.

The meeting of experts identified a data gap to address the atmospheric fate and behaviour of MITC including global warming (ozone depletion), long-range transport and deposition. In the resubmission dossier, experimental values have been provided by the applicant showing that half-lives in the atmosphere, when all possible degradation processes are considered (direct and oxidative indirect photolysis), will be in the range of 4.8 – 6.3 d. This half life is still longer than the 2 d trigger considered for alerting on potential long-range transport. Therefore, the critical area of concern on potential long-range transport of MITC through the atmosphere remains. The available data suggest that MITC might have a low potential for ozone depletion. The potential for contribution to global warming of MITC has not been directly addressed within the information provided in the resubmission dossier. In practice, any meaningful global warming assessment would need to consider the overall amount of MITC released to the atmosphere (including sources other than metam) and an assessment restricted to the European geographical region might have limited relevance in this context.

The notifier and the RMS proposed in the DAR that due to the method of application of metam-sodium, the risk to birds and mammals was considered acceptable for the representative field uses. Member States experts suggested that the most probable contaminated food items for birds and mammals would be the soil invertebrates (including earthworms). The experts in the PRAPeR 53 meeting agreed that the notifier should provide an acute risk assessment to assess the effects of metam-sodium and its metabolite MITC to terrestrial vertebrates feeding on soil invertebrates. The acute risk assessment should also be provided for the metabolite MITC using the lowest endpoint available of 100 mg a.s./kg bw, which was agreed during the meeting. A higher tier assessment of the risk of MITC to insectivorous and vermivorous birds and mammals was carried out, based on the higher tier studies in the resubmission dossier. Birds and mammals censuses were performed on sterilized and unsterilized carrot plots in France to derive focal species and ecological data. The study was deemed valid only for the identification of focal species. In a second field study, residues in invertebrates and in carrots were measured. It was agreed to use the highest residue as RUD (13.3 mg /kg). Overall, it was concluded that the risk of metam-sodium and MITC to birds and mammals was assessed as high, for all the field representative uses, with the exception of the use on potato. Therefore a data gap has been identified to further address the risk for insectivorous and vermivorous birds, for all field representative uses except on potato.

Metam-sodium and its relevant metabolite MITC were very toxic to aquatic organisms based on the available data. Due to the rapid degradation of metam-sodium in soil, surface water contamination with the parent molecule could be excluded. Aquatic organisms may be exposed to the metabolite MITC as result of the drainage and run-off. The fate and behaviour section considered that PEC_{sw} from FOCUSsw step 3 can be considered valid only for the representative use on potato, but not for the other representative uses. The PEC_{sw} values from $FOCUS_{sw}$ Step 4 were not considered valid in the fate and behaviour section. The TERs values were calculated on the basis of new PECsw values from FOCUS step 3. The TERs values were above the Annex VI trigger values for most of the $FOCUS_{sw}$ step 3 scenarios for the representative use on potato, indicating a low risk of MITC to aquatic organisms for the representative use on potato. For the representative field uses evaluated other than the use on potato, a data gap was identified to assess the risk of MITC to aquatic organisms based on the new PEC_{sw}.

An extended laboratory study was conducted with *Aleochara bilineata* and this aged residue study demonstrated that *A. bilineata* was able to recolonise the field after 55 days. From an extended laboratory study it was only possible to assess the potential for re-colonisation, but not the actual recovery. A field trial was presented in the resubmission dossier. The field trial was carried out to determine the effects of metam-sodium on the non-target arthropods of arable land in France after one application in spring. The test demonstrates that actual recovery in the field occurred for the most important taxa within one year. For 2 % of pitfall sampling taxa recovery was still ongoing in the next spring. Due to the high mortalities of arthropods found in the in-field area, probably the recolonisation may occur from non-treated field. Therefore the risk of MITC to non-target arthropods was considered to be low.

An earthworm field study was conducted with the metam-sodium. The experts agreed that after the application of the 608.4 kg a.s./ha, there was no clear indication of full recovery after one year. A further refinement was required from the notifier to address concerns on recovery/recolonisation of earthworms this should be include considerations on effects on recovery of different ecological groups as well as known data on migration distances. Information on the migration distances of earthworm species was submitted in the resubmission dossier. However, available data on migratory distances could not be used in the risk assessment. Therefore a data gap remains.

The risk of metam and its metabolite MITC to other soil macro-organisms was assessed. A field trial to demonstrate the effects of metam-sodium on non-target macro-organisms on arable land in France

after one application in spring was submitted in the resubmission dossier. All affected soil-dwelling invertebrates had recovery in abundance within the same season and no adverse effects extended into the year after the treatment. Therefore the risk of metam-sodium and MITC to soil macro-organisms was assessed as low for all of the representative uses.

The risk of metam and its metabolite MITC to bees, soil micro-organisms, non-target plants and biological method of sewage treatment was assessed as low for the field uses.

The risk of metam and its metabolite MITC to terrestrial vertebrates, aquatic organisms, bees, non-target arthropods, soil micro-organisms and biological methods of sewage treatment was assessed to be low for the representative greenhouse uses.

KEY WORDS

metam, metam-sodium, metam-potassium, peer review, risk assessment, pesticide, nematicide, fungicide, herbicide and insecticide

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BACKGROUND

Legislative framework

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000 as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State (RMS). Metam is one of the 84 substances of the third stage, part B, covered by the Regulation (EC) No 1490/2002 designating Belgium as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Belgium submitted the report of its initial evaluation of the dossier on metam, hereafter referred to as the draft assessment report (Belgium, 2007), received by EFSA on 10 September 2007. Following an administrative evaluation, the draft assessment report was distributed for consultation in accordance with Article 11(2) of the Regulation (EC) No 1490/2002 as amended by the Regulation (EC) 1095/2007, on 3 December 2007 to the Member States and on 4 October 2007 to the main notifier Taminco as identified by the rapporteur Member State. The DAR is only based on the Taminco dossier. The European Metam Sodium Task Force that is composed of the companies FMC Foret and Lainco has submitted a dossier that was considered incomplete.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, EFSA identified and agreed on lacking information to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the requested information received from the notifier, a scientific discussion took place in expert meetings in June – July 2008. The reports of these meetings were made available to the Member States electronically.

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 set out in the EFSA Conclusion issued on 26 November 2008 (EFSA, 2008).

Following the Council Decision of 13 July 2009 (2009/562/EC)[8] concerning the non-inclusion of metam in Annex I to Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Taminco N.V. made a resubmission application for the inclusion of metam in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008.[9] The resubmission dossier included further data in response to the issues identified in the conclusions leading to the Decision on non-inclusion, as set out in the Review Report (SANCO/206/2008; European Commission, 2009) as follows:

- the risk to consumers given the data gaps identified in the residue section and the possible impact of the relevant impurity DMTU; as a consequence, the consumers risk assessment could not be finalised;
- the fate and behaviour in soil and water due to inadequate information on the major metabolite MITC and impurity DMTU. As a consequence, the risk to groundwater could not be finalised;
- MITC is volatile and long-range transport and potential effects on the atmosphere need to be further addressed;

[8] OJ L 196, 28.7.2009, p. 22
[9] OJ L 15, 18.01.2008, p. 5

- The risk assessment of acute effects of metam and its metabolite MITC to terrestrial vertebrates feeding on soil invertebrates
- Further information is required to address the recovery potential of the non-target arthropods, earthworms and non-target soil macro-organisms.

And concerns were identified with regard to

- the potential for contamination of groundwater by the major metabolite MITC in some scenarios
- the risk assessment for operators and workers in greenhouses
- risk to aquatic organisms.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Belgium, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report (Belgium, 2010). The Additional Report was received by the EFSA on 31 August 2010.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 14 September 2010. The EFSA collated and forwarded all comments received to the European Commission on 28 October 2010. The collated comments were also forwarded to the RMS for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 2 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report and the comments received, the European Commission decided to further consult the EFSA. By written request, received by the EFSA on 3 December 2010, the European Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on metam within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicant in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the European Commission on 25 November 2010; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that there was a need for EFSA to organise a consultation with Member State experts in the areas of environmental fate and behaviour and ecotoxicology, and that further information should be requested from the applicant in the areas of physical and chemical properties, residues and ecotoxicology.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in July – August 2011.

The conclusion from the original review was reached on the basis of the evaluation of the representative uses as presented in the DAR, i.e. use as a nematicide, fungicide, herbicide and insecticide by soil fumigation prior to the planting of carrot, lamb's lettuce, cucumber, aubergine, pepper, potato, strawberry, tomato and grape. The conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the same representative uses. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A.

The documentation developed during the resubmission peer review was compiled as a **peer review report** (EFSA, 2011). The peer review report comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the rapporteur Member State's additional report,
- the Reporting Table (25 November 2010),
- the Evaluation Table (12 July 2011),
- the report(s) of the scientific consultation with Member State experts (where relevant),
- the comments received on the assessment of the points of clarification (where relevant),
- the comments received on the draft EFSA conclusion.

Given the importance of the Additional Report including its addendum (compiled version of May 2011 containing all individually submitted addenda; Belgium, 2011) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion. The documents of the Peer Review Report and the final addendum developed and prepared during the course of the initial review process are made publicly available as part of the background documentation to the original conclusion, issued on 26 November 2008 (EFSA, 2008).

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Metam is the ISO common name for methyldithiocarbamic acid (IUPAC). Due to the fact that metam-sodium is a variant of metam and is used in the formulated product, it should be noted that the evaluated data belong to the variant metam-sodium (sodium methyldithiocarbamate, IUPAC), unless otherwise specified.

Metam is a MITC[10] generator and this is the moiety that has the biological activity, the compound dazomet is also a MITC generator.

MITC interferes at the level of enzymatic activity. It disturbs the absorption of oxygen during the process of cellular respiration by chelating enzymes having a metal radical. The efficacy against nematodes is probably due to the ability of MITC to deactivate the sulfuric groups of essential enzymes.

The representative formulated product for the evaluation was “Metam sodium 510 g/L” a soluble concentrate (SL), registered under different trade names in Europe.

The evaluated representative uses are as a nematicide, fungicide, herbicide and insecticide by soil fumigation prior to the planting of carrot, lamb’s lettuce, cucumber, aubergine, pepper, potato, strawberry, tomato and grapes. Full details of the GAP can be found in Appendix A

CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The purity range of metam-sodium TK is 400 g/kg-442 g/kg (reference source). The calculated minimum purity of metam-sodium on a dry weight basis is 965 g/kg. The FAO specification 20.1Na/13/S/15, published in AGP:CP/82 (1979) states the following “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.” The technical material is in compliance with the FAO specification. The technical material contains MITC and DMTU[11] which have to be considered as relevant impurities. The maximum content in the technical material should not be higher than 23 g/kg DMTU on a dry weight basis and 12 g/kg for MITC on a dry weight basis (both values derived from the FMC Foret source).

According to the equivalence assessment of the different technical materials it is concluded that the reference source is the Taminco metam-sodium. The Taminco metam-potassium was considered to be equivalent to the sodium salt on the basis of a Tier II equivalence assessment. During the peer review process it was considered that the sodium and potassium salts were proposed for a full assessment and data gaps were identified for the sodium salt and potassium salt. However, during the writing of the conclusion it was discovered that toxicology and ecotoxicology had only considered it for equivalence. As this is the case, this conclusion is only based on the sodium salt and only the equivalence of the potassium source is considered.

The Lainco source did not have a supported specification and therefore it will not be considered further. The FMC Foret source is not equivalent at Tier I but ecotoxicology and mammalian toxicology considered it as equivalent in a Tier II assessment in accordance with Sanco/10597/2003 – rev. 8.1-1 (European Commission, 2003). (See section 2)

The content of metam-sodium in the representative formulation is 510 g/L (pure).

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[10] MITC: methyl isothiocyanate
[11] DMTU: N,N’-dimethylthiourea

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of metam-sodium, metam-potassium or the respective formulation. However, the following data gap was identified:

– Storage stability data with analysis of the relevant impurities before and after storage.

The main data regarding the identity of metam-sodium and its physical and chemical properties are given in Appendix A. This Appendix also contains some data on MITC that have been used in the risk assessment.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of metam in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.

Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor MITC in plant commodities, soil, water and air. Only single methods for the determination of residues are available since a multi-residue-method like the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Residues of MITC in products of plant origin are analysed by GC-MS with an LOQ of 0.01 mg/kg. Soil, water and air are analysed by GC-NPD. The LOQs are 0.02 mg/kg soil, 0.1 µg/L water and 0.5 µg/m³ air. For confirmation a column of different polarity is used.

An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2)

As the breakdown product MITC is classified as very toxic, methods have been supplied for body fluids and tissues. Blood, plasma and urine are analysed by LC-MS with confirmation by LC-MS/MS with a LOQ of 0.05 mg/L for the analyte (*N*-acetyl-*S*-[(methylamino)carbothioyl]cysteine. The method for tissues is GC-NPD and confirmation is by using a column of different polarity. The LOQ was 0.1 mg/kg for the analyte MITC.

2. Mammalian toxicity

Metam was discussed in the PRAPeR meeting of experts 54 (subgroup 1) held in Parma in July 2008.

The meeting discussed the identity of the a.s. under peer review, whether it was metam or variants metam-sodium or metam-potassium. It was noted that bridging data are available on metam-sodium and metam-potassium. The phys-chem opinion is that the active substance is metam. The meeting agreed the active moiety is metam; results in the endpoint list and in the conclusion will be expressed as metam-sodium as the majority of studies have been performed with this variant. However a conversion factor of 1.2 from metam-sodium to metam based on molar conversion was defined.

The toxicological profile of metam was discussed in relation to the toxicological role of MITC, which is a major metabolite of metam. Degradation of MITC into the metabolites carbon disulfide (CS_2) and carbonyl sulfide (COS) in the rat is only a minor metabolic pathway, while most is eliminated following conjugation. MITC has lower toxicological endpoints compared to parent. It was noted that metam is almost instantly hydrolysed to MITC, so it was discussed whether the interest should be focused on MITC instead of metam, although metam is heavily classified. For operators applying metam, the relevant assessment is for MITC. The meeting agreed that the operator, worker and bystander risk assessment should be performed for MITC.

Experts discussed the impurities, which were described in the DAR and were considered of possible relevance. The impurities below 1 g/kg were not considered to be of toxicological concern. The experts agreed on the relevance of the impurity N,N'-dimethylthiourea (DMTU). This impurity was present at 1% (equivalent to 23 g/kg on dry weight basis) in a lot of the tox batches used (metam sodium TK, FMC source) thus not giving rise to any toxicological concern (the specification of the reference source being 7 g/kg on dry weight basis). MITC was considered as relevant but extensively covered by toxicological studies where specific reference values have been established.

Beside the reference source, two additional sources (FMC and Lainco) were presented. From the comparison with the reference source, the experts did not expect a different toxicological profile. In particular, for FMC the equivalence check was performed based on tier 2, whereas for Lainco that was not possible. During the resubmission, based on the available information, the RMS considered that the significantly higher level of MITC in the FMC source (approximately 55-fold concentration) was unacceptable, and concluded that it could not be considered to be technically equivalent to the reference source. However, from a toxicological point of view, it was agreed during the PRAPeR meeting that batches containing no MITC or containing 12 g/kg MITC (FMC) were equivalent, as metam will completely degrade to MITC within 24h after application.

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

Oral absorption of metam is rapid and almost complete (85%) based on urinary and expired air excretion (50 and 35%, respectively). Metam is uniformly distributed with slight accumulation in the thyroid. The metabolism is extensive and rapid, suggesting a decomposition of metam into MITC, CO_2, and COS. MITC is further conjugated to glutathione and excreted in urine while CO_2 and COS are excreted via expired air. The other significant pathway for metam is the release of CS_2, which could be related to the acidic conditions in the stomach of the rat (pH=3.8-5) following oral ingestion. Excretion is almost complete within 24-48 h after administration, with minor portions excreted up to 168 h after dosing.

2.2. Acute toxicity

Metam

Metam-sodium is harmful by oral ingestion and inhalation (R22 and R20 proposed).

In irritation tests, metam-sodium was not irritant to eyes but was corrosive to skin, therefore R34 ("Causes burns") was proposed. Metam-sodium is a skin sensitiser (R43 proposed).

MITC

MITC is toxic via ingestion (R25 proposed) and via inhalation (R23 proposed). It is harmful in contact with skin (R21 proposed). In skin irritation tests it was corrosive to skin (R34 proposed). It was also irritative to the respiratory system (R37 proposed). It is a skin sensitiser (R43 proposed).

2.3. Short term toxicity

Metam-sodium

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, 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 0.5 mg/kg bw/day.

In mice, mucosal hyperplasia and epithelial eosinophilia were apparent in the urinary bladder. Nasal cavity was not affected. An NOAEL at 0.8 mg/kg bw/day was proposed.

In a 90-day inhalation study in rats (5 days of exposure per week), the NOAEL was set at 6.5 mg/m³ (corresponding to 1.75 mg/kg bw/day) based on a mild degree of mucigenic epithelial hyperplasia as well as lymphocitic rhinitis in nasal passages, as well as pulmonary histiocytosis and gastric erosions of the stomach.

In dogs, metam-sodium was given in capsules for 90 days and caused treatment-related hepatitis at 5 mg/kg bw/day onwards. During the meeting it was discussed whether the increase of Alanine Transaminase ALT (starting around 13th week) in one female in the 1 mg/kg bw/day dose group should be regarded as an outlier or as the LOAEL. The finding appeared to be dose related (effect also seen in the one year study). It was difficult to determine its significance, as in the 90-day study no changes in liver weights or histopathology data in the liver at 1 mg/kg bw/day were observed. Although only one dog was affected at 1 mg/kg bw/day, the number of animals treated was small. The majority of experts agreed it was a NOAEL. After 1-year, hepatotoxicity was more evident in female dogs as suggested by increased ALT and some liver histopathological findings. The relevant NOAEL was agreed at 0.1 mg/kg bw/day based on histopathological liver findings.

During the meeting, the RMS proposal of R48/22 ("Danger of serious damage to health by prolonged exposure if swallowed") for the occurrence of severe hepatotoxicity in dogs at 10 mg/kg bw/day in the 90-day study was discussed. It was noted that at the top-dose of 10 mg/kg bw/day, 2/8 animals were terminated because of severe hepatic dysfunction (liver enzymes, hepatitis). Hepatitis with histopathological signs was observed in 5/8 and 8/8 animals at 5 and 10 mg/kg bw/day respectively. Although the classification assessment criteria do not mention other species (e.g. dogs) but rats, it was considered that findings in other species may be taken into account if appropriate. Overall, it was agreed that R48/22, as proposed by the RMS, should be left in place.

Rabbits did not show systemic toxicity after dermal exposure for 21 days to metam-sodium. The NOAEL for local effects was 31.25 mg/kg bw/day based on local skin reactions such as erythema, oedema and rhagades at higher doses.

MITC

A 4-week inhalation rat study was performed with MITC. At doses of 100 mg/m^3, lung weight was increased, and was associated with bronchopneumonia and epithelial proliferation in bronchi and bronchioles. At this dose level, proliferation in tracheal epithelial cells, 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. A NOAEL for systemic effects was proposed at 5 mg/m^3 (1.35 mg/kg bw/day) and agreed in the meeting. A local NOAEL was established at <1.35 mg/kg bw/day.

In a 90-day dog study by gavage with MITC, at dose levels of 0.4 mg/kg bw/day onwards, thymus involution and liver toxicity was suggested by periportal hepatocyte vacuolation and lipid deposition.

During the meeting the relevance of thymus involution and liver vacuolation at 0.4 mg/kg bw/day was discussed. Some experts considered effects at mid-dose level (0.4 mg/kg bw/day) were not marked, but could not be compared with findings from a one year dog study. The study showed inconsistency in findings. However the majority of effects were indicating treatment related effects, consistent at the highest dose tested. Therefore it was agreed the NOAEL is 0.4 mg/kg bw/day.

2.4. Genotoxicity

Metam

Metam-sodium was evaluated in a battery of *in vivo* and *in vitro* tests.

Metam-sodium revealed a slight clastogenic activity in the presence and absence of metabolic activation in a first chromosome aberration test, and only in the presence of metabolic activation system in a second test, both performed in human lymphocytes. Increases in structural chromosomal aberrations were observed at cytotoxic concentrations, impairing chromosomal morphology, and thus preventing metaphases from accurate analysis for structural chromosomal aberrations.

In the *in vitro* UDS assay metam-sodium did not induce unscheduled DNA synthesis even at concentrations that are cytotoxic. Metam-sodium did not induce micronuclei in bone marrow polychromatic erythrocytes in CD-1 mice. In the *in vivo* chromosome aberration test performed in Chinese hamsters, Metam-sodium was not clastogenic.

The genotoxicity testing and potential of metam was discussed at the meeting. Equivocal effects were recorded in the HPRT test, but dose-response was not clear. In two chromosomal aberration tests rather weak findings were observed. Two *in vivo* studies showed negative results. However, in hamster bone marrow cells, there was a slightly increased incidence of polyploid cells, but likely due to cytoxicity/systemic toxicity. Overall the RMS considered that the compound was devoid of genotoxic potential. The meeting agreed with this conclusion.

MITC

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. The conclusion that MITC was not genotoxic, was supported by studies from open literature.

2.5. Long term toxicity

Metam

Metam-sodium was administered to rats in drinking water for 2 years. Rats showed reduced bodyweight gain, specific lesions within the nasal passages, and changes in some haematology parameters and spleen (haemosiderin depots) and a slight increase in the severity but not incidence of degenerative myopathy of the voluntary muscle. The incidence of haemangiosarcoma 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 was concluded that metam-sodium is not carcinogenic in rats. An NOAEL was established at 1.5 mg/kg bw/day.

Mice received metam-sodium in their drinking water for 24 months. The relevant NOAEL of the 2 year drinking study in mice was discussed in the meeting. There was a treatment-related increased incidence of angiosarcomas, in the spleen in the males and the females at the mid- and the top-dose (combined incidence 5/3/11/19). However, it was noted there was no clear dose-dependency in other organs such as the liver (0/6/3/7 on a total of 55 male animals). Overall, tumour incidence was increased only at the highest tested dose. However, as the overall incidence was 7/12/12/27 in the males (4/2/6/10 in the females), the carcinogenicity NOAEL at the *lowest* dose was questioned. The control group incidence was well within the range of historical control data (5-18%), while the incidence in the treated groups (22-51%) exceeded this range. The RMS considered that the incidence was not exceeded in the spleen at the lowest dose, but the picture is confused by an inconsistently increased tumour incidence seen in other organs, including the liver, at the lowest dose tested, however with a lack of dose-responsiveness. Whereas it was agreed that the tumours are treatment-related, it was thought initially that a NOAEL could not be set, although the dose response was not clear. The mechanism of action for the angiosarcoma tumours remained unexplained. No information was available on the historical background range of incidences in particular organs (only the total incidence at any site available). It was reported that the US Environmental Protection Agency (US EPA) agreed on a NOAEL =0.019 mg/kg bw/day, based on systemic effects (bodyweight changes).

However, the EPA report further highlighted that a statistical increase was observed in the males at the two top-doses in the decedents (12/14/*32/***49%), and at the top-dose in the terminally sacrificed animals (14/35/11/*50%), further indicating the lack of meaningful effects at the lowest dose. Later in the meeting, the RMS asked to reopen the discussion regarding the angiosarcoma incidence (liver and global), and the experts agreed that the lowest dose used was a NOAEL rather than a LOAEL, taking account that the findings in the liver showed no dose response. The experts agreed that a classification as Carc. Cat 3 (R40, "Limited evidence of carcinogenic effect") was justified, based on the effects seen in the spleen only.

MITC

Rats received MITC via drinking water at 2, 10 or 50 ppm over 104 weeks. White blood cell parameters, histopathological findings such as bone marrow hyperplasia, increased kidney microcalculi, liver effects, and spleen hyperplasia/increased haematopoiesis were reported at the highest dose (1.6 mg/kg bw/day) and could be related to MITC exposure.

MITC was not carcinogenic under these experimental conditions. A NOAEL=10 ppm (0.44 mg/kg bw/day) was proposed. The experts discussed the use of proposed MITC intake in the 2 year rat study with MITC. The derivation of doses tested was discussed due to the fact that MITC is not stable in aqueous solution, with different degradation rates at different doses tested. It was noted this is a problem for all studies as MITC is a volatile compound, not just for the 2 year rat study. The RMS calculated the ingested doses using a correction factor of 87.7%, obtained using the analytical measurements of the 10 ppm dose group, in the drinking water bottles used during the greatest part of the study. The correction factor for this was considered acceptable.

In mice, a NOAEL was set at 20 ppm (3.3 mg/kg bw/day) taking into account the different slight effects seen at 80 ppm (12 mg/kg bw/day), 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.

2.6. Reproductive toxicity

Metam

In rats, metam-sodium was tested in a multigenerational drinking water study. At the top dose, body weight and food consumption were 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, together with degeneration/ disorganization/atrophy of the olfactory epithelium. 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 occurred spontaneously in the strain used and was 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/day. Maternal toxicity started at 10 mg/kg bw/day (reduced body weight gain). Reproduction parameters were not affected. At 40 mg/kg, bw/day there was also some evidence for foetotoxicity. Foetotoxicity was evident at 80 mg/kg bw/day with a reduced mean foetal weight. A significantly increased post-implantation loss was reported at 120 mg/kg bw/day. At 120 mg/kg bw/day, the number of live foetuses was reduced and mean foetal weight was significantly lower. Major defects were reported at 120 mg/kg bw/day, two foetuses/1 litter exhibited a meningocele (neural tube closure defect) and another foetus had bilateral microphthalmia. At 80 mg/kg bw/day, one foetus had a meningocele. At 60 mg/kg bw/day 5 foetuses/5 litters were affected: defects of eyes (3 foetuses with other head defects); 1 foetus had a shortened jaw and cleft lip, 1 had meningocele, 1 foetus had unossified 2nd, 3rd and 4th arches of the cervical vertebrae, and one foetus displayed an abnormal zygomatic arch. None of which has been seen historically in controls in the laboratory. At 20 mg/kg, one foetus had four major defects, including a shortened lower jaw, which has not been seen in historical data. At 5 mg/kg bw/day, two foetuses 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.

During the meeting the relevant NOAEL of the developmental toxicity study in rat with metam (Tinston 1993) was discussed. The RMS considered that some effects were dose dependent. 5 mg/kg bw/day was proposed as the NOAEL for maternal findings. For foetal findings, there were clear treatment related effects for major malformations. The proposal from the RMS of 5 mg/kg bw/day for the developmental NOAEL was agreed, for both maternal and developmental toxicity.

In rabbits, body weight gain of dams at 100 mg/kg bw/day was decreased on most days of treatment. At 60 mg/kg bw/day, dams lost considerable weight after the start of dosing and food consumption was reduced. Similar but less marked changes were seen in the 20 mg/kg bw/day group.

At 100 mg/kg bw/day, 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/day, and reduced number of live foetuses/pregnant female was seen at 30, 60 and 100 mg/kg bw/day. At 60 mg/kg bw/day, foetal weight was decreased. Percentage of male foetuses was reduced and litters containing five or less foetuses did not include males. Two foetuses in two litters of 100 mg/kg bw/day 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. Foetuses showed retarded ossification in the head but also in limbs, thoracic vertebrae, sternum, and these effects were seen at doses with maternal toxicity.

The proposed classification as Repr. Cat.3 (R63 “Possible risk of harm to the unborn child”) was discussed.

The malformations occurred at low incidences (sometimes in singularity), but in a consistent manner, at the top-doses, and in the presence of quite severe maternal toxicity. In certain studies, single rare malformations were also present at lower doses, however in these cases, no dose-dependency was demonstrated. Concerns were expressed during the meeting whether Cat. 2 (R61?) may be justified as effects were clearly treatment related. However, they were associated with maternal toxicity, which would lead to Cat. 3 classification. Overall, it was agreed the European Chemical Agency would reflect further on this.

MITC

In a 2 generation rat drinking water study, 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 decreased 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. The parental, reproductive and offspring NOAELs were 0.7, >3.6 and >3.6 mg/kg/bw/day respectively.

In a developmental rat study, MITC was given by gavage at 0, 3, 10 or 30 mg/kg bw/day. Before gavage several dams at top dose had sticky and/or moist fur in the area of the snout and after gavage 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/day. Reproduction data were not significantly affected in the groups. The number of foetuses weighing <75% of the mean foetal weight/litter was increased, and 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/day. 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. The relevant maternal and developmental NOAELs in rat were 3 and 10 mg/kg bw/day.

In rabbits, MITC was given by gavage at 1, 3 or 10 mg/kg bw/day. 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 weights of foetuses were not affected. Sex ratio was similar in all groups. Investigations of the crania and body cavity and skeleton of the foetuses did not show compound-related effects. The relevant maternal and developmental NOAELs in rabbit were 3 and 10 mg/kg bw/day.

2.7. Neurotoxicity

An acute neurotoxicity study was performed with metam-sodium administered to rats. The NOAEL for systemic toxicity was <50 mg/kg bw/day and no neurotoxicity was seen in this study (NOAEL acute neurotoxicity >1500 mg/kg bw/day). In a repeat dose study, where metam-sodium was administered in drinking water at doses up to 15-18 mg/kg bw/day, there were no signs of neurotoxicity.

2.8. Further studies

The toxicity of MITC was investigated by the company and a full dossier is included and reported in parallel to metam-sodium.

During the meeting it was noted that according to guidance on the relevance of metabolites in groundwater, if the parent was classified as Cat. 3, the metabolites should be considered relevant (European Commission, 2003b). DMTU may occur in groundwater above 0.1 µg/L; however DMTU is an impurity, not a rat metabolite and no further studies are available. Its toxicity was considered equivalent to the toxicity of the parent compound based on chemical structure, based on the lack of data on DMTU and considering the toxicological properties of the parent compound. Since metam-sodium was tested with batches containing 1% of DMTU, it was considered that all toxicity endpoints and related classifications sufficiently covered the toxicity of this impurity. It was noted that metam applied at a rate of 612 kg/ha would result in approximately 4 kg/ha of DMTU.

2.9. Medical data

No medical surveillance data for manufacturing plant personnel was found for metam-sodium.

After an accidental spillage in California in 1991, over 700 persons in the area sought medical attention for symptoms ranging from nausea and dizziness to irritation of the eyes and upper respiratory tract. A number of persons reported exacerbation or induction of asthma following exposure. The follow up of the involved people during the first month post-spill included headache (64%), nausea (46%), eye irritation/blurring (40%), dizziness (30%), shortness of breath (27%) and diarrhoea (25%). Complaints of depression, disorientation, drowsiness, dry mouth, earache, fatigue, fever, hot flashes, irritability, memory reduction, nosebleed, numbness, pain in the arms or legs, tinnitus (ringing in the ear) and sweating were also reported at medical centres. Sixty-one percent of the spill residents showed clinical abnormalities. Significantly higher blood pressure and less fluctuation of salivary cortisol levels were found. More neurological, memory and concentration, anxiety, depression, sleep disorders, headaches, visual, olfactory, dermatological, gastro-intestinal and cardiac symptoms were reported than the controls.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

Reference values of metam-sodium and MITC were agreed on in the meeting.

<u>ADI</u>

Metam

The ADI proposed by the RMS in the DAR was 0.001 mg/kg bw/d, based on 1 year dog study with SF 100. It was considered that the Margin of Safety (MOS) of 7200× to the long-term mouse study LOAEL (tumourigenic effects at 7.2 mg/kg bw/d and above) was sufficiently high. The meeting therefore agreed that the ADI was acceptable.

MITC

ADI proposed by the RMS was 0.0004 mg/kg bw/day based on the 90-day dog study, with SF 100. The NOAEL agreed for the 90-day dog study in the expert meeting is now 0.4 mg/kg bw/day, it was agreed to establish the ADI at 0.004 mg/kg bw/day applying a SF of 100.

AOEL

Metam

The AOEL originally proposed was 0.005 mg/kg bw/day, based on the 90-day rat drinking water study, with a 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).

MITC

The RMS proposed an AOEL of 0.0135 mg/kg bw for MITC, based on a rat 4 wk inhalation study. It was noted that the overall database for MITC was on oral studies, but inhalation was the critical route of exposure. However, as the inhalation study was somewhat limited in duration (only 4 wk study), it was therefore considered whether to use a NOAEL from the 90-day oral dog study, as this was a more adequate duration for the operator exposure assessment. Also, the AOEL is normally based on oral exposure studies, and the dog was also a more sensitive species. However, the RMS stressed that the 4 wk study on MITC was also supported by the 90-day inhalation study using metam (where the NOAEL of metam, applying a molar conversion factor, would indicate a NOAEL for MITC of about 1 mg/kg bw/day, in line with the NOAEL in the 4 wk MITC study).

On balance the experts agreed the 90-day dog study on MITC should be used to set the AOEL, as it was considered that a 4-week study would not be sufficient to cover the application window (especially if the a.s. was applied by contractors). This study was also used for the ADI. The AOEL agreed was 0.004 mg/kg bw/day for MITC.

ARfD

Metam

The ARfD proposed was based on a developmental study in rat with SF 100: 0.05 mg/kg bw. The meeting considered whether a SF of 100 was sufficiently high. The meeting agreed the ARfD is 0.1 mg/kg bw based on overall rat developmental study and supported by rabbit developmental study.

MITC

The meeting agreed an ARfD of 0.03 mg/kg bw based on the NOAEL for rat maternal toxicity with SF 100.

2.11. Dermal absorption

The new data provided by the RMS were discussed during the meeting. About 1% dermal absorption for the concentrate was shown. There was discussion whether a value should be used for dilution (12% is available for this). Overall the experts agreed 1% for the concentrate, and 12% for the dilution. The studies were performed with the representative formulation METAM 510 g/L SL.

2.12. Exposure to operators, workers and bystanders

METAM 510 g/L SL is an aqueous solution containing about 510 g/L a.s. and is equivalent to the technical active substance as manufactured. Metam-sodium is a soil fumigant used to prepare soils for planting as well as drip irrigation in greenhouses.

Application of metam-sodium is carried out by a soil-injection technique using tractor-mounted equipment as well as by drip irrigation in greenhouses. For the application by soil injection automated direct transfer systems are used for the mixing/loading procedure. When metam-sodium comes into contact with soil it decomposes into gaseous MITC within a few hours, which is in fact the active ingredient.

Operator exposure

Metam

Only the UK POEM and the German model are available for the estimation of operator exposure to metam-sodium during the preparation of equipment (mixing/loading) for drip irrigation and for soil injection application. However, the models are not suitable as metam is used as it is, and is not subject to M/L steps. Further the technical a.s. is not sprayed but the liquid applied by mechanised soil incorporation or drip irrigation.

MITC – drip irrigation in greenhouse

During the original review a field study in greenhouse using soil incorporation was discussed during the meeting. It was noted that the study was only on a small scale, and commercially a greater area would be treated. Also the working rate was only 2 hrs. The RMS reported that due to the technique used in the study, exposure was above the original AOEL. There was agreement not to use this study due to these limitations. No safe use for glasshouse application was demonstrated (there was no information on drip irrigation available at that time.

To fulfill this data gap, during the resubmission, a new field study in greenhouse was submitted, with only 2 subjects monitored (therefore its representativeness was limited). However, the requirement of wearing a respirator with A1P2 filter, which decreased the exposure from 145% to 2.9% of the AOEL, gave sufficient reassurance that the operator exposure would be below the AOEL with the use of Respiratory Protective Equipment (RPE) considered in the field study design. The exposure duration considered was 7 hours.

MITC – soil injection

During the PRAPeR meeting the field studies summarized in the DAR were discussed. Some of them showed some outliers with regard to the AOEL, but the RMS assessed the risk considering the average exposure values (which indicated exposure below the original AOEL). It was agreed that the outliers in the studies (i.e. measurements exceeding the AOEL) should be considered as they reflect actual conditions of use. It was also agreed that the RMS should re-calculate the exposure estimates based on the field studies worst case values (and not the average), using the revised AOEL.

The exposure to MITC was shown to be above the AOEL for the operator, in the absence of RPE. With the use of RPE, the measured exposure was about 9% of the AOEL.

Exposure assessment for spot application (injection in soil at 40 cm depth) on grapes was not provided however it's unlikely that a concern could occur for operator wearing appropriate PPE and RPE.

Worker exposure:

MITC – soil injection

Under field conditions, for a 7 hour working day, worker re-entry exposure calculations based on measurements of MITC concentrations in air are below the AOEL proposed by the RMS.

The exposure of the worker to MITC, on d14 following application of metam did not give rise to concern in the open field. According to revised input parameters exposure to MITC is demonstrated at around 30% (using the new AOEL, 8 hrs exposure and 60 kg bw).

MITC – greenhouse

During the resubmission, worker exposure (8 hours) was assessed in the new greenhouse study as well, and was below the AOEL at day 18 after application without RPE (any re-entries before day 18 requires the use of RPE; for an occasional re-entry for 15 minutes shortly after treatment the exposure was calculated to be below the AOEL by wearing RPE with 98% protection).

Bystander exposure:

Taking into the rapid degradation of metam-sodium, and the particular way of application in the soil (soil injection or drip irrigation), the issue of bystander exposure to metam itself was considered irrelevant.

MITC – soil injection

Inhalation exposure of bystanders might occur for MITC, the volatile degradation product of metam-sodium. The company provided studies where MITC concentrations in air were measured directly during and after application of metam-sodium. Based on these studies, it can be estimated that bystander exposure for 1 hour to MITC during or after application of metam-sodium is below the AOEL proposed by the RMS.

As for MITC, the exposure of a bystander, staying 1h in the neighbourhood of a freshly fumigated field was estimated to be below the AOEL, amounting to 19% of the AOEL in the worst case.

MITC – greenhouse

According to the field study submitted during the resubmission, bystander exposure (60 min.) is above the AOEL at 1-12 m from the source of exposure (it was reported that the door to the poly-tunnel was kept open during fumigation, leading to high MITC concentrations outside the greenhouse). Data were not available to support the risk mitigation measures proposed by the RMS (closure of the door and distance of safety).

Resident exposure was estimated to be below the AOEL at 140 m from the application site onwards.

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

Metabolism studies were conducted using *N*-methyl-^{14}C-(thiocarbonyl)-metam. The metabolism of metam 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, and leafy and fruiting vegetables and therefore can be considered to cover the representative uses on carrot, lamb's lettuce, cucumber, aubergine, pepper, potato, strawberry, tomato and grapes by soil injection or drip-irrigation of metam on the planting row.

In radish roots and leaves, neither the parent compound nor its soil metabolite MITC (which is the biologically active compound) and the methylthiourea/ureas derivates 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 methylureas/methylthioureas or MITC 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 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 radioactivity over a variety of natural products such as cellulose, hemicellulose, starch, proteins, pectin and lignin. The radioactive residues of metam 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 meeting of experts discussed the fact that all the studies except turnip were underdosed, and it was considered that if they had been dosed at the correct level maybe, some metabolites could have been identified. The meeting concluded that as long as environmental fate and behaviour confirms that there are no other significant metabolites in soil then the plant metabolism studies could be accepted. In the resubmission it was confirmed that this is the case and the metabolism data are acceptable. From the metabolism data it can be concluded that the residue definition for risk assessment and monitoring is MITC because of its high toxicity.

Usually the impurities in the technical material are not of a concern for residues. However, as the application rate is so high, they will be applied in kg/ha rates and could therefore be present in crops at harvest. In the original review the meeting of experts considered a case from the notifier and concluded that for one of the impurities this was not an issue. For the two organic impurities the meeting of experts rejected the case and therefore the notifier was required to explain further why these compounds are not relevant for consumer risk. In the resubmission residue trials data were provided that showed that the most pertinent significant impurity is not taken up by plants and it can be concluded from this and the fate and behaviour data that the impurities will not give residues in crops.

In the resubmission the residue data set was completed and it was demonstrated that there will be no residues in crops (<0.01 mg/kg). Given the no residue situation processing studies are not required.

3.1.2. Succeeding and rotational crops

The need for data for rotational crops was not triggered as the DT_{90} in soil was less than 100 days. In the meeting of experts this was discussed further and it was considered that, given the use pattern as a soil sterilent before the crop is planted, the primary plant metabolism would cover rotational crops.

3.2. Nature and magnitude of residues in livestock

The need for livestock metabolism studies and feeding studies was not triggered.

3.3. Consumer risk assessment

Intakes are less than 3 % of the ADI and less than 6 % of the ARfD, the consumer risk assessment is finalised.

3.4. Proposed MRLs

An MRL of 0.01* mg/kg can be proposed for all representative crops.

4. Environmental fate and behaviour

The fate and behaviour of metam in the environment was discussed in the meeting of experts PRAPeR 52 (July 2008) on basis of the DAR (August 2007) and the addendum to B8 (June 2008). The resubmission evaluation was discussed in the meeting of experts PRAPeR TC 52 (March 2011).

The fate and behaviour assessment has considered the application rate range of 153 – 612 kg a.s. / ha as the range covering the majority of representative uses. A special case is the application rate proposed for the use on grape (1020 kg a.s./ha). In this crop metam is intended to be applied locally by incorporation on the root zone of each plant, which is expected to result in an overall application rate lower than the nominal rate notified. Assessment of the application rate of 1200 kg a.s. / ha would require further refinement taking into consideration the particularities of the spot treatment. However, this refinement would need to be appropriately justified by data to ensure the reduction of the application rate represents a realistic worst case.

4.1. Fate and behaviour in soil

4.1.1. Route of degradation in soil

The metabolism of metam in soil was investigated in a study that was found not acceptable by the RMS due to the lack of transparency of the study report with respect to the analytical procedures and the identification of metabolites.

Degradation of metam and its known active metabolite MITC in soil under dark aerobic conditions at 20 °C was investigated in a study with four soils (metam: pH 5.4 – 7.7; OM 1.87 – 6.97 %; clay 11.89

-33.68 %; MITC: pH 4.5 – 7.6; OM 1.53 – 12.41 %; clay 9.58 – 35.45 %) with the compounds ^{14}C labelled at the thiocarbonyl. No other metabolites were identified in these experiments. Radioactivity in the NaOH trap was assumed to be CO_2 and reached levels of 46 – 86 % AR after 21 d. Unextracted radioactivity in soil amounted up to 9.9-38.4 % AR after 21 d. Further details on methodological aspects of this study were provided by the RMS in the addendum (Belgium, 2008). The meeting of experts discussed this additional information related to the mode of application of the substances in the studies, the sampling and identification of volatiles, the analytical methods, the nature of the degradation and the kinetic analysis. Experts agreed that the analytical methods, the sampling scheme and the identification of volatiles in the study were appropriate or acceptable. It was also agreed that the degradation observed was probably of microbial origin, since no pH dependence was apparent. However, the experts in the meeting were not confident that these experiments provided a realistic representation of the fate and behaviour of metam and MITC in soil mainly due to the mode of application used in the study with respect to the application in field were volatilisation is minimized by compacting soil or with plastic films.

A degradation study of metam in soil under dark anaerobic conditions is available in the dossier. The RMS considered that the study was not acceptable. No further study has been required since anaerobic conditions are considered not relevant for the representative use proposed.

A photolysis study in soil was available in the dossier. The study was considered not acceptable by the RMS. No further study has been required to investigate photolysis in soil since for the representative use incorporation would prevent direct exposition of metam to light once applied.

Some studies that investigate the dissipation of metam under field conditions are available in the dossier. 1,3-dimethyl urea was found as a soil metabolite in these studies. However, the RMS did not consider the field studies relevant for the EU risk assessment since the application technique did not reflect the representative uses in EU. Furthermore, field studies were not triggered based on the laboratory data available in the dossier.

Taking into consideration the application rates of metam other than for grape (306 – 612 kg/ha), during the peer review it was considered that impurities present in the technical material need to be addressed for the potential environmental and ground water contamination. For example, an impurity present at 1 % (w/w) in the technical material is applied to the field at levels of up to 6 kg/ha. This rate of application is substantially higher than the rate at which most common pesticides are applied. Since the properties of the impurities may diverge considerably from those of the pure active substance, potential effect of impurities into the environment and contamination of ground water may not be precluded based solely on the assessment of the active ingredient. The notifier submitted an overview of the main impurities present in the technical material that was summarized by the RMS in the addendum (Belgium, 2008). Many of the impurities are also environmental transformation products of the parent and have been addressed as such. However, the impurity DMTU was considered to be a possible impurity of concern. The notifier claimed that the substance tested in ecotoxicological studies already contained this impurity. With respect to the potential ground water contamination the meeting decided to address a question to the toxicology experts meeting on the toxicological relevance of this impurity. The meeting agreed that in case the impurity was considered toxicologically relevant, a ground water assessment would be necessary. The meeting of experts in toxicology agreed that the impurity DMTU should be regarded as toxicologically relevant and therefore a ground water exposure assessment was needed.

The route and rate of degradation of the relevant impurity DMTU in four soils (pH 5.74 – 7.27; OC 0.98 – 2.72 %, clay 9.4 – 42.1 %) under aerobic conditions was investigated in one study submitted with the resubmission dossier. Two major metabolites were identified: M1 (max 47.5% AR after 1 d) and M4 (15.4 % AR after 3d). Mineralization measured as CO_2 amounted to 49.6 % AR and non-extractable residue 34.8 % AR at the end of the study (145 d).

4.1.2. Persistence of the active substance and their metabolites, degradation or reaction products

Rate of degradation of metam and its active metabolite in soil was investigated in the same study commented in the route section. In this study metam and MITC were very low and low persistent in soil respectively (metam DT_{50} = 9 – 17 min; MITC DT_{50} = 1.0 – 2.9 d). With respect to the kinetic analysis, the experts meeting agreed with the RMS that the use of linear regression of data (instead of non-linear) would not have a significant impact in the half lives calculated in this case. Even some deficiencies were identified in some of the experiments, the derivation of kinetic parameters was considered acceptable. However, the meeting noted that a number of scientific studies investigating the persistence of metam and MITC are available in the public domain and to regulatory authorities eg. dazomet DAR (Belgium, 2007b) and California evaluation on MITC (California Environmental Protection Agency, 2002) and the references there in. Some of this information has already been considered by regulatory authorities in EU Member States. The information available in the dazomet DAR was briefly discussed by the meeting of experts. In this dossier, a study is available were half life of MITC was between 5 to 13.6 d. The metam notifier claimed that the difference in the half lives may be due to a slower formation of MITC from dazomet; however, the RMS confirmed after the meeting of experts that in the dazomet study the half life was derived by kinetic analysis and represents true degradation, not dependant on the rate of formation from the parent. Consequently, 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 the metam EU risk assessment.

In the resubmission dossier the applicant presented a number of studies from the scientific literature. The teleconference of experts PRAPeR TC 52 discussed these studies and those available in the dazomet dossier and the possible reasons for discrepancies in the rate of degradation end points derived. The meeting agreed that the available scientific literature allows a relationship between the concentration of MITC in soil and its rate of degradation to be established. MITC degrades slowly at higher concentration rates. Whereas the GLP study available in the original dossier (Hall, 2004; summarized in the DAR of Belgium, 2010) was considered scientifically acceptable, it was performed with a MITC concentration in the low range of the ones that would result from the representative uses proposed for metam. It was agreed that only the use in potatoes (153 kg metam /ha) could be considered covered by the end points derived from this study. A new data gap was identified to address those situations where the soil concentrations of the metabolite MITC due to the use of metam are expected to be significantly higher than the concentration used in the available GLP study. Preferably a study following the relevant guidelines and conducted to simulate the specific application method at a range of concentrations covering those expected to occur from the representative uses should be used to derive end points relevant to all representative uses.

The rate of degradation of the relevant impurity DMTU in soil under aerobic conditions was investigated in the same study used to establish the route of degradation and presented in the resubmission dossier. DMTU may be considered to be very low persistent in soil ($DT_{50\ lab\ 20\ °C}$ = 0.09 – 0.24 d).

PEC soil for metam and MITC were calculated for the worst case use other than grape, in field tomato (612 kg a.s. / ha) assuming 15 cm incorporation. Time dependent PEC soil need to be updated once the data gaps identified for persistence in soil are solved. Initial PECs in soil may be used for the EU risk assessment.

4.1.3. Mobility in soil of the active substance and their metabolites, degradation or reaction products

Mobility of metam was investigated by the HPLC method. Metam-sodium was eluted from the column more quickly than acetaniline (reference standard for the lowest literature value of K_{oc}). Therefore, metam may be considered to be very highly mobile in soil (K_{oc} < 17.8 mL/g). Whereas the HPLC method is generally not considered to provide reliable values for the adsorption in soil, no further data have been required since the worst case is covered by the result obtained. Additionally, if the low half life in soil is confirmed, the relevance of metam mobility is low with respect to its metabolite MITC.

In the original review a batch adsorption / desorption study was available for MITC in four soils (pH 6.2 – 7.6; OC 0.69 – 2.56 %; clay 7.2 – 23.8 %). This compound exhibits very high mobility in these soils. Of the four experiments, three were considered not appropriate by the meeting of experts (only 3 – 4 % MITC found back on the soil) (K_{Foc} = 27 mL / g). The meeting of experts concluded that adsorption in this study may have been overestimated due to the fact that experimental Koc values are simultaneously affected by degradation and volatilisation during the experiment. The experts in the meeting considered that the adsorption study was not conducted in an appropriate manner for a low adsorbing substance with regard to the soil water ration and the OC content of the soil types used. Therefore, 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). A new study is available in the resubmission dossier that investigates adsorption / desorption of MITC in five soils (pH 4.78 – 7.25; OC 1.02 – 4.03 %; clay 6 – 44 %). The very high mobility of MITC is confirmed by these experiments (K_{FOC} = 9 – 20.2 mL / g).

In the original review a data gap was identified by EFSA to address the mobility of impurity DMTU in soil in order to obtain adequate input parameters for ground water modelling. A new study presented in the resubmission dossier investigates adsorption / desorption of DMTU in five soils (pH 5.4 – 7.36; OC 0.98 – 3.93 %; clay 6.4 – 42.1 %). According to the results of these experiments it may be expected that DMTU will exhibit very high mobility in soil (K_{FOC} = 7 – 10 mL / g).

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Hydrolysis of metam in buffered aqueous solutions (pH 5, 7 and 9) at 25 °C was investigated in one acceptable study. Hydrolysis is relatively fast at any pH being slightly faster at the more acidic ones (pH 5: DT_{50} = 1.9 d; pH 7 DT_{50} = 2.2 d; pH 9 DT_{50} = 4.5 d). Major hydrolysis metabolites identified were MITC (max. 60 % AR after 5 d at pH 7 and max 20 % AR at pH 5 and 9) and MCDT (16 % AR at pH 9 after 5.4 d, end of the study). Hydrolysis of MITC in buffered aqueous solutions (pH 4, 7 and 9) at 15 °C 25 °C and 50 °C was investigated in one study that was considered acceptable as supportive information. At 25 °C half lives for MITC were ≈ 40 d (pH 4), 50 d (pH 7) and 11 d (pH 9). Major hydrolysis products of MITC were DMU, DMTU and MDTA (metam). The fact that one of the major metabolites of MITC is metam indicates that metam and MITC may be interconverted under these conditions.

The aqueous photolysis of metam was investigated in a study at pH 7 under artificially simulated sunlight. Degradation of metam in this experiment is very fast (DT_{50} = 12 min; equivalent to 27.8 min at 38 °N). The major degradation products in these experiments were *N*-methylthioformamide (max. 22 % AR after 25 min), MCDT (sodium methylcarbamo(dithioperoxo)thioate; max. 14 % AR after 25 min), MITC (max. 16 % AR after 25 min), methylamine (18 % AR after 25 min; already detected at time 0 at 14 % AR).

No acceptable ready biodegradation study is available and therefore the substance is considered to be not readily biodegradable.

Degradation / dissipation of metam (potassium salt) in the aquatic environment was investigated in a water sediment system (pH_{water} 7.4; pH_{sed} 6.7; OC 4.3 %; clay 10 %) under dark aerobic and anaerobic conditions at 25 °C. In the aerobic experiment metam degrades rapidly in the whole system ($DT_{50whole\ system}$ = 0.32 h). During the peer review the notifier was requested to calculate the formation fraction and whole system degradation rates for the active metabolite MITC and to provide an evaluation of the effect of the temperature on the results of these studies with respect to the volatilisation of MITC. Temperature used in this study was in the higher part of the range allowed by OECD guidance (10 - 30

°C). The experts in the meeting considered that the range is set to allow testing of the most relevant worst case conditions. In this case, a lower temperature would result in a more representative worst case due to the high volatilisation of MITC. Studies used for EU risk assessment are generally performed at 20 °C and the meeting did not find any reason that justifies the use of a higher temperature. The meeting agreed that the information provided by the notifier did not allow any quantitative estimation of the effect of temperature on the volatilisation. Since in the dossier vapour pressure measurements at 15 and 25 °C are available, a more quantitative assessment should be possible. Consequently, in the original review the meeting of experts identified a data gap to address the effect of temperature on the dissipation of MITC from water by volatilisation. In the resubmission dossier a theoretical calculation on the dependence of volatilisation on the temperature is presented. According this calculation volatilisation rates are about half at 12 °C than at 25 °C but it is still expected that $DissT_{50}$ would be shorter than 1 d. No new water sediment study at lower temperature was provided in the resubmission. The data from the anaerobic water sediment study was considered not relevant for the representative uses, and to average dissipation rates from aerobic and anaerobic experiments was not found scientifically justified.

During the peer review a clarification was required with respect to metabolite DMTD. This metabolite reaches 24 % AR after 2 h, 13 % AR after 4 h and is not detected after 8 h. Since the metabolite is produced directly from metam and not from MITC the meeting agreed that it does not need to be addressed if significant direct exposure of surface water to metam may be precluded from the representative uses.

Due to the data gaps identified on the derivation of various key modelling input parameters and to the fact that FOCUS SW modelling does not consider volatilisation-deposition route of entry in surface water, the available PEC_{SW} were not considered appropriate for the EU risk assessment. The meeting of experts identified 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. The experts also agreed that the observed dissipation of MITC in these experiments is due to volatilisation and not to degradation. Therefore, they agreed that a kinetic formation fraction and degradation rate cannot be properly calculated. The half life for MITC resulting from the kinetic analysis presented in the addendum (June 2008) was reclassified by the meeting of experts as a dissipation half life from water phase. In the resubmission dossier a new surface water assessment has been provided with calculation of PEC SW for the active metabolite MITC. FOCUS SW Step 3 calculations presented in this reassessment may be used as worst case in the aquatic risk assessment (FOCUS, 2001); however, FOCUS SW Step 4 calculations provided by the applicant assume 97.5 % run off mitigation, well above the 90 % maximum run off mitigation considered feasible by FOCUS Landscape (FOCUS 2007). Furthermore, it is expected that for a substance with a K_{FOC} as low as MITC, the vegetative buffer zone will not be effective in mitigating the run off. Additionally the applicant has provided an estimation of the PEC SW resulting from volatilisation deposition of MITC. Without further mitigation, the exposure to the aquatic environment resulting from this route of exposure can be considered covered by the assessment performed for the edge-of-field exposure.

4.2.2. Potential for ground water contamination of the active substance their metabolites, degradation or reaction products

According to the FOCUS GW modelling presented by the notifier the limit of 0.1 μg / L may be exceeded by MITC for the 80^{th} percentile concentration at 1 m depth in some ground water scenarios (up to a maximum of 8.97 μg / L for carrots use in Hamburg) (FOCUS 2000). Since data gaps were identified during the peer review for half life and adsorption / desorption properties in soil of MITC the available PEC_{GW} calculations were not considered reliable by the meeting of experts. The meeting also agreed that FOCUS GW was probably not completely satisfactory for volatile compounds such as MITC, but considered that it is the best available tool at the moment.

In the original review the meeting of experts identified the need to recalculate MITC PEC GW with adequate input parameters (when available) using FOCUS GW or a higher tier approach if appropriate. In the resubmission dossier new PEC GW calculations were provided for MITC. However, the persistence end point available for this substance was considered by the peer review to represent only situations were the substance is applied at lower application rates, such as the representative use in potato (153 kg metam /ha; equivalent to 86.6 kg /ha). Potential groundwater contamination was assessed for the use in potato by FOCUS GW (PELMO 3.3.2 and PEARL 3.3.3) calculations of 80th percentile concentration at 1 m depth assuming rotation and applications once every third year. With these restrictions the limit of 0.1 μg / L is exceeded in 5 of the 9 scenarios simulated. Additionally the 10 μg / L are exceeded in two of the scenarios with a calculated maximum of 197.73 μg MITC / L in Jokioinen (PELMO 3.2.2 calculation).

In the original review, a data gap was identified by EFSA to address the potential ground water contamination of impurity DMTU. In the resubmission dossier, potential groundwater contamination by impurity DMTU has been addressed by FOCUS GW (PELMO 3.3.3 and PEARL 3.3.3) calculations for uses in carrots, cabbage (surrogate for lamb's lettuce) and tomatoes by calculation of 80th percentile leachate concentration over 20 yr of continuous application. In the calculations a worst case application rate of 7 kg DMTU / ha (corresponding to an application rate of 1020 kg / ha metam) was assumed for this impurity. The trigger of 0.1 μg / L is not exceeded for any of the scenarios and uses simulated.

4.3. Fate and behaviour in air

MITC is a very volatile compound. Half life of MITC in the troposphere due to photochemical degradation was estimated to be 78.6 d by Atkinson calculation. Potential long-range transport cannot therefore be excluded from the available information. The meeting of experts identified a data gap to address the atmospheric fate and behaviour of MITC including global warming (ozone depletion), long-range transport and deposition.

In the resubmission dossier, experimental values have been provided by the applicant showing that half-lives in the atmosphere, when all possible degradation processes are considered (direct and oxidative indirect photolysis), will be in the range of 4.8 – 6.3 days (a half life of 4.5 d was estimated in the dazomet evaluation). This half-life is still longer than the 2 d trigger considered for alerting on potential long-range transport. Therefore, the critical area of concern on potential long-range transport of MITC through the atmosphere remains.

With respect to the ozone depletion potential, however, the low rate of photochemical degradation (including reaction with ozone) discussed above suggests that MITC might have a low potential for ozone depletion. The potential for contribution to global warming of MITC has not been directly addressed within the information provided in the resubmission dossier. The applicant presented arguments that contribution to the greenhouse effect and global warming is not expected to be significant for substances with atmosphere residence times shorter than 1yr. In practice, any meaningful global warming assessment would need to consider the overall amount of MITC released to the atmosphere (including sources other than metam) and an assessment restricted to the European geographical region might have limited relevance in this context.

5. Ecotoxicology

Metam-sodium was discussed at the PRAPeR experts' meeting on ecotoxicology (PRAPeR 53) in July 2008 on basis of the DAR, the Addendum Vol 3 B.9 and subsequent Metam Revised Vol. 3 B .9. The resubmission evaluation was discussed in the meeting of experts PRAPeR TC 54 (April 2011).

The fate and behaviour assessment considered the application rate range of 153 – 612 kg a.s. / ha as the range covering the majority of representative uses proposed. A special case is the application rate proposed for the representative use on grape (1020 kg a.s./ha). In this crop metam is intended to be applied locally by incorporation in the root zone of each plant, which is expected to result in an overall application rate (i.e. rate per hectare) which is lower than the nominal rate notified. It is pointed out that the risk of metam to non-target organisms for the use on grape (local application on the root at 40 cm depth), was considered covered by the risk assessment provided for other soil injection representative uses (i.e. carrots). EFSA considered this approach as feasible. However given the higher application rate, it would need to be appropriately justified that overall application rate (i.e. rate per hectare) is lower than the nominal rate notified.

The representative uses evaluated were the uses as a soil fumigant (nematicide, fungicide, herbicide, insecticide) in carrot (Field), lamb's lettuce (F), cucumber (Glasshouse), aubergine (G), pepper (G), potato (F), strawberry (F) , tomato (F, G), grape (F) at the application rate of 153-612 kg a.s./ha (local application of 1020 kg a.s./ha in the case of grape).

Metam-sodium rapidly degrades into methylisothiocyanate (MITC), which is active on living organisms present in the soil and water.

DMTU (N,N'-dimethylthiourea) is an impurity applied together with the active substance at rates up to 1 – 7 kg / ha. DMTU was considered as a relevant impurity; however, ecotoxicological studies were not available in the original DAR. Therefore, a data gap was identified for submission of ecotoxicological information with the DMTU.

The risk assessment was conducted according to the following guidance documents: Risk Assessment for Birds and Mammals. SANCO/4145/2000 September 2002 (European Commission, 2002c); Aquatic Ecotoxicology, SANCO/3268/2001 rev.4 final, October 2002 (European Commission, 2002b); Terrestrial Ecotoxicology, SANCO/10329/2002 rev.2 final, October 2002 (European Commission, 2002); Risk Assessment for non-target arthropods, ESCORT 2, March 2000, SETAC (SETAC, 2001).

5.1. Risk to terrestrial vertebrates

Birds and mammals were not exposed to metam-sodium in the glasshouse uses, therefore the risk to birds and mammals for the use of metam in glasshouse was assessed as low.

The acute and short-term endpoints for birds were obtained from *Colinus virginianus* and *Anas platyrhynchos* studies, respectively. The acute and short-term endpoints LD_{50}/LC_{50} for birds were 211 mg/kg bw (equivalent to 119 mg MITC /kg bw) and > 324 mg/kg bw/day (equivalent to 183.4 mg MITC /kg bw /day), respectively. The lowest acute and long-term endpoints in mammals were observed in rat LD_{50} = 896 mg a.s./kg bw and NOAEL = 1.5 mg a.s./kg bw/day.

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 to prevent evaporation. After a waiting period of at least two weeks, the soil would be cultivated. The notifier and the RMS proposed in the DAR that due to the method of application of metam-sodium, no contaminated food would be available for birds and mammals in the field (no contaminated crop or weeds, no contaminated earthworms or insects). The RMS considers that the risk to birds was considered low for the representative field uses. MS Experts at PRAPeR 53 discussed the risk assessment for birds and mammals exposed to metam-sodium and to the main metabolite (MITC). Member States experts suggested that the most probable contaminated food items for birds and mammals would be the soil invertebrates (including earthworms). The experts agreed that even if the soil invertebrates were expected to be killed, birds and mammals may feed on them. Therefore, an acute risk assessment for insectivorous birds and mammals should be provided. Long-term exposure to birds and mammals is not expected. Therefore a chronic risk assessment for birds and mammals is not needed. An acute risk assessment for insectivorous and vermivorous birds and mammals was provided in the resubmission dossier.

A higher tier assessment of the risk of MITC to insectivorous and vermivorous birds was carried out, based on the higher tier studies in the resubmission dossier. Birds censuses were performed on sterilized and unsterilized carrot plots in France to derive focal species and ecological data. A PT of 0.66 was suggested to be used in the risk assessment. Due to the opportunist behaviour of birds it is not possible to exclude higher PT. Member States experts at PRAPeR TC 54 did not consider acceptable the use of a PT refinement for acute exposure, and the study was deemed valid only for the identification of focal species.

In a second field study, residues in invertebrates and in carrots were measured. Several uncertainties were pointed out by the experts at the teleconference regarding the representativeness of invertebrates and soil properties. Therefore, it was agreed to use the highest residue measured in the study as RUD (13.3 mg /kg).

Even using this RUD value, a high acute risk cannot be excluded for the representative uses on carrots, strawberry, tomato and lamb's lettuce. However, the acute risk to insectivorous and vermivorous birds was assessed as low for the representative use on potato. Therefore a data gap was identified to further address the risk for insectivorous and vermivorous birds, for all representative field uses except on potato.

Member States experts agreed that an acute risk assessment was necessary for the metabolite MITC for mammals. The endpoint for MITC from the dazomet DAR is lower than the endpoint used in the metam-sodium DAR. Member State experts agreed that lowest endpoint could be used in the risk assessment in accordance with previous assessments of active substances with common metabolites, unless scientific reasons suggest not to use it. Otherwise the RMS should provide a risk assessment for the metabolite MITC using the lower endpoint of 100 mg/kg_{bw} obtained from a mouse oral toxicity study in the dazomet DAR.

The risk assessment was done based on the use of the lowest endpoint LD_{50} = 100 mg $MITC/kg_{bw}$. A higher tier risk assessment of MITC to insectivorous and vermivorous mammals was carried out, based on the higher tier studies in the resubmission dossier. A survey of small mammals on sterilised and unsterilized carrot plots and the field perimeter in a commercial arable field in France was performed. The aim of the study was to propose a list of small mammal species in the selected carrot field that can be used as focal species. A field study was conducted to determine the residues in carrots field invertebrates as potential food items for the small mammals in France. The Member State experts at PRAPeR TC 54 discussed the use of both studies in the refined risk assessment. The experts agreed that PT could not be derived to be used in the risk assessment. The study can be considered acceptable only to derive the focal species. Due to the uncertainties identified (soil properties; representativeness of invertebrates) the experts agreed to use the highest measured residue level (13.3 mg /kg) to derive the RUD value. The acute risk of metam-sodium and MITC to insectivorous and vermivorous mammals was assessed as high for the representative uses on strawberry, tomato, carrot and lamb's lettuce. However, the acute risk to insectivorous and vermivorous mammals was assessed as low for the representative use on potato. Therefore a data gap was identified to further address the risk for insectivorous and vermivorous mammals, for all representative field uses, except for use on potato.

Overall, it was concluded that the acute risk of metam-sodium and MITC to birds and mammals was assessed as high for all the representative uses in the field, with the exception of the use on potato.

No risk assessment for secondary poisoning was triggered for metam-sodium since the log P_{OW} = -2.91.

5.2. Risk to aquatic organisms

The greenhouse uses poses no concern for the surface water contamination, based on the Dutch Model approach (0.1 % of the highest application rate proposed is 61.2 kg as/ha that can reach the surface water).

Based on the available information metam-sodium was considered to be very toxic to aquatic organisms. The metabolite MITC was more toxic than metam-sodium. Application of metam-sodium is such that no drift exposure of the surface water was expected. The unique ways of exposure were through run-off and drainage, and due to the rapid degradation of metam-sodium in soil (DT_{50} in soil between 9 and 17 minutes), surface water contamination with the parent molecule could be excluded. Aquatic organisms might be exposed to the metabolite MITC as a result of the drainage and run-off. The lowest endpoints driving the aquatic risk assessment were obtained in studies with fish, daphnids and algae. The LC_{50}/EC_{50} for fish, *Daphnia*, higher aquatic plants and algae were 0.0531, 0.076, 0.59 and 0.28 mg MITC/L, respectively. With regards to chronic toxicity fish was the most sensitive group. Results from the fish prolonged toxicity test with the metabolite MITC (Munk R., 1990) showed that at the three highest tests measured concentrations were <80 % of the nominal concentrations. Therefore, the experts in PRAPeR 53 agreed that the NOEC from this study should be provided using the third highest concentration expressed in mean measured. The RMS presented the new NOEC = 0.004 mg MITC/L (mean measured concentrations) for *Oncorhynchus mykiss* in the Metam Revised Vol. 3 B.9 that was submitted in August 2008.

The RMS based the aquatic risk assessment on the estimation of the TER values for the metabolite MITC.

The fate and behaviour section considered that PEC_{sw} from $FOCUS_{sw}$ step 3 can be considered as valid only for the representative use on potato, but not for the other representative uses. The PEC_{sw} values from $FOCUS_{sw}$ Step 4 were not considered valid in the fate and behaviour section.

The TERs values were calculated on the basis of a new PECsw values from FOCUS step 3. The TER values were above the Annex VI trigger values for the representative use on potato. Therefore the TERs values were above the Annex VI trigger values for more than half of the $FOCUS_{sw}$ step 3 scenarios (5 out of 9 scenarios for fish, 6 out of 9 for aquatic invertebrates and for all relevant scenarios for algae and aquatic plants), indicating a low risk of MITC for this representative use. For the representative field uses evaluated other than the use on potato, a data gap was identified to assess the risk of MITC to aquatic organisms based on the new PEC_{sw}.

No bioconcentration study with fish is triggered since the log P_{ow} of metam is < 3.

5.3. Risk to bees

The application of metam-sodium was on bare soil; the product was incorporated into the soil (soil injection or drip irrigation) and thereafter the soil was compressed with a roller. After a waiting period of 2 weeks the soil would be cultivated. There was no direct application onto plant material. Bees were not at risk in-field and off-field since no exposure to contaminated crops or weeds was expected. Consequently, the risk of metam-sodium and its metabolite MITC to bees was assessed as low.

The risk of metam-sodium to bees for the use in greenhouse was considered to be low, since bees were not exposed.

5.4. Risk to other arthropod species

The notifier proposed that due to the application method, there was no exposure to standard foliage dwelling arthropods, such *Typhlodromus pyri* and *Aphidius rhopalosiphi*. Therefore studies with standard foliage-dwelling arthropods should not be required. Only the soil-dwelling arthropods would be exposed to the metam fumigation. The notifier provided an extended laboratory study conducted with (soil-dwelling) rove beetles (*Aleochara bilineata*). This aged residues study was performed with treated soil after 55 days of aging under field conditions. No biologically relevant effects were observed for the reproduction (14.6%) at the application rate of 1 x 1200 L Sodium-metam/ha (608.4 kg a.s./ha). This aged residue study demonstrated that *A. bilineata* could be recolonised in the field after 55 days. The RMS proposed that the risk of metam-sodium and its metabolite MITC should be addressed in terms of recovery in the field. A field trial was presented in the resubmission dossier. The field trial was carried out to determine the effects of metam-sodium on the non-target arthropods of arable land in France after one application in spring. The study was discussed at the PRAPeR TC 54 meeting. Metam-sodium at the highest application rate, other than for the use on grape, of 612 kg a.s./ha had initial adverse effects on soil arthropods living in the soil and at the soil surface. The test demonstrates that actual recovery in the field occurred for the most important taxa within one year. For 2 % of pitfall sampling taxa recovery was still ongoing in the next spring. Due to the high mortalities of arthropods found in the in-field area, probably the recolonisation may have occurred from non-treated field. The recolonisation is depending on the size of the treated area. 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.

The risk of metam-sodium to non-target arthropods for the use in greenhouse was considered to be low, since non-target arthropods were not exposed in the greenhouse.

5.5. Risk to earthworms

An earthworm field study (Lührs U. 2002 in Belgium 2007) was conducted with two different concentrations 152.1 and 608.4 kg a.s./ha during one year. After this period the earthworm abundance and earthworm biomass were comparable to the agricultural controls. The abundance of juvenile earthworm was comparable to the agricultural control at the lowest test dose (152.1 kg a.s./ha); however, at the higher test treatment (608.4 kg a.s./ha) there was a statistically significant difference with the agricultural controls. The experts agreed that after the application of the 608.4 kg a.s./ha, there was no clear indication of 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 notifier to address concerns on the recovery/recolonisation of earthworms. This should include considerations of effects on recovery of different ecological groups as well as known data on migration distances.

Information on the migration distances of earthworm species was submitted in the resubmission dossier. Two literature papers were used to provide migration distances for earthworm species. Nevertheless, it was not possible to check the whole reports, to validate the migration distances proposed. Therefore, available data on migratory distances could not be used in the risk assessment and a data gap remains.

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) the risk to earthworms cannot be excluded with the available data, so restriction to exclude uses in temporary greenhouses would be appropriate.

5.6. Risk to other soil non-target macro-organisms

As metam-sodium is used as soil fumigant, it was expected that metam-sodium would have effects on the entire soil flora and fauna including the Collembola populations. Therefore the risk of metam-sodium and its metabolite MITC should be addressed. An extended laboratory study was presented in the DAR (Meister A., 2002 in Belgium 2007), however, the RMS did not consider this study to be valid.

The risk from metam and its metabolite should be addressed in terms of recovery in the field. The RMS suggested that a semi-field or field study should demonstrate the recolonisation of the fields.

A field trial to demonstrate the effects of metam-sodium on non-target macro-organisms on arable land in France after one application in spring was submitted in the resubmission dossier. The study included the assessment of soil non-target macro-organisms such as *collembola* and *gamasida*. There is no evidence from the results in the test that long-term effects on soil macro-organisms occurred due to the metam-sodium treatment. All affected soil-dwelling invertebrates had recovery in abundance within the same season and no adverse effects extended into the year after the treatment. Therefore the risk of metam-sodium and MITC to soil macro-organisms was considered to be low for all of the representative uses.

5.7. Risk to soil non-target micro-organisms

No effects of >25 % on soil respiration and nitrification were observed in tests with metam-sodium up to concentration of 608.4 kg a.s./ha indicating a low risk to soil non-target micro-organisms for the representative uses evaluated.

5.8. Risk to other non-target-organisms (flora and fauna)

The application of metam-sodium was on bare soil; the product was incorporated into the soil and thereafter the soil was compressed with a roller. The mode of application excludes the off-field exposure by drift. In conclusion the risk of metam-sodium and its metabolite MITC to non-target terrestrial plants was expected to be low.

5.9. Risk to biological methods of sewage treatment

Technical metam-sodium inhibits the respiration of activated sewage sludge at a concentration giving an EC_{50} (activate sludge, 3h) = 4.36 mg a.s./L. It is not expected that the concentrations of metam-sodium in biological sewage treatment plants would reach a concentration of more than 0.142 mg a.s./L if the product is applied according to the GAP, and therefore the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

6.1. Soil

Definitions for risk assessment:	metam-sodium, MITC, DMTU (impurity)
Definitions for monitoring:	MITC

6.2. Water

6.2.1. Ground water

Definitions for exposure assessment:	MITC, DMTU (impurity)
Definitions for monitoring:	MITC

6.2.2. Surface water

Definitions for risk assessment:	MITC
Definitions for monitoring:	MITC

6.3. Air

Definitions for risk assessment:	MITC
Definitions for monitoring:	MITC

6.4. Food of plant origin

Definitions for risk assessment:	MITC
Definitions for monitoring:	MITC

6.5. Food of animal origin

Definitions for risk assessment:	Not required.
Definitions for monitoring:	Not required.

7. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

7.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
metam	Very low persistence (DT_{50} = 9 – 17 min)	Further information was required to address the risk to earthworms. The risk to soil macro-organisms was assessed as low.
MITC	Low persistence when metam is applied at rates not higher than 153 kg / ha (equivalent to 86.6 kg MITC / ha) ($DT_{50\ 20°C}$ = 1.0 – 2.9 d). A new data gap was identified to address those situations where the soil concentrations of the metabolite MITC due to the use of metam are expected to be significantly higher than the concentration used in the available GLP study (all the representative uses evaluated except potato).	Further information was required to address the risk to earthworms. The risk to other soil macro-organisms was assessed as low.
DMTU (impurity applied together with the active ingredient at rates up to 4 – 7 kg / ha)	Very low persistence in soil ($DT_{50\ lab\ 20\ °C}$ = 0.09 – 0.24 d).	Data gap.

7.2. Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
MITC	very high mobility (K_{FOC} = 9 – 20.2 mL / g)	Only use in potato can be assessed with the available persistence end point. FOCUS: Yes, the limit of 0.1 µg / L is exceeded in 5 of the 9 scenarios simulated. Additionally the 10 µg / L are exceeded in two of the scenarios with a calculated maximum of 197.73 µg MITC / L in Jokioinen.	Yes	Yes	Very toxic to the aquatic organisms. The risk of MITC to aquatic organisms was assessed as low for the use on potato.
DMTU (impurity applied together with the active ingredient at rates up to 4 – 7 kg / ha for representative uses other than the use on grape)	very high mobility (K_{FOC} = 7 – 10 mL / g)	FOCUS GW: No (for the uses carrot, cabbage (surrogate for lamb's lettuce) and tomato assuming a worst case application of 7 kg/ha of DMTU).	Data gap	Not required for the proposed uses. (agreed as relevant during PRAPeR 59 due to the lack of information)	Data gap

7.3. Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
MITC	Very toxic to the aquatic organisms. The risk of MITC to aquatic organisms was assessed as low for the use on potato.

7.4. Air

Compound (name and/or code)	**Toxicology**
MITC	Toxic via inhalation (R23 proposed)

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

- 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, ongoing proposed submission date February 2012, refer to section 1).
- A data gap was identified by the meeting of experts (PRAPeR TC 52, March 2011) to address those uses where soil concentrations of the metabolite MITC are expected to be significantly higher than the concentration used in the Hall 2004 study (Belgium, 2010) to determine the half life of this active metabolite. Preferably, a study following the relevant guidelines and conducted at a range of concentrations covering those expected to occur from the representative uses should be used (relevant for all representative uses except potato).
- A data gap was identified by EFSA to provide PEC_{SW} for MITC using adequate input parameters (when available) for all field uses except potato (proposed submission date unknown).
- 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 a higher tier approach if appropriate (relevant for all uses evaluated except potato, data gap identified at the meeting of experts PRAPeR 52, data gap only fulfilled in the resubmission for uses at rates of 153 kg / ha or lower, refer to section 4.2.2).
- The risk to insectivorous and vermivorous birds and mammals needs to be further refined (relevant for all field representative uses evaluated, except for the use on potato; submission date proposed by the notifier: unknown).
- The risk of MITC to aquatic organisms should be assessed based on the new PEC_{SW} (relevant for the representative field uses evaluated except for the use on potato; submission date proposed by the notifier: unknown; refer to section 5.2).
- Notifier to address the concerns on the recovery/recolonisation of earthworms, this should include consideration of effects on recovery of different ecological groups as well as data on migration distances (relevant for all field representative uses evaluated except for the use to potatoes; submission date proposed by the notifier: unknown; refer to section 5.5).
- Data to address the ecotoxicological relevance of the impurity DMTU in comparison with metam-sodium is required (relevant for all representative uses; submission date proposed by the notifier: unknown).

Conclusions and Recommendations

Overall conclusions

This conclusion from the original review was reached on the basis of the evaluation of the representative uses as a nematicide, fungicide, herbicide and insecticide by soil fumigation prior to the planting of carrot, lamb’s lettuce, cucumber, aubergine, pepper, potato, strawberry, tomato and grapes. The conclusion of the peer review of the resubmission was reached on the basis of the evaluation of the same representative uses. Full details of the representative uses can be found in Appendix A.

The representative formulated product for the evaluation was “Metam sodium 510 g/L”, a soluble concentrate (SL), registered under different trade names in Europe.

Adequate methods are available to monitor all compounds given in the respective residue definition. Only single methods for the determination of residues are available since a multi-residue-method such as the German S19 or the Dutch MM1 is not applicable due to the nature of the residues.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Storage stability data where the relevant impurities are analysed for was identified as a data gap. Spectra are available for the relevant impurity MITC and also for the relevant impurity DMTU.

As for mammalian toxicology, metam-sodium is harmful by oral ingestion and inhalation (R22 and R20 proposed). In irritation tests, metam-sodium was not irritant to eyes but was corrosive to skin, therefore R34 ("Causes burns") was proposed. Metam-sodium is a skin sensitiser (R43 "May cause sensitisation by skin contact" proposed). The relevant short-term No Observed Adverse Effect Levels (NOAELs) are 0.1, 0.5 and 0.8 mg/kg bw/day in dogs, rats and mice, respectively. In particular, the occurrence of severe hepatotoxicity in dogs was considered to support the proposal of R48/22 ("Danger of serious damage to health by prolonged exposure if swallowed") to the European Chemicals Agency (EChA). Metam did not show any genotoxic potential, but caused angiosarcomas in mice (therefore R40 "Limited evidence of a carcinogenic effect" was proposed). The relevant long-term NOAEL was 1.5 mg/kg bw/day based on reduced bodyweight gain, specific lesion within the nasal passages, and changes in some haematology and spleen (haemosiderin depots) parameters in rats. In multigeneration tests, the relevant parental, reproductive and offspring NOAELs were 4, 12 and 4 mg/kg bw/day, respectively. Tested in developmental toxicity studies, metam-sodium caused an increased incidence of variations and retardations at maternally toxic dose in rats and decreased number of live foetuses, and increased number of dead implants in rabbits, with relevant maternal and developmental NOAEL in rats of 5 mg/kg bw/day and of 5 and 10 mg/kg bw/day, respectively, in rabbits. The malformations occurred at low incidences (sometimes in singularity), but in a consistent manner, at the top-doses, in the presence of quite severe maternal toxicity. Effects were clearly treatment related and associated with maternal toxicity: the classification as R63 ("Possible risk of harm to the unborn child") was proposed for consideration to the EChA. The Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 0.001 mg/kg bw/day, based on the 1-year dog study NOAEL with a Safety Factor (SF) 100; the Acute Reference Dose (ARfD) is 0.1 mg/kg bw based on an overall rat developmental toxicity NOAEL and supported by rabbit developmental study (SF 100).

MITC is toxic via ingestion (R25 proposed) and via inhalation (R23 proposed). It is harmful in contact with skin (R21 proposed). In skin irritation tests it was corrosive (R34 proposed). It was also irritative to the respiratory system (R37 proposed). It is a skin sensitiser (R43 proposed).

The relevant NOAEL for short-term exposure to MITC is 0.4 mg/kg bw/day, based on body weight decrease, haematological findings and blood chemistry at 2 mg/kg bw/day (in the 90d dog study). MITC did not show any genotoxic, carcinogenic, reproductive or developmental toxicity potential. The relevant NOAEL for long-term toxicity is 0.44 mg/kg bw/day based on haematological changes in rats; the relevant parental NOAEL is 0.7 mg/kg bw/day, the reproductive and offspring NOAEL is >3.6 mg/kg bw/day. The relevant maternal and developmental toxicity NOAELs in rats are 3 and 10 mg/kg bw/day. The ADI and AOEL are 0.004 mg/kg bw/day based on the 1 year and 90-day studies in dog, respectively; the ARfD is 0.03 mg/kg bw based on a NOAEL for rat maternal toxicity with SF 100. The operator exposure in open field is below the AOEL with the use of Respiratory Protective Equipment (RPE); the bystander exposure for applications in the open field is below the AOEL and worker exposure for applications in the open field is below the AOEL without the use of Personal Protective Equipment (PPE). The operator exposure for drip irrigation in greenhouses is 2.9% of the AOEL with the use of RPE. The worker exposure is below the AOEL even without RPE 18 days after application. Bystander exposure exceeds the AOEL 10 hours after application within 12 metres of the greenhouse. The PRAPeR meeting of experts considered the impurity DMTU as relevant.

Metabolism studies were supplied but no metabolites were identified. It was noted that the majority of the metabolism studies were under dosed. The meeting of experts considered the under dosing and lack of identification and it was concluded that as long as fate and behaviour had not identified any significant metabolites in soil then the metabolism data could be accepted. In the resubmission it was confirmed by fate and behaviour that no other significant metabolites (other than MITC) are present and therefore the metabolism data are acceptable. In the resubmission the residue trials data set was completed and it can be concluded that the uses do not lead to residues >0.01 mg/kg. It can be concluded that there is no need for processing studies, rotational crop studies or livestock studies. The risk assessment can be finalised and MRLs are proposed for all representative crops at 0.01* mg/kg.

Degradation of metam and its known active metabolite MITC in soil was investigated in four soils under dark aerobic conditions at 20 °C. The experts in the meeting were not confident that these experiments provided a realistic representation of the fate and behaviour of metam and MITC in soil mainly due to the mode of application used in the study with respect to the application in field where volatilisation is minimized by compacting soil or with plastic films. However, the meeting noted that a number of scientific studies investigating the persistence of metam and MITC are available in the public domain and to regulatory authorities. Consequently, in the original review a data gap was identified to address the range of half-lives available for metam and MITC and whether they are applicable to the metam EU risk assessment. In the resubmission dossier the applicant presented a number of studies from the scientific literature. Available scientific literature allows a relationship between the concentration of MITC in soil and its rate of degradation to be established. MITC degrades slowly at higher concentration rates. Whereas the GLP study available in the original dossier (Hall, 2004; summarized in the DAR of Belgium 2010) was considered scientifically acceptable, it was performed with a MITC concentration in the low range of the ones that would result from the representative uses proposed for metam. It was agreed that only the use in potato (153 kg metam /ha) could be considered covered by the end points derived from this study. A new data gap was identified to address those situations where the soil concentrations of the metabolite MITC due to the use of metam are expected to be significantly higher than the concentration used in the available GLP study.

Taking into consideration the application rates of metam other than for the use on grape (306 – 612 kg / ha), during the peer review it was considered that impurities need to be addressed for the potential environmental and ground water contamination. The notifier submitted an overview of the main impurities present in the technical material that was summarized by the RMS in the addendum (Belgium, 2008). The meeting of experts in toxicology agreed that the impurity DMTU should be regarded as toxicologically relevant and therefore a data gap was identified in the original review for a ground water exposure assessment. The route and rate of degradation of the relevant impurity DMTU in four soils under aerobic conditions was investigated in one study submitted with the resubmission dossier. DMTU may be considered to have very low persistence in soil.

PEC soil for metam and MITC were calculated for the worst case use other than grape, in field tomato (612 kg a.s. / ha) assuming 15 cm incorporation. Time dependent PEC soil need to be updated once the data gaps identified for persistence in soil are solved. Initial PECs in soil may be used for the EU risk assessment.

Mobility of metam was investigated by the HPLC method. According this experiment metam may be considered to be very high mobile in soil. In the original review a batch adsorption / desorption study was available for MITC in four soils. This compound was very high mobile in these soils (K_{foc} = 27 – 46 mL / g). The meeting of experts concluded that adsorption in the study may have been overestimated due to the fact that experimental Koc values are simultaneously affected by degradation and volatilisation during the experiment. A new study is available in the resubmission dossier that investigates adsorption / desorption of MITC in five soils. The very high mobility of MITC is confirmed by these experiments (K_{FOC} = 9 – 20.2 mL / g).

In the original review a data gap was identified by EFSA to address the mobility of the impurity DMTU in soil in order to obtain adequate input parameters for ground water modelling. According to the new study available in the resubmission dossier it may be expected that DMTU will exhibit very high mobility in soil (K_{FOC} = 7 – 10 mL / g).

Hydrolysis of metam is relatively fast at any pH. Hydrolysis of MITC at 25 °C occurs with half-lives of ≈ 40 d (pH 4), 50 d (pH 7) and 11 d (pH 9). Major hydrolysis products of MITC were DMU, DMTU and MDTA (metam). The fact that one of the major metabolites of MITC is metam indicates that in water metam and MITC are in equilibrium.

Aqueous photolysis of metam under simulated sunlight is very fast (DT_{50} = 12 min; equivalent to 27.8 min at 38 °N). No ready biodegradation study is available and therefore the substance is considered to be not readily biodegradable.

In the aerobic water /sediment experiment (25 °C) metam degrades rapidly in the whole system ($DT_{50whole\ system}$ = 0.32 h). The meeting agreed that the information provided by the notifier did not allow any quantitative estimation of the effect of temperature on the volatilisation. Consequently, in the original review the meeting of experts identified a data gap to address the effect of temperature on the dissipation of MITC from water by volatilisation. In the resubmission dossier a theoretical calculation on the dependence of volatilisation on the temperature is presented. According to this calculation volatilisation rates are about half at 12 °C than a 25 °C but it is still expected that $DissT_{50}$ would be shorter than 1 d. No new water sediment study at lower temperature was provided in the resubmission. The data from the anaerobic water sediment study was considered not relevant for the representative uses and it was not considered scientifically justified to average dissipation rates from aerobic and anaerobic experiments.

Due to the data gaps identified on the derivation of various key modelling input parameters and to the fact that FOCUS SW modelling does not considers volatilisation-deposition route of entry in surface water, the available PEC_{SW} were not considered appropriate for the EU risk assessment. The meeting of experts in the original review identified 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. In the resubmission new calculations of PEC SW for the active metabolite MITC have been provided. FOCUS SW Step 3 calculations presented in this reassessment may be used as a worst case in the aquatic risk assessment; however, FOCUS SW Step 4 calculations provided do not follow FOCUS Landscape recommendations. Additionally the applicant has provided an estimation of the PEC SW resulting from volatilisation deposition of MITC. Without further mitigation, the exposure to aquatic environment resulting from this route of exposure can be considered covered by the assessment performed for the edge-of-field exposure.

The meeting of experts identified the need to recalculate MITC PEC_{GW} values with adequate input parameters (when available) using FOCUS GW or a higher tier approach if appropriate. In the resubmission dossier new PEC GW calculations were provided for MITC. However, the persistence end point available for this substance was considered by the peer review to represent only situations where the substance is applied at lower application rates such the representative use in potato (153 kg metam /ha; equivalent to 86.6 kg /ha). Potential groundwater contamination was assessed for the use in potato assuming rotation and applications once every third year. With these restrictions the limit of 0.1 μg / L is exceeded in 5 of the 9 scenarios simulated. Additionally the 10 μg / L are exceeded in two of the scenarios with a calculated maximum of 197.73 μg MITC / L in Jokioinen (PELMO 3.2.2 calculation).

In the original review, a new data gap was identified by EFSA to address the potential ground water contamination of impurity DMTU. In the resubmission dossier, potential groundwater contamination by the impurity DMTU has been addressed. The trigger of 0.1 μg / L is not exceeded for any of the scenarios and uses simulated.

The meeting of experts identified a data gap to address the atmospheric fate and behaviour of MITC including global warming (ozone depletion), long-range transport and deposition. In the resubmission dossier, experimental values have been provided by the applicant showing that half-lives in the atmosphere, when all possible degradation processes are considered (direct and oxidative indirect photolysis), will be in the range of 4.8 – 6.3 d. This half life is still longer than the 2 d trigger considered for alerting on potential long-range transport. Therefore, the critical area of concern on potential long-range transport of MITC through the atmosphere remains. The available data suggest that MITC might have a low potential for ozone depletion. The potential for contribution to global warming of MITC has not been directly addressed within the information provided in the resubmission dossier. In practice, any meaningful global warming assessment would need to consider the overall amount of MITC released to the atmosphere (including sources other than metam) and an assessment restricted to the European geographical region might have limited relevance in this context.

No risk assessment for terrestrial vertebrates was presented in the DAR. Experts suggested that the most probable contaminated food items for birds and mammals would be the soil invertebrates (included earthworms). An acute risk assessment should be also done for the metabolite MITC using the lowest endpoint available of 100 mg a.s./kg bw agreed during the meeting. A higher tier assessment of the risk of MITC to insectivorous and vermivorous birds and mammals was carried out, based on the higher tier studies in the resubmission dossier. Birds and mammals censuses were performed on sterilized and unsterilized carrot plots in France to derive focal species and ecological data. The study was deemed valid only for the identification of focal species. In a second field study, residues in invertebrates and in carrots were measured. It was agreed to used the highest residue as RUD (13.3 mg /kg). Overall, it was concluded that the acute risk of metam-sodium and MITC to birds and mammals was assessed as high, for all the field representative uses, with the exception of the use on potato. Therefore a data gap has been identified to further address the risk for insectivorous and vermivorous birds, for all field representative uses except on potato.

Metam-sodium and its relevant metabolite MITC are very toxic to aquatic organisms. Due to the rapid degradation of metam-sodium in soil, surface water contamination with the parent molecule can be excluded. Aquatic organisms may be exposed to the metabolite MITC as result of the drainage and run-off. A new risk assessment for aquatic organisms was submitted in the resubmission dossier. The fate and behaviour section considered that PEC_{sw} from $FOCUS_{sw}$ step 3 can be considered as valid only for the representative use on potato, but not for the other representative uses. The PEC_{sw} values from $FOCUS_{sw}$ Step 4 were not considered valid in the fate and behaviour section. The TERs values were calculated on the basis of new PECsw values from FOCUS step 3 for the use on potato. The TERs values were above the Annex VI trigger values for most of the scenarios $FOCUS_{sw}$ step 3 for the representative use on potato, indicating a low risk of MITC to aquatic organisms on the representative use on potato. A data gap was identified pending on the fate section. Once the new PEC_{sw} values are available, the risk of MITC to aquatic organisms should be assessed for the representative field uses evaluated other than for the use on potato.

An extended laboratory study was conducted with *Aleochara bilineata* and this aged residue study demonstrated that *A. bilineata* was able to re-colonise the field after 55 days. From an extended laboratory study it was only possible to assess the potential for recolonisation, but not the actual recovery. A field trial was presented in the resubmission dossier. The field trial was carried out to determine the effects of metam-sodium on the non-target arthropods of arable land in France after one application in spring. The test demonstrates that actual recovery in the field occurred for the most important taxa within one year. For 2 % of pitfall sampling taxa recovery was still ongoing in the next spring. Due to the high mortalities of arthropods found in the in-field area, probably the recolonisation may occur from non-treated field. Therefore the risk of MITC to non-target arthropods was considered to be low.

An earthworm field study was conducted with the metam-sodium. At the lower dose of 152.1 kg a.s./ha earthworm abundance and biomass had recovered to levels of that in the agricultural controls. The experts agreed that after the application of the 608.4 kg a.s./ha, there was no clear indication of full recovery after one year. A further refinement was required to the notifier to address concerns on the recovery/re-colonisation of earthworms this should include considerations on effects on recovery of different ecological groups as well as known data on migration distances. Information on the migration distances of earthworm species was submitted in the resubmission dossier. However, available data on migratory distances could not be used in the risk assessment. Therefore a data gap remains.

The risk of metam and its metabolite MITC to other soil macro-organisms was assessed. A field trial to demonstrate the effects of metam-sodium on non-target macro-organisms on arable land in France after one application in spring was submitted in the resubmission dossier. All affected soil-dwelling invertebrates had recovery in abundance within the same season and no adverse effects extended into the year after the treatment. Therefore the risk of metam-sodium and MITC to soil macro-organisms was assessed as low for all of the representative uses.

The risk of metam and its metabolite MITC to bees, soil micro-organisms, non-target plants and biological method of sewage treatment were assessed as low for the field uses.

The risk of metam and its metabolite MITC to terrestrial vertebrates, aquatic organisms, bees and non-target arthropods, soil micro-organisms and biological methods of sewage treatment were assessed to be low for the representative greenhouse uses.

9. Particular conditions proposed to be taken into account to manage the risk(s) identified

- Use of respiratory protective equipment (RPE) to be considered for operator exposure to MITC during field (soil injection) and greenhouse applications; for greenhouse applications any re-entries before day 18 requires the use of RPE; for an occasional re-entry shortly after treatment for 15 minutes, the worker must wear RPE with 98% protection.
- The groundwater assessment for the active relevant metabolite MITC is only finalized for the representative use in potato assuming a maximum application rate of metam of 153 kg metam /ha (equivalent to 86.6 kg MITC /ha) every third year. In the simulation it is also assumed that no other substances generating the active metabolite MITC are applied between the metam applications.
- For uses in permanent glasshouses the risk to earthworms was considered as low by EFSA. For uses is temporary greenhouses (e.g. polythene tunnels) that include natural soil (non-artificial substrate), the risk to earthworms cannot be excluded with the available data, so a restriction to exclude uses in temporary greenhouses would be appropriate.

10. CONCERNS

10.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

1. The groundwater contamination level by the active relevant metabolite MITC for all representative uses except for the use in potato (max application rate of 153 kg metam/ha) has not been finalized.

2. The risk assessments for metam-sodium and MITC to birds and mammals could not be finalised with the available data for all the representative field uses except for the use on potato.

3. The risk of MITC to aquatic organisms could not be finalised with the available data for the representative field uses except for the use on potato.

4. The risk assessments for earthworms could not be finalised with the available data for all the representative field uses except for the use on potato.

10.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive

91/414/EEC, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

5. Environmental exposure assessment (including potential ground water contamination) can not be finalised for uses at application rates higher than 153 kg metam / ha, however a high potential for groundwater exposure by relevant metabolite MITC can be anticipated. The assessment of the use in potatoes (153 kg metam/ ha, every third year) indicates that the active relevant metabolite MITC may exceed 0.1 μg/L in five of the nine FOCUS scenarios simulated (with a maximum of 49.3 – 197.7 μg/L in Jokioinen).
6. The active metabolite MITC is volatile and has a measured half-life in the atmosphere due to direct and indirect photolysis processes in the range of 4.8 – 6.3 days. This half life is still longer than the 2 d trigger considered for alerting on potential long-range transport.[12]

For the only representative use for which the risk assessment was finalised (potato), a critical concern has been identified. See summary of representative uses in section 11 for further details of the areas of concern identified for the individual uses.

[12] Note this is not a criteria in the Uniform Principles of Annex VI to Directive 91/414/EEC for decision making on product authorisations, but is a criteria that managers from Member States have asked to be informed about in relation to obligations Member States have under certain international treaties.

11. Overview of the assessments for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 9, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

Representative use		Carrot (April-June)	Carrot (Oct-Dec)	Lamb's lettuce	Cucumber (greenhouse)	Aubergine (greenhouse)	Pepper (greenhouse)
Operator risk	Risk identified						
	Assessment not finalised						
Worker risk	Risk identified						
	Assessment not finalised						
Bystander risk	Risk identified				X	X	X
	Assessment not finalised						
Consumer risk	Risk identified						
	Assessment not finalised						
Risk to wild non target terrestrial vertebrates	Risk identified						
	Assessment not finalised	X[2]	X[2]	X[2]			
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified						
	Assessment not finalised	X[4]	X[4]	X[4]			
Risk to aquatic organisms	Risk identified						
	Assessment not finalised	X[3]	X[3]	X[3]			
Groundwater exposure active substance	Legal parametric value breached						
	Assessment not finalised						
Groundwater exposure metabolites	Legal parametric value breached						
	Parametric value of 10µg/L[(a)] breached						
	Assessment not finalised	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]
Comments/Remarks							

The superscript numbers in this table relate to the numbered points indicated as concerns in section 10.
(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003.

Representative use		Potato	Strawberry	Tomato (field)	Tomato (greenhouse)	Grape
Operator risk	Risk identified					
	Assessment not finalised					
Worker risk	Risk identified					
	Assessment not finalised					
Bystander risk	Risk identified				X	
	Assessment not finalised					
Consumer risk	Risk identified					
	Assessment not finalised					
Risk to wild non target terrestrial vertebrates	Risk identified					
	Assessment not finalised		X[2]	X[2]		X[2]
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified					
	Assessment not finalised		X[4]	X[4]		X[4]
Risk to aquatic organisms	Risk identified					
	Assessment not finalised	4/9 FOCUS scenarios	X[3]	X[3]		X[3]
Groundwater exposure active substance	Legal parametric value breached					
	Assessment not finalised					
Groundwater exposure metabolites	Legal parametric value breached	5/9[5] FOCUS scenarios				
	Parametric value of 10µg/L[(a)] breached					
	Assessment not finalised		X[1]	X[1]	X[1]	X[1]
Comments/Remarks						

The superscript numbers in this table relate to the numbered points indicated as concerns in section 10.
(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003.

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APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

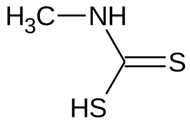
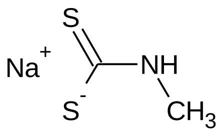
Identity, Physical and Chemical Properties, Details of Uses, Further Information

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) ‡	methyldithiocarbamic acid Variant*:* sodium methyldithiocarbamate
Chemical name (CA) ‡	*N*-methylcarbamodithioic acid Variant: sodium *N*-methylcarbamodithioate
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 ‡	<u>Technical concentrates (TK):</u> metam-sodium TK: min. 400 g/kg – max. 442 g/kg metam-potassium TK: min. 520 g/kg – max. 560 g/kg <u>Dry weight basis (calculated):</u> metam-sodium: min. 965 g/kg metam-potassium: min. 990 g/kg
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	methylisothiocyanate (MITC) - max. 12 g/kg on dry weight basis (metam-sodium); - max. 0.42 g/kg on dry weight basis (metam-potassium) *N,N'*-dimethylthiourea (DMTU) - max. 23 g/kg on a dry weight basis (metam-sodium) - max. 6 g/kg on a dry weight basis (metam-potassium)
Molecular formula ‡	$C_2H_5NS_2$ Variant : $C_2H_4NNaS_2$
Molecular mass ‡	107.2 u

	Variant: 129.2 u
Structural formula ‡	 metam  metam-sodium

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) ‡	$5.75 .10^{-2}$ 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)	Solubility at 20°C in g/L (99.9%)

	solubility at 20°C (g/L)
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_{OW} ≤ - 2.91 at 20 °C (pH 6.9) (99.9%)
	No significant pH-effect expected (cfr. dissociation constants)
Dissociation constant (state purity) ‡	pKa_I = 2.99; pKa_{II} = 11.06 (99.2%)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	

	λ_{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 $Pa.m^3.mol^{-1}$
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:

	λ_{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

Summary of representative uses evaluated (metam-sodium)

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/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.	45000-180000	459	n.a.	see note ** below table
Aubergine (eggplant)	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.	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.	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.	see note **** below table
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.	60000-240000	612	n.a.	see note ** below table

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/hl 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.	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 10 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/m²)	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.

**: 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.

**** One application every three years in potato.

- * 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

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
Food of animal origin		None
Soil		MITC
Water	surface	MITC
	drinking/ground	MITC
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 = 0.1µg/L (MITC)
Air (analytical technique and LOQ)	GC-NPD (conf. technique: column of different polarity): LOQ = 0.5 µg/m³ (MITC)
Body fluids and tissues (analytical technique and LOQ)	HPLC-MS (conf. technique: LC-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)

	RMS/peer review proposal
Active substance	R31

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 0.4 mg/kg bw/day	
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	

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**
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	

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	rat, developmental study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation (e.g. name 50 % ECMonam)	Concentrate: 1 %; 12% : for the dilution Rat *in vivo* and comparative *in vitro* (human/rat skin)

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 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]
Workers exposure to metam-sodium	Not relevant: metam-sodium decomposes very rapidly into MITC.
Workers exposure to 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
Bystanders exposure to metam-sodium	Not relevant: metam-sodium decomposes very rapidly into MITC.
Bystanders exposure to MITC	**Bystander exposure:** -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 (60 min. exposure)
Resident exposure to MITC	**Resident exposure:** drip irrigation in greenhouse, 10 h after application, 140-220m distance of greenhouse: **94%** of AOEL

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

	RMS/peer review proposal
Substance classified (metam-sodium)	Repr. Cat 3; R63 : Carc. Cat 3; R 40: Xn; R48/22: Xn; R20/22: C; R34: R43

	RMS/peer review proposal
Substance classified (MITC)	C ; R34 : T; R23/25: Xn ; R21 : R43; R37

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	-Root and Tuber vegetables (radish & turnip), -Leafy Brassica (Chinese cabbage), -Fruiting vegetables (Tomato).
Rotational crops	Rotational crops studies are not required considering the DT_{50}/DT_{90} 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?	N/A
Processed commodities	Not required.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	N/A
Plant residue definition for monitoring	MITC
Plant residue definition for risk assessment	MITC
Conversion factor (monitoring to risk assessment)	N/A

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

Animals covered	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 P*o/w*: -2.9 at 20 °C).

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

	Not relevant

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

	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)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	N/A	N/A	N/A
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/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		-	

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 Southern Region Field or glasshouse,	Trials results relevant to the representative uses (a)	Recommendation/comments	**MRL** estimated from trials according to representative use	**HR** (c)	**STMR** (b)
Lettuce	Indoor	**MITC**: <0.01 mg/kg		0.01* mg/kg	0.01	
Pepper	Indoor	**MITC**: 3x <0.01 mg/kg **DMTU**: na; 2x <0.01 mg/kg		0.01* mg/kg	0.01	
Tomato	Indoor	**MITC**: 5x <0.01 mg/kg **DMTU**: na; 4x <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	
Aubergine	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 [(1).]	-	
Potato		No residue trial provided		0.01* mg/kg [(1).]	-	
Grapes		No residue trial provided		0.01* mg/kg[(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

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	N/A
TMDI (% ADI) according to national (to be specified) diets	N/A
TMDI (% ADI) according to EFSA PRIMo Model rev.2A	Highest TMDI: 2.5 % ADI (PT general population)
IEDI (WHO European Diet) (% ADI)	N/A
NEDI (specify diet) (% ADI)	N/A
Factors included in IEDI and NEDI	N/A
ARfD	0.03 mg/kg bw for MITC
IESTI (% ARfD)	5 % Potatoes 2 % Table grapes 2 % Carrots 2 % Peppers 2 % Cucumbers
NESTI (% ARfD) according to national (to be specified) large portion consumption data	N/A
Factors included in IESTI and NESTI	N/A

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	
Not required				

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*
	Lamb's lettuce (F)	0.01*
	Cucumber (G)	0.01*
	Aubergine (G)	0.01*
	Pepper (G)	0.01*
	Potato (F)	0.01*
	Strawberry (F)	0.01*
	Tomato (F/G)	0.01*
	Grapes (F)	0.01*

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), [^{14}C-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), [^{14}C-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.

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[13]	PH (water)	t. °C / % MWHC	DT_{50} /DT_{90} (minutes)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	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 d*		

*This end point should only be used to assess uses with application rates lower or equal to 153 kg metam / ha. Longer half lives are expected to be observed when higher application rates are used. A data gap to determine the degradation rate of MITC to address situations were metam is intended to be applied at higher rates has been identified by the peer review of the resubmission dossier.

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		

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

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: data available in the public scientific literature and to other regulatory authorities has been evaluated but no regulatory endpoints can be derived since the data were considered as not reliable quantitatively. However, the data provide useful qualitative information such as the dependence of the MITC degradation rate with its concentration in soil (slower degradation at higher concentration)	

pH dependence ‡ (yes / no) (if yes type of dependence)	-
Soil accumulation and plateau concentration ‡	Not required

Laboratory studies ‡

Parent, MITC	Anaerobic conditions
Not required	

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡
HPLC determination: Koc < 17.8 mL/g at pH 4 and 9

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

Impurity DMTU ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Clay	1.75	7.20	-	-	0.175	10	0.75
Loamy sand	2.16	5.40	-	-	0.152	7	0.73
Silty clay	3.93	7.36	-	-	0.290	7	0.82
Sandy loam	0.98	6.40	-	-	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)

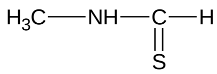
Parent Method of calculation	DT_{50} (metam-sodium): 0.0118 days (17 minutes) Kinetics: 1st order Representative worst case from laboratory study.
Application data	Crop: field tomato Depth of soil layer: 15 cm Soil bulk density: 1.5 g/cm^3 % plant interception: 0% Number of applications: 1 Interval (d): - Application rate(s): 612 kg as/ha

$PEC_{(s)}$ (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application 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 DT_{50} (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 Actual	Single application Time weighted average	Multiple application Actual	Multiple application 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, r^2=0.98) MITC: 20 % AR (1.8 d)
	pH 7: DT50 a.s. : 2.2 d at 25 °C (1st order, r^2=0.92) MITC: 60 % AR (5 d)
	pH 9: DT50 a.s. : 4.5 d at 25 °C (1st order, r^2=0.98) MITC: 20 % AR (5.4 d)
	pH 4: 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)
Photolytic degradation of active substance and metabolites above 10 % ‡	DT_{50} = 12 min (equivalent to 27.8 min of natural summer sunlight at latitude 38° N) *Major degradation products (≥ 10% of applied radioactivity AR):* - N-methylthioformamide (*syn*- and *anti*- rotamer): 22% of AR after 25 min  - MCDT (sodium methylcarbamo(dithioperoxo)thioate): 14% of AR after 25 min - MITC (methylisothiocyanate): 16% of AR after 25 min - Methylamine: 18% of AR after 25 min (zero-time sample contained 14% methylamine)
Quantum yield of direct phototransformation in water at Σ > 290 nm	Not required

Readily biodegradable ‡ (yes/no)	No information available; considered to be not readily biodegradable.

Degradation in water / sediment

Metam-potassium	Distribution (less than 1%AR after 1 day in whole system)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} Water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Non-sterile aerobic	7.4	6.7	25	0.32/1.09 h	0.946	-	-	-	-	Linear 1st ord.
Sterile anaerobic	7.4	6.7	25	1.59/5.28 h	0.928	-	-	-	-	Linear 1st ord.
Non-sterile anaerobic	7.4	6.7	25	2.87/9.53 h	0.976	-	-	-	-	Linear 1st ord.
Geometric mean/median										

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 1st ord.
Non-sterile anaerobic	7.4	6.7	25	-	0.995	13.44/44.65h	0.995	-	-	Non-lin 1st 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 FOCUSsw step 1 and 2	Not required, since metam-sodium itself is subject to rapid degradation (laboratory DT_{50}'s ranged from 4 - 23 minutes) and is not expected to reach surface water
Parameters used in FOCUSsw step 3 (if performed)	Not required
Application rate	Not required

Metabolite MITC Parameters used in FOCUSsw step 3	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 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 DT_{50} (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	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-potatoes (FOCUS, 2002)

Scenario	Emergence date	Harvest date	Possible window of application	Application date generated by PAT *
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 (1st crop)	10-Apr	15-Jul	01 Sep-01 Oct	04-Sep-1986
D6 (2nd 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

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 (1st crop)	Ditch	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000	0.0000
D6 (2nd 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	1.5550	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

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 contact between downward moving water and MITC in soil.

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	Metam-sodium Not required , since the a.s. itself is subject to rapid degradation (laboratory DT_{50}'s ranged from 4 - 23 minutes) and is not expected to reach groundwater MITC 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: potato Molecular Mass (g mol^{-1}): 73.12 Vapour Pressure (Pa): 1739 at 20ºC Aqueous Solubility (mg/L):8940 at 20ºC Soil Adsorption Coefficient (mean K_{oc}) (ml/g): 13.5 (Kom = 7.83) Freundlich Exponent ($^1/_n$): 0.83 Arithmetic mean $DT_{50\ laboratory}$ (days): 2.10 at 20ºC and pF2 Plant Uptake Coefficient: 0 Impurity DMTU 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 lamb's lettuce), tomato Molecular Mass (g mol^{-1}): 104.18 Vapour Pressure (Pa): 832.95 at 20ºC Aqueous Solubility (mg/L):581980 at 20ºC Soil Adsorption Coefficient (mean K_{oc}) (ml/g): 9(Kom = 5) Freundlich Exponent ($^1/_n$): 0.76 Arithmetic mean $DT_{50\ laboratory}$ (days): 0.121 at 20ºC and pF2 Plant Uptake Coefficient: 0
Application rate	MITC:

<u>Potato</u>
Application rate: 86.60 kg MITC/ha.
No. of applications: 1/every three years
Time of application (month or season): see below
Incorporation (cm): 25

<u>Impurity DMTU:</u>
<u>Carrot, cabbage (surrogate for lamb's lettuce), tomato:</u>
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	
Lamb's lettuce			
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	
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	**80th Percentile Annual Average PEC_{GW} (µg/L)**					
						FOCUS-potatoes
Châteaudun						**0.001**
Hamburg						10.308
Jokioinen						197.734
Kremsmünster						0.540
Okehampton						1.208
Piacenza						0.645
Porto						**0.000**
Sevilla						**0.000**
Thiva						**0.000**

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	**80th Percentile Annual Average PEC_{GW} (µg/L)**					
						FOCUS-potatoes
Châteaudun						**0.066**
Hamburg						6.456
Jokioinen						49.264
Kremsmünster						0.827
Okehampton						1.947
Piacenza						0.591
Porto						**0.000**
Sevilla						**0.000**
Thiva						**0.000**

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	**80th 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	80th 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

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	MITC - short range transport (relevant for soil and surface water assessment). .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 DT_{50} water (d): 50 DT_{50} soil (d): 2.1 DT_{50} 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	$µg/kg_{wwt}$
Pore water of agricultural soil	5.15E-03	µg/L
Natural soil	4.12E-03	$µg/kg_{wwt}$
Industrial soil	4.12E-03	$µg/kg_{wwt}$
Sediment	0.015	$µg/kg_{wwt}$

PEC$_{(gw)}$ From lysimeter / field studies

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

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

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

Direct photolysis in air ‡	(see table below)
Quantum yield of direct phototransformation	Not reported
Photochemical oxidative degradation in air ‡	DT_{50} of metam 1.997 hours based on 24h-day derived by the Atkinson model (version v1.90). OH concentration assumed = 1.5 x10^{6} OH/cm³ DT_{50} of MITC = 78.6 days based on 12 h-day derived by the Atkinson model (version v1.92). OH concentration assumed = 1.5 x10^{6} OH/cm³
Volatilisation ‡	from plant surfaces (BBA guideline): not available
	from soil surfaces (BBA guideline): not available
Metabolites	MITC

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

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, DMTU (impurity) Surface Water: MITC Sediment: MITC Ground water: MITC, DMTU (impurity) 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.
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.

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)

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 ‡				
Colinus virginianus	metam-sodium	Acute	LD_{50} = 211[1]	-
Colinus virginianus	metam-sodium	Short-term	LC_{50} > 448	> 5000
Anas platyrhynchos	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 **LD_{50} = 119 mg MITC/kg b.w.**
[2] corresponding to **LC_{50} > 183.4 mg MITC/kg b.w./day**
[3] for the risk assessment the worst case acute toxicity endpoint for MITC (from the dazomet dossier), **LD_{50} (female mouse) = 100 mg MITC/kg b.w.** was used.

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

Crop and application rate : strawberry, tomato, 612 kg a.s./ha (346 kg MITC/ha)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[1]
Higher tier refinement (Birds)				
(1) Insectivorous birds based on FIR/bw =1.20 and RUD = 0.083				
Starling	acute	34.6	**3.44**	10
(2) Vermivorous birds based on FIR/bw = 1.1 and RUD = 0.083				
Mistle thrush	acute	31.7	**3.75**	10
Higher tier refinement (Mammals)				
(1) Insectivorous mammals based on FIR/bw =1.18 and RUD = 0.083				
Wood mouse	acute	34.1	**2.94**	10
(2) Vermivorous mammals based on FIR/bw = 1.4 and RUD = 0.083				
Wood mouse	acute	40.4	**2.47**	10

[1] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

Crop and application rate : carrot, 408 kg a.s./ha (230 kg MITC/ha)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[1]
Higher tier refinement (Birds)				
(1) Insectivorous birds based on FIR/bw =1.20 and RUD = 0.083				

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[1]
Starling	acute	23.0	**5.17**	10
(2) Vermivorous birds based on FIR/bw = 1.1 and RUD = 0.083				
Mistle thrush	acute	21.1	**5.64**	10
Higher tier refinement (Mammals)				
(1) Insectivorous mammals based on FIR/bw =1.18 and RUD = 0.083				
Wood mouse	acute	22.6	**4.42**	10
(2) Vermivorous mammals based on FIR/bw = 1.4 and RUD = 0.083				
Wood mouse	acute	26.9	**3.72**	10

[1] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

Crop and application rate : lamb's lettuce, 306 kg a.s./ha (173 kg MITC/ha)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[1]
Higher tier refinement (Birds)				
(1) Insectivorous birds based on FIR/bw =1.20 and RUD = 0.083				
Starling	acute	17.3	**6.87**	10
(2) Vermivorous birds based on FIR/bw = 1.1 and RUD = 0.083				
Mistle thrush	acute	15.9	**7.50**	10
Higher tier refinement (Mammals)				
(1) Insectivorous mammals based on FIR/bw =1.18 and RUD = 0.083				
Wood mouse	acute	17.0	**5.87**	10
(2) Vermivorous mammals based on FIR/bw = 1.4 and RUD = 0.083				
Wood mouse	acute	20.2	**4.95**	10

[1] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

Crop and application rate : potato, 153 kg a.s./ha (86.3 kg MITC/ha)

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger[1]
Higher tier refinement (Birds)				
(1) Insectivorous birds based on FIR/bw =1.20 and RUD = 0.083				
Starling	acute	8.64	13.8	10
(2) Vermivorous birds based on FIR/bw = 1.1 and RUD = 0.083				
Mistle thrush	acute	7.92	15.0	10
Higher tier refinement (Mammals)				
(1) Insectivorous mammals based on FIR/bw =1.18 and RUD = 0.083				
Wood mouse	acute	8.49	11.8	10
(2) Vermivorous mammals based on FIR/bw = 1.4 and RUD = 0.083				
Wood mouse	acute	10.1	10	10

[1] If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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				
Lepomis macrochirus	metam-sodium	96 h (static)	Mortality, LC_{50}	> 0.175 mg a.s./L (measured at 96 h)
Oncorhynchus mykiss	Vapam	96 h (static)	Mortality, LC_{50}	0.24 mg form/L (0.078 mg a.s./L) (nom)
Lepomis macrochirus	Vapam	96 h (static)	Mortality, LC_{50}	1.19 mg form/L (0.389 mg a.s./L) (nom)
Cyprinodon variegatus	Vapam	96 h (static)	Mortality, LC_{50}	1.3 mg form/L (0.425 mg a.s./L) (nom)
Striped *Majatis*	Vapam	96 h (static)	Mortality, LC_{50}	1.5 mg form/L (0.491 mg a.s./L) (nom)
Oncorhynchus mykiss	MITC	96 h (semi-static)	Mortality, LC_{50}	**0.0531 mg/L** (mm)
Oncorhynchus mykiss	MITC	96 h (flow-through)	Mortality, LC_{50}	0.094 mg/L (mm)
Lepomis macrochirus	MITC	96 h (flow-through)	Mortality, LC_{50}	0.142 mg/L (mm)
Oncorhynchus mykiss	MITC	28 d (flow-through)	Growth NOEC	0.004 mg/L (mm)
Aquatic invertebrate				
Daphnia magna	Metam-Fluid 510 g/L	48 h (static)	Mortality, EC_{50}	2.34 mg form/L (0.99 mg a.s./L) (nom)
Daphnia magna	MITC	48 h (semi-static)	Mortality, EC_{50}	**0.076 mg/L** (mm)
Daphnia magna	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 Koc, 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).				

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Algae				
Pseudokirchneriella subcapitata	Metam-Sodium 510 g/L	96 h (static)	Biomass: E_bC_{50} (72 h) Growth rate: E_rC_{50} (72 h)	0.556 mg a.s./L 1.08 mg a.s./L (initially measured)
Pseudokirchneriella subcapitata	MITC	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**0.28 mg/L** 0.58 mg/L (initially measured)
Anabaena flos-aquae	MITC	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	2.12 mg/L 3.72 mg/L (initially measured)
Higher plant				
Lemna gibba	MITC	7 d (semi-static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**0.59 mg/L** 1.18 mg/L (mean measured initial)
Microcosm or mesocosm tests				
Not required.				

[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)

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

Test substance	Scena-rio	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	*Oncorhynchus mykiss*	96 h	0.0531	1 m	0.0319	1665	100
	D 4	pond				1 m	0.5980	**88.8**	100
	D 4	stream				1 m	3.3540	**15.8**	100
	D 6	ditch (1st crop)				1 m	0.0000	>10000	100
	D 6	ditch (2nd 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	*Daphnia magna*	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 (1st crop)				1 m	0.0000	>10000	100
	D 6	ditch (2nd 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	*Pseudokirch-neriella subcapitata*	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 (1st crop)				1 m	0.0000	>10000	10

	D 6	ditch (2nd 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	*Lemna gibba*	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 (1st crop)				1 m	0.0000	>10000	10
	D 6	ditch (2nd crop)				1 m	9.0840	64.9	10
	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

Bioconcentration				
	metam-sodium	MITC	Metabolite2	Metabolite3
$\log P_{O/W}$	- 2.91	1.05	-	-
Bioconcentration factor (BCF)[1] ‡	Not required.			
Annex VI Trigger for the bioconcentration factor	-	-	-	-
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 ^{14}C or on specific compounds

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

No data available; not required.

Hazard quotients for honey bees (Annex IIIA, point 10.4)

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 low for the representative uses.

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

Laboratory tests with standard sensitive species

No data available; 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
Aleochara bilineata	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 residues
[2] for preparations indicate whether dose is expressed in units of a.s. or preparation
[3] 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
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 well reported (evaluations by different statistical methods). Metam-sodium application at the highest rate other than for grape, 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 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.

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			
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. The risk of metam-sodium and its metabolite MITC to non-target soil macro-organisms is low for the representative 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]			
An earthworm field study (Lührs 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. **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 address concerns 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. However, available data on migratory distances could not be used in the risk assessment.			

[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

Not necessary to be calculated.

Soil organisms (non-target arthropods, earthworms (permanent greenhouse only), soil macro-organisms and soil micro-organisms) are not exposed to the uses in greenhouse.

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 low for the representative 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)

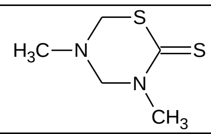
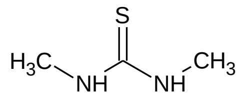
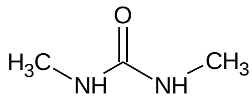
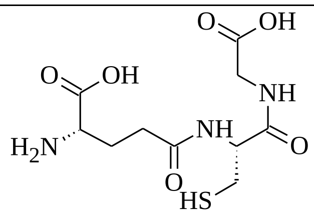
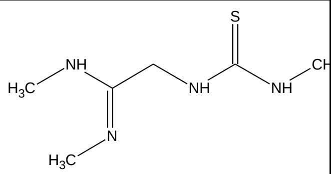
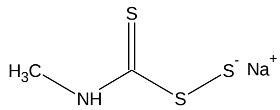
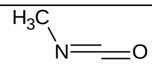
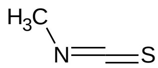
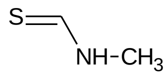
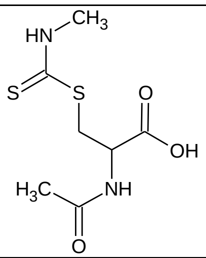
Compartment	
soil	metam-sodium, MITC
water	MITC
sediment	MITC
groundwater	MITC

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	metam-sodium : N, R50
Metabolite	MITC : N, R50

	RMS/peer review proposal
Preparation	Not required. The formulated product is equivalent to the active substance.

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name**	Structural formula**
COS	thioxomethanone	O=S
CS_2	carbon disulphide	S=S
Dazomet	3,5-dimethyl-1,3,5-thiadiazinane-2-thione	
DMTU Dimethyl thiourea	*N,N'*-dimethylthiourea or 1,3-dimethylthiourea	
DMU **M1** (soil metabolite of DMTU)	*N,N'*-dimethylurea or 1,3-dimethylurea	
Glutathione	L-γ-glutamyl-L-cysteinylglycine	
M4 (soil metabolite of DMTU)	(1*Z*)-*N*,*N*'-dimethyl-2-[(methylcarbamothioyl)amino]ethanimidamide	
MCDT	sodium (methylamino)(thioxo)methanesulfenothioate	
MIC	methylisocyanate or isocyanatomethane	
MITC	methyl isothiocyanate or isothiocyanatomethane	
methylamine	methanamine	$H_3C\text{-}NH_2$
N-methylthioformamide	*N*-methylthioformamide	
N-acetyl-S-[(methylamino)carbothioyl]cysteine	*N*-acetyl-*S*-(methylcarbamothioyl)cysteine	

*The metabolite name in bold is the name used in the conclusion.

**ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).

ABBREVIATIONS

λ	wavelength
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticides Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
G	glasshouse
GAP	good agricultural practice
GC-MS	gas chromatography – mass spectrometry
GC-NPD	gas chromatography nitrogen phosphorous detection
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC-UV	high performance liquid chromatography with ultra violet detector
HPLC-MS	high performance liquid chromatography – mass spectrometry
HPLC-MS/MS	high performance liquid chromatography with tandem mass spectrometry
HPRT	Hypoxanthine-guanine phosphoribosyl transferase
ILV	inter laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry

K_{oc}	organic carbon adsorption coefficient
kg	kilogram
L	litre
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
mN	milli-newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
Pa	pascal
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
pH	pH-value
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between n-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
STMR	supervised trials median residue
TER	toxicity exposure ratio
TLC	Thin layer chromatography
TMDI	theoretical maximum daily intake
UV	ultraviolet
UDS	unscheduled DNA synthesis
WBC	white blood cell
WHO	World Health Organisation
WG	water dispersible granule

yr	year