Conclusion regarding the peer review of the pesticide risk assessment of the active substance

oxydemeton-methyl

finalised: 23 June 2006

SUMMARY

Oxydemeton-methyl is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[1], as amended by Commission Regulation (EC) No 1490/2002[2]. This Regulation requires the European Food Safety Authority (EFSA) to organise 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 one year a conclusion on the risk assessment to the EU-Commission.

France being the designated rapporteur Member State submitted the DAR on oxydemeton-methyl in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 3 May 2004. Following a quality check on the DAR, the peer review was initiated on 4 August 2004 by dispatching the DAR for consultation of the Member States and the applicant, the oxydemeton-methyl Task Force which originally consisted of Bayer AG and United Phosphorus Limited. The Task Force membership changed. Bayer AG has transferred the property of oxydemeton-methyl to IRVITA Plant Protection Branch. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 18 May 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in September 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 6 June 2006 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicant which comprises application by orchard air-blast sprayers and by tractor mounted hydraulic sprayers to control aphids in pome fruit and cereals (excluding oats). The maximum total dose for cereals is 0.25 kg oxydemeton-methyl (ODM) per hectare and for pome fruit it is 0.75 kg ODM per hectare.

[1] OJ No L 53, 29.02.2000, p. 25
[2] OJ No L 224, 21.08.2002, p. 25

The representative formulated product for the evaluation was Metasystox 250 EC, an emulsifiable concentrate (EC).

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in pome fruit can be analysed with a multi-method (The German S16 method has been validated). For the other matrices only single methods are available to determine residues of oxydemeton -methyl.
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.

Oxydemeton-methyl is toxic if swallowed, in contact with skin and by inhalation. It is irritating to eyes and may cause sensitisation by skin contact. The main acute, short-term or long-term toxic effect is an inhibition of blood and brain cholinesterase activities in all tested mammalian species. Another target organ in rodents is the epididymis, but the mode of action is not fully understood and the relevance for humans is unknown. Oxydemeton-methyl is not teratogenic, not oncogenic in rodents, and shows no evidence of delayed neurotoxicity (in hens). The compound has clear mutagenic and clastogenic properties *in vitro* but has no genotoxic potential *in vivo*.
The agreed Acceptable Daily Intake (ADI) is 0.0003 mg/kg bw/day, the agreed Acceptable Operator Exposure Level (AOEL) 0.001 mg/kg bw/day, and the agreed Acute Reference Dose (ARfD) 0.0015 mg/kg bw/day, with the use of a safety factor of 100. The estimated and measured operator exposures are higher than the AOEL for the use on pome fruits and cereals (>70 times the AOEL without PPE in the German model), even with the use of personal protective equipment (>3 times the AOEL in the German model). The worker and bystander exposures exceed the AOEL in the pome fruit scenario.

The metabolism of oxydemeton-methyl has been investigated in apples. Initial reactions are the oxidation of the sulphur in the side chain leading to M01[3], demethylation of the ester moieties and hydrolysis of the P-S-bond, followed by further oxidation processes. M01 and metabolite M07[4] have to be considered due to their structural profile as cholinesterase inhibitors. In metabolism studies performed on other crops, another metabolite with the intact organophosphorous structure was identified (metabolite M06[5]). As the metabolic pattern in plant commodities at harvest indicates that metabolites may contribute significantly to the toxicological burden, the residue definition for risk assessment in plant products is proposed to include the parent compound, and metabolites M01, M06 and M07, to allow a reliable assessment of the safety of the consumer to be conducted. The residue definition for monitoring can be restricted to the parent compound and M01, as indicator compounds. A metabolism study on cereals is required for confirmation of the validity of these residue definitions for this crop group.

[3] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate. Pesticide common name:demeton-S-methylsulphon
[4] M07: O-methyl-S-[2(ethylsulfonyl)ethyl] phoshorothioate.
[5] M06: O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate.

The conducted supervised residue trials analysed only the parent compound and M01 and due to deficiencies are not appropriate for MRL setting. A complete data base of supervised residue trials should be submitted with analysis of residues according to the residue definition for risk assessment.
The provided information on processed commodities is very limited and suggests that residues are transferred to apple juice and sauce. However the information is restricted to the levels of the parent compound and its sulfone metabolite, and no balance studies are provided. The need for further information in particular on the effect of processing on the nature of the residues should be examined at Member State level, given the high toxicity of oxydemeton-methyl, and considering the results of the required residue trials.
No residues are expected in following crops and no plant-back interval is needed.
The animal metabolism was investigated in ruminants and poultry, and different metabolic patterns are observed. In ruminants the major constituents of the residues are the parent compound and M01, while metabolite M07 is clearly the dominant compound in poultry tissues and eggs. The residue definitions for monitoring and risk assessment in animal commodities are proposed to include the parent compound, M01 and metabolite M07 in a conservative approach. No MRL proposal for animal commodities can be made given the lack of information on the actual level of exposure of animals to toxicologically relevant compound.
A reliable consumer risk assessment could not be performed at this stage as no reliable information is available on the residue levels in plant commodities.

In soil oxydemeton-methyl exhibited very low to low persistence. Significant sinks for the ^{14}C-radiolabel used in the aerobic laboratory studies were residue not extracted by methanol or methanol/water (17-20% of applied radioactivity (AR) after 90 days ethane label and 20% AR after 49 days methoxy label) and mineralisation to CO_2 (6.6-38%AR after 90 days ethane label & 79% AR after 49 days methoxy label) The breakdown products identified in soil extracts were: M01 (max. 6.3%AR at 3 days), M05[6] (max. 9.5%AR at 4 days), M09[7] (max. 39%AR at 2 days), M10[8] (max. 26.5%AR at 365 days) and DMP[9] (max. 45.8%AR at 1 day). These breakdown products all exhibited very low or low persistence with the exception of M05 which exhibited moderate persistence. Under anaerobic conditions in soil laboratory studies the breakdown products M02[10] (max 6.2%AR at 13 days), and M22[11] (max 22%AR at 13 days) not found under aerobic conditions were identified. Oxydemeton-methyl, M01, M09, M10 and M02 exhibited very high soil mobility in guideline batch adsorption studies. M05 would be expected to exhibit very high mobility on the basis of quantitative structure activity relationship (QSAR) computer modelling.
In aerobic laboratory natural sediment water system experiments (22°C), oxydemeton-methyl exhibited low persistence (dissipation DT_{50} in water 2.3-3.4 days) primarily as a consequence of biodegradation. In the water phase the metabolites M01 (max. 0.9%AR), M02 (max. 3.4%AR), M06

[6] M05: 1-(ethylsulfonyl)-2-(methylsulfonyl) ethane.
[7] M09: 2-ethylsulfinyl ethane sulfonic acid.
[8] M10: 2-ethylsulfonyl ethane sulfonic acid.
[9] DMP: dimethyl phosphate.
[10] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate. Pesticide common name: demeton-S-methyl
[11] M22: 2-ethylthio ethane sulfonic acid.

(max. <9.4%AR) M07 (max. 18%AR), M09 (max. 9.9%AR), M10 (max. 5.1%AR) and M11[12]/M21[13] (max 22.3%AR) were identified and considered to need addressing in the aquatic risk assessment. Partitioning of extractable parent oxydemeton-methyl and the metabolites to sediment was limited, however residues not extracted from sediment by methanol or methanol:water represented a significant sink for the applied radioactivity (45-66%AR at study end, 91 days). Mineralisation to CO_2 of the ethane-^{14}C- radiolabel used accounted for 29-31 % AR by 91 days. Investigations with oxydemeton-methyl with a methoxy radiolabel were not available. Therefore it cannot be excluded that DMP may be present in significant amounts in natural water systems. The available surface water exposure assessment just considered the spray drift route of entry to surface water. The potential exposure of surface water with the soil metabolites M05, M09 and DMP has not been assessed in the available EU level exposure assessment. Member States should therefore carry out a surface water exposure and consequent aquatic risk assessment for M05, M09 and DMP from the runoff and drainage routes of exposure to surface water at the national level, should oxydemeton-methyl be included in Annex 1.

Appropriate FOCUS groundwater modelling is available for oxydemeton-methyl and its soil metabolites: M01, M09 and M10 for some of the potential applied for representative uses on cereals and the use on apples. Modelling was also available for the soil metabolite M05 but data gaps were identified for further substance properties for this metabolite. Consequently the groundwater exposure estimates available for M05 discussed in this conclusion are preliminary. Based on the groundwater modelling results annual average recharge concentrations leaving the top 1m soil column (that do not cover all the possible applied for representative uses on cereals) were < 0.1µg/L for oxydemeton-methyl, M01 and M09 at all 9 FOCUS groundwater scenarios. For 2 of the 9 scenarios concentrations of M10 were predicted to be >0.1 µg/L (up to 0.23 µg/L). Using the available results for M05 that may underestimate leaching potential, the annual average recharge concentrations were >0.1 µg/L at all 9 FOCUS groundwater scenarios. (Preliminary values ranged from 0.17-2.86µg/L. Therefore non relevance assessments were triggered for M05 and M10.

A clarification is needed whether or not the test material used in the section on ecotoxicology covers the specification of the technical material regarding the impurities and furthermore the composition of the tested premix products needs to be clarified.

A potential high risk to birds was identified. The experts' meeting accepted the residue data, the residue decline data, the use of a MAF and food in take values (except for yellow wagtail). Further justification of the relevance of focal bird species to southern Member States is required as well as a consideration of the skylark as a focal species in cereals in northern Member States. As regards the other refinements factors, the meeting had reservations and hence further justification is required before these can be incorporated into a refined risk assessment. A PD of 0.764 large insects/0.236 small insects was accepted for yellow wagtail.

[12] M11: bis-2-[(ethylsulfinyl)-ethyl]disulfide
[13] M21: 2-ethylsulfinyl-ethyl mercaptan

Also a potential high risk to mammals was identified. As for birds the meeting accepted the new residue data, the residue decline data and the use of a MAF figure. As regards the other refinement options, the meeting had reservations and hence further justification is required before these can be incorporated in a refined risk assessment.
Furthermore, the risk to birds and mammals from the metabolite M01 needs to be addressed.

Chironomus riparius is the most sensitive aquatic organisms on an acute time-scale when tested with the lead formulation Metasystox R 250 EC. As the EC_{50} for this species is at least 10 times lower than the EC_{50} for *D. magna*, the EFSA considers a chronic study on *Chironomus* sp. necessary. A high risk to aquatic organisms from oxydemeton-methyl was identified for which risk mitigation measures such as bufferzones of 15 m in cereals and 100 m in orchards are considered necessary. The acute studies on *D. magna* with oxydemeton-methyl 50% premix and the metabolite M02 should be repeated as the test concentrations were not analytically verified.
Based on the available assumption for *C. riparius* a high risk was identified for M01 and M02 for both representative uses evaluated. The acute risk from M07, M09, M10 and M11 to aquatic organisms can be regarded as low for both representative uses evaluated. The experts' meeting decided that the long term risk to aquatic invertebrates of the metabolites M07, M09 and M11 needs to be addressed. The EFSA considers such a study also necessary for metabolite M10 as this is a major metabolite in groundwater. Studies to address the risk from the metabolites M05, ~~*M06*~~, M21 and DMP are considered necessary.

A high risk to bees was identified which must be managed at Member State level. The available studies were not sufficient to establish a withholding period. Application should be avoided when there are likely to be any bees in the crop.

A high risk to non-target arthropods was observed in the laboratory and extended laboratory studies. Further higher tier studies were submitted to address this risk. The EFSA is of the opinion that further data is needed to address the risk to non-target arthropods for both uses evaluated.

The risk to earthworms and soil-micro-organisms from oxydemeton-methyl, M01, M09 and M10 can be regarded as low. Further studies to address the risk to earthworms and soil-micro-organisms from the metabolite DMP are considered necessary.

M01 and M02 have a comparable insecticidal activity as the parent compound. A further clarification of the tested dose rates in the biological screening data for M07 and M10 is needed to conclude on the biological relevance of these metabolites. A study on the effects of oxydemeton-methyl on non-target plants was still awaited during the EPCO meeting. Biological screening data for the ground water metabolite M05 and DMP are considered necessary.

The risk to soil non-target macro-organisms and biological methods of sewage treatment can be regarded as low.

Key words: oxydemeton-methyl, peer review, risk assessment, pesticide, insecticide

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Oxydemeton-methyl is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating France as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, France submitted the report of its initial evaluation of the dossier on oxydemeton-methyl, hereafter referred to as the draft assessment report, to the EFSA on 3 May 2004. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the draft assessment report was distributed for consultation on 4 August 2004 to the Member States and the main applicant the oxydemeton-methyl Task Force which originally consisted of Bayer AG and United Phosphorus Limited. The Task Force membership changed. Bayer AG has transferred the property of oxydemeton-methyl to IRVITA Plant Protection Branch as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 18 May 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in experts' meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticides Safety Directorate (PSD) in York, United Kingdom in September 2005. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 6 June 2006 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 8(7) of the amended Regulation (EC) No 451/2000, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received
- the resulting reporting table (rev. 1-1 of 8 June 2005)
- the consultation report

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 19 June 2006)

Given the importance of the draft assessment report including its addendum (compiled version of March 2006 containing all individually submitted addenda) 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.

By the time of the presentation of this conclusion to the EU-Commission, the rapporteur Member State has made available amended parts of the draft assessment report which take into account mostly editorial changes. Since these revised documents still contain confidential information, the documents cannot be made publicly available. However, the information given can basically be found in the original draft assessment report together with the peer review report which both is publicly available.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Oxydemeton-methyl is the ISO common name for *S*-2-ethylsulfinylethyl *O*,*O*-dimethyl phosphorothioate (IUPAC).

ODM, belongs to the class of aliphatic organothiophospahte insecticides such as cadusafos and ethion. ODM is systemic and acts by stomach and contact action. It works by inhibiting acetylcholinesterase.

The representative formulated product for the evaluation was Metasystox 250 EC, an emulsifiable concentrate (EC), registered under different trade names in Europe.

The evaluated representative uses are as an insecticide which comprises application by orchard air-blast sprayers and by tractor mounted hydraulic sprayers to control aphids in pome fruit and

cereals(excluding oats). The maximum total dose for cereals is 0.25 kg oxydemeton-methyl (ODM) per hectare and for pome fruit it is 0.75 kg ODM per hectare.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of ODM as manufactured should not be less than 85 %, however as the active substance is unstable it is necessary to stabilise it at the point of manufacture. Therefore it is diluted with solvent to form a pre-mixture which has a minimum ODM content of 50 %. This complies with the FAO specification which states "The oxydemeton-methyl content shall be declared within the limits 50-55% w/w and when determined, the content obtained shall not differ from that declared by more than ± 2 percentage units". It should be noted that there is no maximum content described in Volume 4 of the DAR however, it must comply with the FAO specification.

However, since clarification is required on the batch data and the methods used to support them, the specification for the technical material as a whole should be regarded as provisional.

The technical material contains *S*-2-ethylthioethyl *O,O*-dimethyl phosphorothioate (demeton-S-methyl[14]) and *S*-2-ethylsulfonylethyl *O,O*-dimethyl phosphorothioate (demeton-S-methylsulphon[14]) both of which are active ingredients in their own right. Both compounds have to be regarded as relevant impurities.

The content of ODM in the representative formulation is 250 g/L (pure).

Beside the specification, the assessment of the data package revealed one other critical areas of concern with respect to the identity, physical, chemical and technical properties of oxydemeton methyl or the respective formulation. The area of concern is the lack of data on the affects of storage on the relevant impurities. In addition the following data gaps were identified.

- Spectra for the relevant impurities (submitted but not evaluated).
- Data on the surface tension at 25 ºC and viscosity at 40 ºC on the undiluted formulation.
- Storage stability data where the relevant impurities demeton S-methyl and demeton S-methylsulphon are analysed for before and after storage.
- Methods of analysis for demeton S-methyl and demeton S-methylsulphon in the formulation.

[14] It should be noted that demeton-S-methyl and demeton-S-methylsulphon are listed in Annex I of Commission Regulation 2076/2002. However, the COM has confirmed that Article 2 of Commission Regulation 2076/2002 is not applicable in this type of situation.

The main data regarding the identity of oxydemeton-methyl and its physical and chemical properties are given in appendix 1.

However, sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that at least limited quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition currently proposed, i.e. oxydemeton-methyl and M01[15] in food of plant origin.

DFG S16 was validated for acidic and high water content matrices but only for the active substance oxydemeton-methyl. Other GC-FID and NPD methods were validated for oxydemeton-methyl, M01 and M02[16].

An acceptable method for products of animal origin is not available however as no MRLs are proposed no further data are required.

For soil the methods in the DAR were found to be unacceptable however in the addendum to B5 validation data for DFG S16 is supplied for oxydemeton-methyl. For the analysis of water a LC-MS/MS method is available for the determination of oxydemeton-methyl, M01 and M02 in drinking water/ground water and for oxydemeton-methyl and M02 in surface water. For air a GC-NPD method is available for the analysis of oxydemeton-methyl.

As oxydemeton-methyl is classified as toxic methods are required for tissue and for body fluids there is a GC-MS method for the analysis of oxydemeton-methyl and M01. However, there is no acceptable method available for tissues and this has been identified as a data gap.

The discussion in the meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material, relevant impurities in the formulation and methods of analysis for blood and tissues.

2. Mammalian toxicology

Oxydemeton-methyl (ODM) was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 33) in September 2005.
Mammalian toxicity studies were performed using either the pure active ingredient or the 50% concentrate. When the 50% concentrate has been used, the administered doses have been converted in

[15] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate. . Pesticide common name:demeton-S-methylsulphon
[16] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate. Pesticide common name: demeton-S-methyl

quantities of technical material by kg of body weight in order to allow comparison between the different studies. For several studies, this conversion has been discussed by the experts, and a new data requirement has been set for clarification. Thus a new addendum has been provided in January 2006, stating the conversion factor used in the rat reproductive studies: 1 ppm of 50% ODM is equivalent to 0.05 mg/kg bw/day expressed as technical ODM.

2.1. ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

ODM is rapidly absorbed and excreted mainly in urine (> 80% within 24 hours). Faeces are only a minor route of excretion of the compound (< 3%). It is extensively distributed in tissues and organs, and shows no potential for accumulation. It is moderately metabolised (50% excreted as the parent compound) by oxidation and hydrolysis.

2.2. ACUTE TOXICITY

ODM is toxic to mammals by oral, dermal and inhalation routes. The oral LD_{50} is 48 mg/kg bw, the dermal LD_{50} 112 mg/kg bw, and the inhalation LC_{50} (4 hour) 0.471 mg/L.

The compound is not a skin irritant but causes eye irritation in rabbits, and is a skin sensitizer (M&K, Buehler with 3 inductions). **The proposed classification is T; R23/24/25 Toxic by inhalation, in contact with skin and if swallowed; R36 Irritating to eyes; R43 May cause sensitisation by skin contact.**

2.3. SHORT TERM TOXICITY

In rats, rabbits and dogs, the main toxic effect is an inhibition of blood and brain acetyl cholinesterase (AChE) activities.

In two 14-day rat studies, the agreed NOAEL is 0.15 mg/kg bw/day based on brain AChE inhibition.

Two dietary 90-day rat studies are presented in the DAR. The first, performed with 93.9% pure compound, is only considered as indicative and shows an NOAEL of 0.08 mg/kg bw/day (1 ppm) based on plasma and erythrocyte AChE inhibition (no brain AChE measurement). The second, performed with a 53.5% concentrate in methyl isobutylketone, results in a NOAEL of 0.08 mg/kg bw/day (1 ppm), based on brain/plasma/erythrocyte AChE inhibition. In addition for this second study, further data on the stability of the test compound in the diet have been provided in an addendum and considered by the experts as demonstrating adequate homogenisation and stability.

EFSA notes: The applicant has to confirm that, in the second study, the degree of purity of the administered concentrate was taken into account in the calculations of the NOAEL.

In the 1-year dog study, the NOAEL is 0.125 mg/kg bw/day, based on brain AChE inhibition. As rats and dogs have a similar sensitivity to the compound, the experts agreed for a relevant short term NOAEL of 0.1 mg/kg bw/day.

Two 21-day dermal studies were performed in rabbits. Based on the inhibition of brain AChE, the agreed dermal NOAEL is 0.5 mg/kg bw/day. In a 21-day inhalation study with rats, an overall NOAEL of 0.00066 mg a.s./L/day was determined, based on the inhibition of brain AChE activity.

2.4. GENOTOXICITY

ODM gives positive results *in vitro* when tested for DNA damage, gene mutation and chromosome mutation, with the exception of a negative response in an UDS test on rat hepatocytes.

In the *in vivo* tests, ODM induces gene mutations in the mouse spot test at the oral toxic dose of 20 mg/kg bw. The compound is negative in a chromosome aberration test in the hamster, a dominant lethal mutation test in the mouse and in an alkaline elution assay in the rat testis at doses inducing general toxicity. The compound is also negative in a sister chromatide exchange in hamster bone marrow and in the mouse bone marrow micronucleus test but in the absence of clinical symptoms or myelotoxicity at the highest dose tested.

In order to complete the genotoxicity data base, an *in vivo* UDS test in rats and a suitable *in vivo* micronucleus test in the mouse were required. The micronucleus test presented in an addendum (July 2005) at the experts' meeting was clearly negative, and the database was considered sufficient to conclude that ODM is not genotoxic *in vivo*.

2.5. LONG TERM TOXICITY

The 27-month rat study has some deficiencies but has been considered suitable for assessing the oncogenic potential of ODM in the rat. There is no evidence of an oncogenic effect and the proposed NOAEL is 0.03 mg/kg bw/day, based on brain AChE inhibition.

In the 90-week mouse study, no oncogenic effect was observed. The proposed NOAEL is 0.5 mg/kg bw/day, based on brain AChE inhibition and epididymis vacuolation. This was discussed at the experts' meeting (see section 2.6).

2.6. REPRODUCTIVE TOXICITY

Among three multigeneration studies in rats presented in the DAR, only one was considered as acceptable. Additional male reproductive studies (up to 8 months) are also provided in the DAR.

ODM induces adverse reproductive and developmental effects consisting in a decrease in fertility, litter size, pup viability and body weight, associated with vacuolisation of the epithelium of epididymis in males and decreased or absent corpora lutea in the ovaries. The effects occurred in the presence of systemic toxicity manifested by inhibition of AChE activities, and lower body weight gain during gestation. An addendum (January 2006) confirmed the conversion of administered concentrate (50%) into the effective intake of technical material. Thus the NOAELs were confirmed to be 0.45 mg/kg bw/day for the offspring and the reproductive parameters, and 0.05 mg/kg bw/day for the systemic effects in adults.

In the additional male reproductive studies, the systemic NOAEL is 0.15 mg/kg bw/day based on a significant depression of AChE activities. The NOAEL for male reproductive parameters is also 0.15 mg/kg bw/day, based on a dose dependent vacuolation in the epithelium of the epididymis (almost completely reversible after 4-5 months). Testis morphology and sperm characteristics were not modified by the test compound.

The overall NOAELs are 0.15 mg/kg bw/day for the parental toxicity, and 0.45 mg/kg bw/day for the offspring and the reproductive parameters.

In the rat teratogenicity study, ODM at maternally toxic doses does not induce embryotoxic, foetotoxic, or teratogenic effects and does not affect survival, growth, and/or development of the neonate. The NOAEL for developmental toxicity and teratogenicity was ≥4.5 mg/kg bw/day (highest dose tested). The NOAEL for maternal toxicity was <0.5 mg/kg bw/day, based on the inhibition of brain AChE activity.
In the rabbit study, no relevant adverse effects on embryo-foetal development were detected. The NOAEL for maternal toxicity was 0.4 mg/kg b.w. based on brain and erythrocyte AChE inhibition, and the NOAEL for developmental toxicity and teratogenicity was ≥ 1.6 mg/kg bw/day.

The relevance of the effects on epididymis, ovaries and fertility in the multigeneration studies was discussed at the experts' meeting. The mechanism of these effects is unknown as well as its relevance for human's safety. It was concluded that there would not be an impact on the overall risk assessment and that an additional safety factor was not needed since all these effects occurred at doses higher than the systemic NOAEL. However, the **classification with R62 'Possible risk of impaired fertility' and R63 'Possible risk of harm to the unborn child'** is proposed with a question mark. The final decision will be taken by ECB.

2.7. NEUROTOXICITY

Oxydemeton-methyl (technical grade and 50% concentrate) did not display clinical, functional or histopathological evidence of acute or subchronic delayed neurotoxicity in hens.

2.8. FURTHER STUDIES

Human studies

The human study presented in the DAR had some deficiencies (no GLP statement, lack of data availability, low number of subjects, non validated assay method for cholinesterase) and was considered by the experts as not acceptable from a scientific point of view. The proposed acute oral NOAEL in male adults was 0.5 mg/kg bw, based on the inhibition of serum/erythrocyte AChE activity. As no effects were observed in six subjects treated for 30 up to 60 days, the proposed subacute NOAEL is 0.05 mg/kg bw/day.

Impurities

The impurity profile of the batch used in the mouse carcinogenicity study was compared to the as yet unsupported technical specification. Toxicological data were provided in an addendum (July 2005) for three impurities shown to be at lower levels in the toxicological batch used in the mouse chronic study. Both **M01 and M02** are genotoxic *in vitro* but not *in vivo*, and have AChE activity. In addition, M02 is at least as acutely toxic as ODM (oral rat LD_{50} 30 mg/kg bw/d). They were considered to be toxicologically equivalent to the parent compound by the experts.
EFSA notes that, as a consequence, the levels in the toxicological batch do not cover the higher levels in the technical specification.
The third impurity was not considered to be toxicologically relevant.

Plant and groundwater metabolites

The plant metabolites **M06**[17] and **M07**[18], having still the organophosphate structure, were considered to be toxicologically equivalent to oxydemeton-methyl by the experts.

The metabolites **M05**[19] and **M10**[20] appear in groundwater above the trigger value of 0.1 µg/L (M10) and 0.75 µg/L (M05) (see section 4.2.2). No toxicological data are available for these metabolites.

EFSA notes: This issue was identified after the experts' meeting. According to the guidance document on the assessment of the relevance of metabolites in groundwater (SANCO/221/2000 – rev 10), the toxicological relevance of M05 and M10 in groundwater cannot be concluded due to the lack of data on their mutagenicity, acute and possible reproductive toxicity (depending on the outcome of the classification of the parent).

2.9. MEDICAL DATA

Occupational medical data provided in the dossier were limited, but no adverse effect was reported in production plant workers. Findings in poisoning cases are typical of AChE inhibition.

2.10. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

ADI

The ADI is based on the NOAEL (0.03 mg/kg bw/day) from the carcinogenicity study in the rat. With the use of a safety factor 100, the agreed **ADI is 0.0003 mg/kg bw/day**.

AOEL

The agreed **AOEL is 0.001 mg/kg bw/day,** based on the overall short term NOAEL, with the use of a safety factor 100.

ARfD

Initially in the DAR, the proposed ARfD is 0.005 mg/kg bw, based on the rat teratogenicity study, with the use of a safety factor 100. The use of the human study was discussed by the experts. As it was not acceptable from a scientific point of view (see 2.8), this study was considered as not appropriate to derive the ARfD, and no similarity between rats, dogs, rabbits and humans could be concluded for the AChE inhibition.

Based on the 14-day rat studies, the agreed **ARfD is 0.0015 mg/kg bw**, with the use of a safety factor 100.

EFSA notes that the JMPR (2002), on the basis of the same studies (two 14-day rat studies) and applying the same safety factor, used the NOAEL value of 0.2 mg/kg bw/day which resulted in an ARfD of 0.002 mg/kg bw/day (see addendum of July 2005).

[17] M06: O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate
[18] M07: O-methyl-S-[2(ethylsulfonyl)ethyl] phoshorothioate
[19] M05: 1-(ethylsulfonyl)-2-(methylsulfonyl) ethane
[20] M10: 2-ethylsulfonyl ethane sulfonic acid

2.11. DERMAL ABSORPTION

Two *in vivo* studies in rats and monkeys, and one *in vitro* study with human and rat epidermal membranes are presented in the DAR.

The *in vivo* rat study was considered as not acceptable, and the *in vivo* monkey study had some deficiencies (lack of details on the dermal exposure conditions). In the female monkeys, the dermal absorption of ODM ranged between 22 to 33% after a 24 hour exposure period.

The *in vitro* studies in human and rat epidermis/skin were performed with Metasystox EC 250. The results indicated a dermal absorption of 18-19% in human against 94-97% in rat (concentrated formulation, 24 hour exposure). However, dermal absorption from diluted formulations (1:50 and 1:500) was lower than from the concentrated one (10 up to 100 fold lower in human skin).

Taking into account the *in vivo* monkey study and the *in vitro* assays the dermal absorption of ODM *in vivo* in human was estimated to be 20% for diluted and undiluted formulations. This was confirmed at the experts' meeting.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Metasystox 250 EC is an emulsifiable concentrate containing 250 g oxydemeton-methyl/L for use on cereals (except oats) and pome fruit (apples and pears).

Operator exposure

According to the intended uses submitted by the applicant the maximum applied single dose is 125 g a.s./ha in cereals, and 375 g a.s./ha in pome fruits. The minimum volumes are 100 L/ha for cereals and 1000 L/ha for pome fruits. The supported applications are tractor mounted hydraulic sprayers or orchard airblast sprayers.

The estimated operator exposure for Metasystox 250 EC is above the AOEL even with PPE, according to both German and UK models. Results are in the following tables.

Estimated exposure for the **cereal use** presented as % of AOEL (0.001 mg/kg bw/day)
(200 L/ha, 50 ha/day, 5 L boxes, 20% derm. abs., tractor-mounted).

Model	No PPE	With PPE
German	7 943	314
UK POEM	12 885	1 823

PPE: personal protective equipment

Estimated exposure for the **apple tree use** presented as % of AOEL (0.001 mg/kg bw/day)
(1000 L/ha, 20 ha/day, 1 L boxes, 20% derm. abs., tractor assisted).

Model	No PPE	With PPE
German	22 489	2 899
UK POEM	34 088	12 713

PPE: personal protective equipment

These results have been confirmed by field studies during application to apple orchards or cereals. The studies showed some deficiencies, but anyhow, the AOEL was exceeded for 3 out of 10 operators. Based on clarifications provided in an addendum (July 2005), it was agreed by the experts that the estimated exposure exceeded the AOEL with both models, even with the use of PPE.

Worker exposure

A German re-entry model[21] was used for the calculations of worker exposure. The estimated worker exposure is 3000% of the AOEL immediately after application on pome fruits, and 83% of the AOEL after application on cereals (the second value was provided after the experts' meeting and not peer reviewed).

Bystander exposure

Bystander exposure was calculated according to a draft document of the ACT (Advisory Committee on Pesticides, meeting 10 July 2002, Bystander risk assessment).
For apple trees, the exposure is above the AOEL (464%). Regarding the cereal scenario, mean exposure estimate was significantly lower than the AOEL (27%) but the maximum exposure, as estimated by the model, was 135 % of the AOEL.
EFSA notes that the input parameters of the bystander exposure estimates are poorly described. Consequently, a refinement of the estimate or measurements of bystander exposure made in the field could be required at a Member State level.

3. Residues

Oxydemeton-methyl (ODM) was discussed at EPCO experts' meeting for residues (EPCO 34) in September 2005.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of oxydemeton-methyl has been investigated in apples, sugar beets and cabbage.
In apples the product was applied in accordance with the supported representative use, with 2 applications in early season and a PHI of 83 days. Samples were taken 30 and 63 days after the

[21] Hoenicke *et al.*, 1998. Hinweise in der Gebrauchsanleitung zum Schutz von Personen bei Nachfolgearbeiten in mit Pflanzenschutzmitteln behandelten Kulturen. Nachrichtenbl. Deut. Pflanzenschutzd. 50 (10), p 267.

second application as well as at harvest. Residues were at each sampling point mostly associated with flesh, which contained about 80 % of the Total Radioactive Residues (TRR) present in whole fruits. The extractability of residue declined with time. At harvest, 13 % of the TRR was present in juice and a further 30 % of the TRR was solvent-extractable from the remaining flesh and peels. Identification of the residues was conducted on the sample taken 63 days after the second application. Oxydemeton-methyl and metabolite M01 were present exclusively in peels, representing 1.7 and 0.2 % of the TRR. Metabolite M07 was present in both peel and flesh, accounting in total for 9.1 % of the TRR. A large fraction of the solvent-extractable radioactivity, could not be identified. The experts' meeting (EPCO 34) did not conclude on whether this was affecting the acceptability of the study.

In sugar beet leaves, at harvest 42 days after one foliar application of the compound, 4 major metabolites, M06, M12[22], M13[23] and M14[24] were identified, each present in amounts ranging from 10 to 14 % of the TRR. In minor amounts were present the parent compound, metabolite M01 and metabolites M11[25].

In cabbage, 14 days after the last of 3 applications, parent compound and metabolite M01 were present at 12 and 8 % of the TRR respectively. However this study is of low value as most of the extractable material (80 % of the TRR) was not identified.

An additional metabolism study performed with demeton-S-methyl in wheat was submitted. This study could not be used as an acceptable basis in support of the representative use in cereals as it was performed with a different active substance and with a too long PHI (60 days instead of 21 days). For cereal, a data requirement is therefore set for a new metabolism study to be carried out with the parent compound and consistently with the supported representative use.

Overall the information provided allows establishing the metabolic pathway of oxydemeton-methyl. Initial reactions are the oxidation of the sulphur in the side chain leading to M01, demethylation of the ester moieties and hydrolysis of the P-S-bond, followed by further oxidation processes. All the metabolites with the intact organophosphorous structure (M01, M06 and M07) were also observed in the rat metabolism and are therefore basically covered by the toxicological studies of the parent compound. However, as specific data on those metabolites were not submitted by the notifier, it was recommended by the experts' meeting on toxicology (EPCO 33) to consider them as toxic as the parent compound. Therefore, although this recommendation was not examined by the experts' meeting on residues (EPCO 34) due to lack of time, the residue definition for risk assessment is proposed by EFSA as the sum of parent compound, metabolite M01, metabolite M06 and metabolite M07, expressed as oxydemeton-methyl, while for monitoring, the definition can be restricted to the sum of parent compound and M01. It must be stated that these residue definitions are subject to reconsideration, depending on the outcome of the required metabolism study in cereals.

Supervised residue trials in accordance with the supported representative uses in pome fruits and cereals were submitted. These trials were conducted in the years 1990 to 1995 and their results were later reassessed, on the basis of a reconsideration of the original chromatograms. These trials suggest

[22] M12: 2-hydroxy-3-[(2-ethylsulfinyl-2-ethyl)-thio]propionic acid
[23] M13: 2-hydroxy-3-[(2-ethylsulfonyl-2-ethyl)-thio]propionic acid
[24] M14: 2-hydroxy-3-[(2-ethylsulfonyl-2-ethyl)-sulfinyl]propionic acid
[25] M11: bis-2-[(ethylsulfinyl)-ethyl]-disulfide

that residues in pome fruits and cereals are generally below the Limit of Quantification of 0.01 mg/kg, but with measurable residues between 0.01 and 0.02 mg/kg in some instances. Nevertheless, due to confusion in the way these trials were reported it is not possible to determine the exact number of individual trials and their relevance for the supported uses. Moreover, in all these trials only oxydemeton-methyl and metabolite M01 were determined and levels of metabolites M06 and M07 are unknown. Therefore a complete data set of trials supporting the uses in pome fruits and cereals is needed with analysis and expression of residues (in pome fruits, cereal grains and straw) according to residue definitions for both monitoring and risk assessment.

Storage stability studies of residues of oxydemeton-methyl and its metabolite M01 were submitted. These data show inconsistencies, with apparent decline of residue during storage for some crops. It is however not possible to determine whether this decline was due to actual degradation of the compounds or due to methodological or analytical difficulties. In addition, no information is available on the storage stability of metabolites M06 and M07. Additional information should be submitted before concluding that the submitted field residue studies are reliable.

Very limited information is available on the effect of processing on residues. Only 2 studies with apples containing measurable residue levels resulting from a treatment close to harvest indicated that residue levels in juice are similar to those in raw apples, while a reduction of the levels was observed in apple sauce. The experts' meeting (EPCO 34) considered that this limited information is sufficient as residues are generally below the LOQ of 0.01 mg/kg. However the available information is restricted to the parent compound and M01. It is therefore the opinion of the EFSA that the need for information on the effect of processing on the nature and the level of residues should be later reconsidered by Member States, on the basis of relevant information on the residue situation in raw commodities, including metabolites M06 and M07, and taking into account the particularly high toxicity of oxydemeton-methyl.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

A confined rotational crop study was conducted using kale, wheat and red beet as following crops. These crops were installed 34, 184 and 351 days after soil application of oxydemeton-methyl at a rate 3.35 kg/ha (corresponding to 5 times the total dose proposed for the representative use in grains). TRR were low in the tested crops at maturity, reaching a maximum of 0.03 mg/kg in wheat straw. Therefore it can be concluded that as a result of the rapid decline of oxydemeton-methyl in soil very low or negligible residues will be taken up by following crops. No MRL and no plant-back restriction are needed.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

The metabolism of oxydemeton-methyl has been investigated in lactating goats and laying hens.

Lactating goats received an oral dose of 7 mg/kg bw for 3 consecutive days and resulting TRR levels were the highest in kidneys (13 mg/kg) and amounted to about 4 mg/kg in milk and muscles. Unchanged parent was present in milk and all edible tissues as major component of the TRR (with amounts ranging from 23 % of the TRR in liver to 61 % of the TRR in milk). Metabolite M01 was also present in all tissues, at lower rate than the parent compound. No other compound was identified,

although the extraction rate of residue was particularly high. No sign of accumulation along the course of the study was observed, with residue levels in milk reaching a plateau at day one of the dosing period. A comprehensive metabolic pathway is not possible to establish due to the lack of information on the nature of all metabolites formed, and a comparison with rat metabolism is difficult to make.

The residue pattern in laying hens is different. After an oral exposure of 7 mg/kg bw for 3 days, TRR levels in eggs and tissues were below 1 mg/kg, except in kidneys where 1.4 mg of TRR/kg were found. Parent compound appeared as a minor component of the residues in tissues and was absent from eggs. The major metabolite found was M07 in muscles, liver and eggs. Levels increased gradually with time in eggs and a plateau level was not reached at the end of the dosing period (3 days).

The experts' meeting (EPCO 34) did not conclude on a residue definition due to lack of time. As conservative approach, considering the recommendation of the experts' meeting on toxicology (EPCO 33) and given the differences noted in the residue patterns between ruminants and poultry, the residue definition in animal products proposed by EFSA for risk assessment and monitoring is the sum of oxydemeton-methyl, metabolite M01 and metabolite M07, expressed as oxydemeton-methyl.

Livestock is potentially exposed to residues resulting from the use of oxydemeton-methyl according to the representative use through consumption of apple pomace as well as of cereal grains and straw. However the potential critical exposure of livestock to all toxicologically relevant residues is currently impossible to determine because information on their amounts present in these feed items is not available. Feeding studies conducted on laying hens and lactating cows at exposure rates of 7.5 and 1 mg oxydemeton-methyl/kg body weight/d respectively, indicate that no residues of the parent compound and its metabolite M01 above 0.01 mg/kg can be expected in animal commodities. Information on residues of metabolite M07 in animal commodities is not available. Due to the here above mentioned missing information no MRL proposal can be made for animal commodities.

3.3. CONSUMER RISK ASSESSMENT

A realistic consumer risk assessment cannot be performed at this stage as no reliable information is available on the residue levels.

Account should also be taken of the ground water metabolite M05, depending on its toxicological relevance.

3.4. PROPOSED MRLS

Due to missing information and uncertainties on the comprehensibility of the available residue data, no MRL can be proposed.

4. Environmental fate and behaviour

The fate and behaviour in the environment of oxydemeton-methyl was discussed in the experts' meeting (EPCO 31) of September 2005 on basis of the addendum to the DAR dated 31 August 2005.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

Soil experiments on 2 different soils were carried out under aerobic conditions in the laboratory (25°C 75% field capacity (FC). The formation of residues not extracted by methanol then methanol:water were a sink for the applied ethane-^{14}C-radiolabel (17-20% of the applied radiolabel (AR) after *ca*. 90 days). Mineralisation to carbon dioxide of the radiolabel accounted for 6.6-38% AR after *ca*. 90 days. In 2 further aerobic laboratory experiments on a further soil at an unreported temperature and 75% FC where both ethane-^{14}C-radiolabel and methoxy-^{14}C-radiolabels were employed the formation of residues not extracted by methanol accounted for 40%AR (ethane-^{14}C-radiolabel) after 57 days and 20% (methoxy-^{14}C-radiolabel) after 49 days (study end). Mineralisation to carbon dioxide accounted for 59%AR (ethane-^{14}C-radiolabel) after 57 days and 79%AR (methoxy-^{14}C-radiolabel) after 49 days.

In these studies and laboratory aerobic experiments carried out on a further 3 soils (20°C and 40% maximum water holding capacity (MWHC)) the breakdown products identified in soil extracts were: M01 (which is the pesticide active ingredient demeton-S-methylsulphon, max. 6.3%AR at 3 days), M05 (max. 9.5%AR at 4 days), M09[26] (max. 39%AR at 2 days), M10 (max. 26.5%AR at 365 days) all ethane-^{14}C-radiolabel experiments and DMP[27] (max. 45.8%AR at 1 day) in the methoxy-^{14}C-radiolabel experiment. The Member State experts identified that a soil exposure estimate was not available for the major soil metabolite DMP. This calculation that used standard assumptions was subsequently provided by the rapporteur Member State in the update to the addendum to B.8 of the DAR rev 2, (dated 15 March 2006).

Under dark laboratory anaerobic conditions in soil, the degradate pattern was different to that identified under aerobic conditions. Whilst M09 was present (max 32%AR at 3 days, a level comparable to the aerobic studies) the additional metabolites M02 (max. 6.2%AR at 13 days) and M22[28] (max. 22.4%AR at 13 days) were identified. It was proposed by the experts from Member States, that in territories where applied for uses might result in significant periods of anaerobic conditions in soil, national Member State assessments should consider the risk to soil organisms from exposure to M02 and M22. In a laboratory soil photolysis study the rate of degradation in irradiated samples was slower than in the dark control.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The rate of degradation of oxydemeton-methyl was estimated from the results of the studies for which a temperature was reported described in 4.1.1 above. DT_{50} were: 0.4 and 3.2 days (single first order 25°C 75%FC, 2 different soils), and <1 day (single first order 20°C 40%MWHC soil moisture 3

[26] M09: 2-ethylsulfinyl ethane sulfonic acid.
[27] DMP: dimethyl phosphate.
[28] M22: 2-ethylthio ethane sulfonic acid.

soils). After normalisation to FOCUS reference conditions[29] (20°C and -10kPa soil moisture content) this range of single first order DT_{50} (from 5 different soils) becomes 0.51-3.79 days (geometric mean that is appropriate for use in FOCUS modelling 0.76 days).

The single first order DT_{50} of the identified degradation products were calculated using the compartment models that were outlined in the addendum to B.8 of the DAR rev 2, (dated 6 September 2005) and the levels measured in the studies for which a temperature was reported described in 4.1.1 above using the ModelMaker 4.0 software. These DT_{50} were: M01 1.08 days (1 soil 25°C 75%FC, 1.28 days at FOCUS reference conditions), M05 14.1 and 31.6 days (2 soils 20°C 40%MWHC, 9.4 and 25.2 days at FOCUS reference conditions), M09 1.13-7.46 days (3 soils 20°C 40%MWHC, 1.08-4.97 days at FOCUS reference conditions) and M10 1.67-3.12 days (3 soils 20°C 40%MWHC, 1.11-2.49 days at FOCUS reference conditions).

In aerobic laboratory studies on 3 soils (20°C 39%MWHC) where M09 and M10 were applied as test substance the calculated single first order DT_{50} were 0.9-1.58 days for M09 (0.86-1.09 days at FOCUS reference conditions) and 1.62-2.0 days for M10 (1.11-1.91 days at FOCUS reference conditions). Using the compartment model that were outlined in the addendum to B.8 of the DAR rev 2, (dated 6 September 2005) and the levels measured in the study where M09 was applied as test substance using the ModelMaker 4.0 software, single first order DT_{50} calculated for M10 were 0.27-0.53 days (0.18-0.51 days at FOCUS reference conditions).

To summarise the range of values at FOCUS reference conditions were: M01, 1.28 days (1 soil); M05, 9.4 and 25.2 days (2 soils); M09, 0.86-4.97 days (3 soils, 6 experiments, geometric mean appropriate for use in FOCUS modelling 1.32 days); M10, 0.18-2.49 days (3 soils, 9 experiments, geometric mean appropriate for use in FOCUS modelling 0.92 days). The meeting of Member State experts concluded that further data on the degradation rate of M05 was necessary as single first order DT_{50} values were only available for 2 soils and there was evidence from a silt soil that the rate of degradation may be longer than indicated by the 2 available DT_{50} values (In this silt soil it was not possible to calculate a DT_{50} as M05 accounted for 7-8%AR from days 1 to 11 (study end) with no clear decline over the duration of the experiment). A data gap was therefore identified. The EFSA has not included the M05 metabolite in the definition for risk assessment to soil dwelling organisms (see section 6) as it was formed at a maximum of 9.5%AR. However the rapporteur Member State proposed this might need to be reconsidered in light of any results that may be provided in the future to close this data gap, should M05 be shown to be significantly more persistent in soil. Although only 1 DT_{50} value was available for M01, Member State experts agreed it was evident that M01 was a transient metabolite and further data on its rate of degradation was not considered necessary to complete the assessment.

[29] Using section 2.4.2 of the generic guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

Field soil dissipation studies were provided from 2 sites in California (USA). Using the residue levels of parent oxydemeton-methyl + M02 (M02 was oxidised to oxydemeton-methyl by the analytical methodology) in the 0-15cm deep soil layer, single first order DT_{50} were 1.6 and 2.2 days (oxydemeton-methyl + M02). For M01 also determined in the 0-15cm deep soil layer a DT_{50} was not calculated but no residue was determined (>0.01mg/kg) by 14 days. In a separate experiment carried out using the same soils in outdoor vessels but 3 years later where radio labelled test substance was applied, for the residues of oxydemeton-methyl, M09 and M10 measured in the 0-3cm soil layer single first order DT_{50} were 1.5-3.8 days (oxydemeton-methyl, with a single compartment model, DT_{90} 4.9-12.7 days) and 7.7 days (M09) and 4.4 days (M10) using the compartment models that were outlined in the addendum to B.8 of the DAR rev 2, (dated 6 September 2005).

The longest available field oxydemeton-methyl, M09 and M10 single first order soil DT_{50} of 3.82, 7.7 and 4.4 days respectively were used in PEC soil calculations. For M01 the laboratory derived value of 2.82 days (1.28 normalised from 20°C to 10°C assuming a Q10 of 2.2) was selected for use. For M05, DMP and the anaerobic metabolites M02 and M22 the rapporteur Member State assumed there was no degradation between applications when carrying out PEC soil calculations.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

The adsorption / desorption of oxydemeton-methyl, M09, M10, M01 and M02 was investigated in four soils in guideline batch adsorptions experiments. The amount of oxydemeton-methyl, M09, M10, M01 and M02 adsorbed to soil was too low to measure with any reliability. Based on these results the experts from Member States agreed K_{foc} value of 0 mL/g and 1/n=0.9 (default) should be used as input to groundwater modelling for these 5 compounds.

No experiments on the adsorption of the soil metabolite M05 were provided. A theoretical quantitative structure activity relationship calculation resulted in an estimated K_{foc} value of 15 mL/g. The experts from Member States agreed that in the absence of any reliable experimental data a K_{foc} value of 0 mL/g and 1/n=0.9 (default) should be used as input to groundwater modelling for M05. Results from satisfactory batch adsorption studies (not currently available) might enable a less precautionary value to be used as modelling input. However adsorption would be expected to be low.

Information on the adsorption to soil of the major soil metabolite DMP is not available. A data gap to assess the potential for DMP to leach to groundwater was therefore identified (see also section 4.2.2).

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Oxydemeton-methyl hydrolysed at 25°C under sterile conditions with single first order DT_{50} of 2.3-2.5 days (pH 9), 39.6-42.3 days (pH 7) 96.3 days, (pH 5) and 92.4 days (pH4). M06 and M21[30] (and / or its dimer M11) were the major (>10%AR) breakdown products, both being present at pH 7. At pH 9 only M21 (and / or its dimer M11) was formed whilst at pH 4/5 only M06 was formed.

The aqueous photolysis of oxydemeton-methyl investigated under sterile pH 5 conditions, was slow (single first order laboratory DT_{50} natural sunlight 38°N in April (unreported day length) was 187 days). The only major (>10%AR) metabolite formed in the study was M10. Photolysis is not expected to be a significant route of dissipation of oxydemeton-methyl in the environment as biodegradation is more rapid.

In aerobic water-sediment studies (2 systems studied at 22°C in the laboratory, sediment pH 6.7-7.7, water pH 7.9-8.9) oxydemeton-methyl (ethane-^{14}C radiolabelled test material used) demonstrated low persistence in both the water phase (single first order DT_{50} 2.3-3.4 days) and in the total system (essentially the same values as partitioning to sediment of oxydemeton methyl was low). The major metabolites in the water analysis were M11 (max. 22.3 % AR at 1 day after treatment) the dimer of M21 (the analysis method employed may have converted M21 to M11, so this residue may have been M21), M07 (max 18%AR at day 91 study end) and M09 (max. 9.9%AR at 7 days). The minor metabolites that may still contain a toxophor and are of potential concern that were also identified in water were: M01 (max. 0.9 % AR at 1-7days), M02 (max. 3.4 % AR at 7 days), M10 (max 5.1%AR at 7 days) and M06 (max. <9.4%AR at 20 days). The terminal metabolite, CO_2, accounted for only 29-31 %AR by 91 days. Residues not extracted from sediment by methanol or methanol:water were a significant sink representing 45-66%AR at study end (91 days). No extractable resolved residue in sediment accounted for more than 3.5 % AR at any sampling time (oxydemeton methyl at 1 day).

Investigations where oxydemeton-methyl was radiolabelled in the methoxy position are not available. Therefore it cannot be excluded that DMP may be a major breakdown product in aerobic aquatic systems as was observed in the available pertinent aerobic soil studies. This was therefore identified as a data gap by the experts from Member States.

The available surface water exposure assessment just considered the spray drift route of entry to surface water. The potential exposure of surface water from the soil metabolites M05, M09 and DMP via the drainage and runoff routes of entry has not been assessed in the available EU level exposure assessment. Member States should therefore carry out a surface water exposure and consequent aquatic risk assessment for M05, M09 and DMP from the runoff and drainage routes of exposure at the national level, should oxydemeton-methyl be included in Annex 1. The EFSA considers that the

[30] M21: 2-ethylsulfinyl-ethyl mercaptan

potential for drainage and runoff of parent oxydemeton-methyl and the other major soil metabolites is limited due to their relatively rapid degradation in soil.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

FOCUSPEARL 2.2.2 was used to appropriately assess the potential for groundwater contamination by oxydemeton-methyl and its aerobic soil breakdown products from some of the possible application patterns applied for as representative uses for Annex 1 listing (see the addendum to B.8 of the DAR rev 2, (dated 6 September 2005, subsequently updated 15 March 2006)). On apples (2 applications in spring, 60 and 70% crop interception assumed) were simulated. On winter cereals, an application in autumn (October-December 25% crop interception) and a second application the following spring (March-May 70% crop interception) were simulated. Acceptable simulations for two applications in the autumn on winter cereals or any applications to spring planted cereals were not available. This was therefore identified as a data gap by the rapporteur Member State. The EFSA agrees these assessments are missing.

The main properties of oxydemeton-methyl and the pertinent aerobic soil degradation used in simulations were: Arithmetic mean 20°C -10kPa single first order soil DT_{50} for oxydemeton-methyl 0.84 days, (comparable to a geometric mean value of 0.76 days, see section 4.1.2); M01, 1.09 days (actually a 25°C 70%FC value, FOCUS normalised value similar at 1.28 days); M05 25.2 days (longest value of 2, however further degradation rate information is considered necessary, see section 4.1.2 where this data gap is discussed further); M09 1.67 days (comparable to a geometric mean value of 1.32 days, see section 4.1.2) and M10 1.22 days (comparable to a geometric mean value of 0.92 days, see section 4.1.2). The kinetic formation fractions used in the simulations were parent oxydemeton-methyl to M01 0.23, parent to M10 0.1, parent to M09 0.29, parent to M05 0.09, M09 to M10 1 and M05 to M10 1. K_{foc} values of 0 mL/g, 1/n 0.9 were used as input for oxydemeton-methyl M01, M05, M09 and M10 as agreed by the experts from Member States.

The results of this modelling indicated that annual average recharge concentrations leaving the top 1m soil layer of a treated field will be below the parametric 0.1 µg/L drinking water limit for oxydemeton-methyl, M01 and M09. However these concentrations were calculated to be above this limit for M10 at 2 of the 9 FOCUS groundwater scenarios (concentrations up to 0.23 µg/L) and M05 at all of the 9 FOCUS groundwater scenarios (concentrations in the range 0.17- 2.86 µg/L). Note further data were considered necessary to finalise the leaching assessment for M05, (see sections 4.1.2, 4.1.3 and list of studies to be generated). A groundwater non relevance assessment was therefore triggered for M10 and there are clear indications that this assessment is also likely to be required for M05, though identified data gaps would need to be closed to confirm the tier of groundwater non relevance assessment that is triggered.

The data necessary to carry out a leaching assessment for the major soil metabolite DMP were not available. This was therefore identified as a data gap at the meeting of Member State experts.

If a Member State identifies that they have vulnerable groundwater aquifers that receive significant recharge from water logged anaerobic top soils and applications in the autumn are requested, the rapporteur Member State and experts from Member States identified that a leaching assessment for the minor (max 6.2%AR) anaerobic but very highly mobile soil metabolite M02 (which is the pesticide active ingredient demeton-S-methyl) is not available and should be considered in assessments for national product authorisation. The EFSA considers this combination of geoclimatic conditions in an area of crop production will occur very rarely, so considers it inappropriate for the leaching potential of M02 to be considered in the EU Annex 1 listing level groundwater exposure assessment. Member States may wish to consider this issue for M02 and the other major anaerobic soil metabolite M22 in national groundwater leaching assessments, should oxydemeton-methyl be included in Annex 1.

4.3. FATE AND BEHAVIOUR IN AIR

Volatilisation of oxydemeton-methyl from soil and wheat plants was estimated to be low (ca. 6% over 24 hours) based on experimental results in an outdoor radiolabelled study where the recovery of radioactivity was quite variable. The vapour pressure of oxydemeton-methyl ($2x10^{-3}$ Pa at 20°C) means that it would be classified under the national scheme of The Netherlands as slightly volatile, indicating some losses due to volatilisation would be expected, but losses from aqueous systems / soil water would be expected to be relatively low due to relatively high water solubility (Henry's Law constant $<4.7x10^{-7}$ $Pa.m^3.mol^{-1}$). Therefore the PECair was considered to be negligible. Calculations using the method of Atkinson for indirect photooxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half life estimated at 1.2 hours indicating the proportion of applied oxydemeton-methyl that did volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Oxydemeton-methyl was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 32) in September 2005 in York (UK).

The batches used in the studies for the section on ecotoxicology were not analytically verified regarding the impurity profile. So it is not known if these studies were performed at the maximum impurity content. Oxydemeton-methyl is not stable and is therefore often tested as a premix. The solvents in these premixes are not known. So differences in species toxicity may not only be attributed to differing species sensitivity. The purity of the active substance is not known in many cases and the stability is poor. Therefore the significance of the test result is not always clear. The EPCO Experts' meeting decided that the applicant should clarify these issues.

5.1. RISK TO TERRESTRIAL VERTEBRATES

In the original DAR the risk to birds and mammals was calculated using residue data outlined in Hoerger and Kenaga (1972). During the evaluation meeting the rapporteur Member State was requested to make a risk assessment available according to the guidance document SANCO/4145/2000 and the applicant was requested to address the acute and long term risk to birds and mammals in cereals and orchards from exposure to oxydemeton-methyl, the lead formulation and the metabolite M01. The EFSA noted some concerns about the risk assessment according to Hoerger and Kenaga (e.g. no conversion to wet weight feed uptake). As meanwhile a risk assessment according to SANCO/4145/2000 is available, no correction of the original risk assessment was considered necessary. The risk assessment according to the guidance document SANCO/4145/2000 is available in the addendum 1 of July 2005 and was the only risk assessment discussed in the EPCO expert's meeting.

Oxydemeton-methyl is intended to be used in cereals and in pome fruit. As the intended use in cereals is from an early to a late crop stage the risk was calculated for a large herbivorous and an insectivorous bird as well as a small herbivorous and insectivorous mammal in cereals. In pome fruit, the risk was calculated for an insectivorous bird and a small herbivorous mammal as foreseen in the guidance document SANCO/4145/2000.

The experts' meeting provisionally agreed on the endpoints for birds and mammals but the rapporteur Member State was requested to verify the dietary endpoint and NOEC for birds and verify the NOEC for mammals. The rapporteur Member State communicated to the EFSA in May 2006 the dietary endpoints for birds: the dietary NOEL is 56.57 mg/kg bw/day for bobwhite quail (food consumption (9 g) and mean body weight (21 g) for 132 ppm) and 119 mg/kg bw/day for the mallard (food consumption (36 g) and mean body weight (181.5 g) for 602 ppm). The EFSA proposes to take this into account when the risk to birds is revised. The conversion to daily dose of the NOEC for birds still needs to be clarified. Also the NOEC for mammals was verified by the rapporteur Member State in May 2006 and the result was communicated to the EFSA: According to the DAR a NOEL of 0.15 mg/kg bw taking into account effects on the male reproduction should be used for risk assessment instead of 0.3 mg/kg bw as was used in addendum 1. The NOEL of 0.15 mg/kg bw was also taken into account in the original risk assessment for mammals in the DAR. The EFSA proposes that this value is taken into account when the risk to mammals is revised.

The experts' meeting decided that multiple applications should be considered in the first tier risk assessment. The EFSA considers that this would not change the outcome of the first tier risk assessment considerably but considers that this should be taken into account in the further refinement steps. Furthermore the meeting decided on a lower endpoint for the short term risk to birds than the value used by the applicant. The value agreed by the meeting is based on the NOEC mortality from the dietary studies as feed avoidance was noted at the higher concentrations tested. Based on this first tier risk assessment a further refinement is necessary for the acute and long term risk of insectivorous and herbivorous birds in cereals, the short term risk for herbivorous birds in cereals and the acute, short and long term risk for insectivorous birds in orchards.

Several refinement options are proposed by the applicant. For most of the proposed options the underlying data were not made available to the rapporteur Member State at the time of the experts' meeting. Therefore the meeting requested that all relevant data should be made available and evaluated by the rapporteur Member State. All options were reviewed by the experts' meeting and will be discussed below.

The first option is a refinement of the RUD (Residue per Unit Dose) by the use of 9 residue trials. These studies were performed in cereals in order to estimate residues in short grass. The meeting accepted these residue data as the trials cover the whole of Europe, were performed at the correct growth stage and cover the intended uses. Furthermore the meeting agreed on the residue decline data which can be used to refine the MAF (Multiple Application Factor) and the f_{twa} (time weighted average factor). The EFSA noted that for the refined f_{twa} the default averaging time of 21 days was taken into account. This averaging time should not be longer than the interval between 2 applications which is only 10 days for this dossier. The EFSA proposes to take this into account when the refined risk assessment is revised. The meeting noted that an interception factor should not be used for insects as feed items as this is already taken into account in the RUD value.

As further refinement options FIR (Food Intake Rate), PD (Proportion in the Diet), PT (Proportion in the Treated area) for several focal species were proposed.

For the herbivorous birds in cereals, the bean goose, white-fronted goose and greylag goose were proposed as focal species. The meeting considered geese as a potential focal species for northern Europe. The meeting felt that there should be a thorough consideration of the dietary data and especially the range of food types consumed (e.g. did some birds consume 100% cereals while others consumed 0%). The FIR for geese was considered acceptable.

As regards the yellow wagtail, proposed for the insectivorous scenario in cereals, the meeting considered that the proposal for PD (0.764 large insects/0.236 small insects) was more or less in line with previous assessments and hence acceptable. It was decided that the FIR of 0.91 used previously in other dossiers for yellow wagtail should be used rather than 0.88. There are insufficient data to define the PT for yellow wagtail. Furthermore the meeting proposed to consider the skylark as a focal species to address the risk to insectivorous birds in cereals in northern Europe.

To address the risk to insectivorous birds in pome fruit the great tit was proposed as a first focal species. The meeting had a concern regarding the appropriateness of the available data set for PD for southern and northern Member States. There was also a question mark over the relevance of the PD data regarding the season of use of oxydemeton-methyl. Further justification of using nestling diet was required. The FIR for great tit was considered acceptable. The proposed PT of 0.48 was considered questionable as it is based on an average proportion of foraging trips.

In addition to the great tit the blackbird was proposed as a focal species to address the risk to insectivorous birds in orchards. The proposed black bird diet was considered acceptable, however further justification for northern Member States was required. The FIR for blackbird was accepted. Further evidence should be provided to support the proposed PT-value.

The applicant is requested to address the relevance of the proposed focal bird species to southern Europe. Furthermore the applicant must clarify whether the data, on which the proposed PD factors

for herbivorous birds are based, addresses the timing and duration of exposure for the representative uses under evaluation. The meeting noted that some of the data referred to are old.
The meeting had a concern in general regarding the relevance of using both PT and PD for the acute risk assessment. It was noted that it might be feasible to refine the risk assessment in line with the PPR Panel opinion for pirimicarb.
Because of the potential of reproductive effects the applicants' proposal to dismiss the long term effects was not considered acceptable.
In conclusion, a potential high risk to birds has been identified. The meeting accepted the residue data, the residue decline data, the use of a MAF and food in take values (except for yellow wagtail). Further justification of the relevance of focal bird species to southern Member States is required as well as a consideration of the skylark as a focal species in cereals in northern Member States. As regards the other refinements factors, the meeting had reservations and hence further justification is required before these can be incorporated into a refined risk assessment.

Also a potential high risk to mammals was identified in the first tier risk assessment, except for the acute risk to insectivorous mammals in cereals which can be regarded as low. Therefore refinements of the acute risk to herbivorous mammals in cereals and orchards and of the long term risk to insectivorous and herbivorous mammals in cereals and of the long term risk to herbivorous mammals in orchards are considered necessary.
As for birds, several refinement options were proposed by the notifier.
The experts' meeting noted that the woodmouse was chosen as a focal species to refine the risk to mammals in cereals and orchards. Whilst the meeting accepted the woodmouse as a focal species for the cereal scenario, a further justification for the orchard scenario was considered necessary as the presence of voles in orchards cannot be excluded. Furthermore a justification is required for the proposed FIR/bw values. It was noted that in the assessment done by the applicant, a deposition factor as well as an amendment of the RUD had been used, i.e. double counting of interception.
As for birds the meeting accepted the new residue data, the residue decline data and the use of a MAF figure. As regards the other refinement options, the meeting had reservations and hence further justification is required before these can be incorporated in a refined risk assessment.

Furthermore the toxicity of the metabolite M01 was discussed at the experts' meeting. M01 is a plant metabolite with a similar molecular structure as oxydemeton-methyl and has insecticidal activity. M01 showed a similar to slightly higher acute toxicity to rats than oxydemeton-methyl. No studies with this metabolite on birds are available. The meeting noted that if it is assumed that the exposure and toxicity of M01 would be similar as for oxydemeton-methyl then a high risk would be predicted. Therefore the meeting decided on a data gap for the applicant to further address the risk to birds and mammals from the metabolite M01.

As the logPow is below 3 the risk from secondary poisoning to birds and mammals is considered to be low.

5.2. RISK TO AQUATIC ORGANISMS

Chironomus riparius is the most sensitive aquatic organism on an acute time-scale when tested with the lead formulation Metasystox R 250 EC. Also *Daphnia magna* is very sensitive on an acute and chronic time-scale when tested with oxydemeton-methyl and the lead formulation Metasystox R 250 EC. The EC_{50} for *C. riparius* is the pivotal endpoint which drives the risk assessment.

The endpoint for fish from the study with the lead formulation Metasystox R 250 EC was wrongly quoted as being expressed in mg a.s./L in the DAR and the list of endpoints. This has been corrected in the final list of endpoints. The correct endpoint is 7.5 mg product/L or 1.88 mg a.s./L. The revised risk assessment is only available in the list of endpoints.

The EC_{50} for *C. riparius* (0.011 mg a.s/L) is at least 10 times lower than the EC_{50} for *D. magna* (0.11-0.34 mg a.s./L). In this situation the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001) states that a chronic study should be conducted with *Chironomus* sp. It could be argued that oxydemeton-methyl does not partition into the sediment in amounts above 10% 14 days after application but in this case *C. riparius* was tested as a second arthropod species and not specifically as a ground dwelling organism. Therefore the EFSA considers a chronic study on *Chironomus* sp. necessary. The need for such a study was not discussed at the EPCO Experts' meeting.

There was a concern during the EPCO meeting that in some of the studies the test concentrations were not analytically verified. It was decided that of these studies the acute studies on *D. magna* with oxydemeton-methyl 50% premix and the metabolite M02 should be repeated.

The risk to aquatic organisms was revised after the EPCO experts' meeting as the PEC values for the metabolites were revised after the experts' meeting on fate and behaviour. This revised risk assessment is only available in the list of endpoints. A high risk to aquatic organisms was identified for which risk mitigation measures such as bufferzones of 15 m in cereals and 100 m in orchards are considered necessary.

The section on fate and behaviour identified the metabolites M07, M09, M11 and M21 as major metabolites. Furthermore data is still awaited regarding the level of exposure from the potentially major aquatic metabolite DMP. The following minor metabolites that may still contain a toxophor and are of potential concern were identified: M01 and M02. Also an assessment for the minor surface water metabolites M10 and M06 might be necessary based on the outstanding data gap regarding the biological screening data for these metabolites.
M01 and M02 retain the insecticidal moiety. For both metabolites an acute toxicity study with fish and *D. magna* is available as well as a long term toxicity study with *D. magna*. No studies on *C. riparius*, the most sensitive organisms to the parent, are available. Therefore the EC_{50} for *C. riparius* of the parent was divided by 10 and compared to the PECsw for M02. The resulting TER (15 and 0.88 for cereals and orchards resp., see list of endpoints) does not meet the trigger of 100. This

calculation was not done for M01 and was not asked for during the experts' meeting as a message from the experts' meeting on fate and behaviour was received during the meeting on ecotoxicology that metabolite M01 should not be taken forward for risk assessment. Meanwhile the opinion of the section on Fate and behaviour has changed and M01 is considered as a metabolite of concern. If the same calculation would be done for M01 the resulting TER would be 44 (1.1/0.025) for the cereal use and 2.6 (1.1/0.42) for the use in orchards. If the trigger is not met the Guidance Document on Aquatic Ecotoxicology (SANCO/3268/2001) states that a toxicity test with a minor metabolite is required. Therefore the EFSA proposes that an acute toxicity study with *C. riparius* and the metabolites M01 and M02 should be provided. Based on this study also a chronic study might be required (see argumentation for the parent above). Also here it could be argued that M01 and M02 do not partition into the sediment in amounts above 10% 14 days after application but as stated above *C. riparius* was tested as a second arthropod species with the parent and not specifically as a sediment dwelling organism. Based on the available assumption for *C. riparius* a high risk was identified for M01 and M02 for both representative uses evaluated.

Acute toxicity studies with fish and *D. magna* are available for the metabolites M07, M09, M10 and M11. All endpoints are above 100 mg/L except for the EC_{50} for *D. magna* with the metabolite M11. But however M11 is less toxic to *D. magna* than the parent with an EC_{50} of 33 mg/L. Based on available studies the acute risk from M07, M09, M10 and M11 to aquatic organisms can be regarded as low for both representative uses evaluated. The experts' meeting decided that the long term risk to aquatic invertebrates of the metabolites M07, M09 and M11 needs to be addressed. This decision was taken on the basis that the long term risk from M01 is greater than the acute risk from this metabolite and there were sublethal effects observed on *D. magna* in the acute studies. The EFSA considers such a study also necessary for metabolite M10 as this is a major metabolite in groundwater.

No studies with the metabolites M21 and DMP are available. The risk from these metabolites to aquatic organisms needs to be addressed. The need for these studies was not discussed at the EPCO meeting. Furthermore also studies with the metabolite M05 are considered necessary as this metabolite occurs above 0.1 µg/L in groundwater.

Oxydemeton-methyl is not an herbicide so studies on aquatic plants are not considered necessary.

As the log Pow is below 3 for oxydemeton-methyl, no study on bioconcentration in fish is considered necessary. The Log Pow for the metabolites M07, M09, M11, M21, M01, M02 and M10 is not known. Therefore the EFSA proposes that the applicant should make these values available.

5.3. RISK TO BEES

An acute contact and oral toxicity study with the lead formulation Metasystox R EC 250 is available. The resulting HQ values breach the Annex VI trigger value indicating a high risk to bees for the representative uses evaluated.

Several field studies were submitted but they could not be validated because a detailed report was lacking, in all cases. Nevertheless they confirm the high toxicity of oxydemeton-methyl in the field.

Furthermore two aged residue studies were submitted. The summaries are available in the addendum of July 2005. In the first study bees were exposed to treated woody apple shoots and in the second study the bees were exposed to stems of *Phacelia tanacetifolia*. In the first study effects on bees were low after 24 hours of exposure if residues were aged for 48 hours or more. Effects on bees remained high, even for 10 day aged residues, if exposed for 48 hours. In the second study a low toxicity to bees was observed independent of the days of ageing or the exposure duration.
The two residue studies were discussed at the EPCO Experts' meeting and the meeting felt that these studies added little to the risk assessment. Based on the available data the meeting decided that there is a potential high risk to bees which must be managed at Member State level. The available studies were not sufficient to establish a withholding period. Application should be avoided when there are likely to be any bees in the crop.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Standard laboratory studies with *Aphidius rhopalosiphi* and *Typhlodromus pyri* are available during which a high toxicity to these standard indicator species was observed. Also in laboratory studies with *Adalia bipunctata* and *Coccinella septempunctata* a high toxicity was observed. It is noted by the EFSA that the field and drift rates, for the HQ calculations, are based on a MAF (multiple application factor) of 1 assuming that the uptake into plant leaves is rapid and no multiplication effects from multiple applications to either apple orchards or cereal crops is expected. The EFSA does not find this argumentation sufficient since no data to support the assumption of rapid uptake via the leaves is available. Therefore the EFSA proposes to take a MAF into account based on the residue decline data, used in the refined risk assessment for birds and mammals, and the interval between two applications. The outcome of the first tier risk assessment by the rapporteur Member State reveals a potential high risk in field and off-field for both representative uses and both indicator species. Only the off-field risk for *T. pyri* in cereals can be regarded as low. The outcome of this risk assessment would not have been altered if a MAF was taken into account.

A higher tier risk assessment is presented in the DAR. For this assessment HQ values were calculated based on LR_{50} values from extended laboratory studies. The EFSA does not agree with this approach as according to Escort II effects should be below 50% at the in-field and/or off-field rate in extended laboratory studies. If an HQ approach is followed, the trigger of 2 will be met if effects are below 50% at half the in-field and/or off-field rate. Furthermore, as described above the EFSA considers that a MAF should have been used. By using the HQ approach, only mortality was taken into account while according to Escort II also reproduction should be looked at in extended laboratory studies. As the EFSA does not agree to the HQ approach in the DAR, all extended laboratory, field and semi-field studies are discussed below taking into account effects on mortality and reproduction at the in-field and off-field dose rate. The risk to non-target arthropods from the a.s. oxydemeton-methyl was not discussed at the EPCO Experts' meeting.

Effects on mortality and reproduction for *A. rhopalosiphi* are far above 50% for the in-field application rate for both representative uses evaluated. Effects are also above 50% for the off-field

rate in orchards. Effects will be below 50% on mortality for the off-field rate in cereals. Effects on reproduction were 70% at 31.24 g a.s./ha, the lowest concentration tested, therefore it is not possible to say what the effects on reproduction at the off-field drift rate in cereals would be.

Also for *T. pyri*, *C. septempunctata* and *C. carnea* effects on mortality were above 50% at the in-field dose rates for both representative uses evaluated. The LR_{50} for *C. septempunctata* from the extended laboratory study is 4.3 g a.s./ha. This rate is just above the off-field rate in cereals but below the off-field rate in orchards. This is also the case for *C. carnea* with an LR_{50} of 13.4 g a.s./ha. For *T. pyri* effects on mortality are below 50% at the off-field rates for both cereals and orchards. For *T. pyri* a 28% and 89% reduction of reproduction was observed at 150 and 300 g/ha respectively. So reproductive effects are above 50% at the in-field rate in orchards but effects are below 50% at the off-field rate in orchards and the in-field and off-field rate in cereals. Effects on reproduction were not assessed for *C. septempunctata* and *C. carnea* as the larval stages were tested for these species.

For *P. cupreus* a 6% effect on mortality and a 33% decrease on feeding activity was observed in a semi-field study at 300 g a.s./ha. This dose rate covers the in-field dose rate in cereals but not in orchards although it is higher than the off-field dose rate in orchards.

Also a semi-field study with *Trichogramma dendrolini* in apple trees is available. The first 2 days after exposure the group treated with 0.1% Metasystox R 250 EC parasitized less host eggs than the control group.

Only an aged residue study with the larval stage of *C. septempunctata* is available. Pre-imaginal mortality was 54% when exposed to 2 days aged residues of 375 g a.s./ha and the corrected mortality was -3% and 26% when exposed to 8 and 10 days old residues respectively.

Furthermore a semi-field study on carabid beetles is available. In this study Metasystox R 250 EC was applied four times at 125 g a.s./ha, i.e. a lower application rate than the representative use in orchards as the application rate per treatment is 375 g a.s./ha (2 applications). In this study an effect of 30% was seen on web spiders for up to 10 days while no effects were observed on rove beetles and slight effects on other invertebrate species.

Finally also 2 field studies are available. One of them is a report on a mite-management program which does not provide much information for this risk assessment. The second study investigated the effects of Metasystox R 250 EC, applied once at 200 g a.s./ha, on *C. septempunctata*. The EFSA noted that this study is a published article in which no exact values are reported (in contrary to the impression which is given in the summary in the DAR in which a table is reported. In the article itself this table is not attributed to a specific insecticide). Furthermore the treated plots were only monitored for 22 days. The conclusion in the DAR that the number of ladybirds in the treated plots was only slightly lower than in the control plots at day 15 after treatment but with a clear tendency for recovery was made based on figure 4 in the original study report. In figure 1 of the original article it can be seen that the number of ladybirds in the treated plots is far below the number observed in the control plots and no tendency for recovery can be observed. The number of beetles observed in the treated and control plots, differs a lot between Figure 1 and 4. In the text of the article it is mentioned that *C. septempunctata* disappeared, and it was only d-14 after application that larvae could be found, although not more than 2 in average of all replications. The discrepancy between figure 1 and 4 can be explained by the fact that these are results from 2 different years. The EFSA considers that the

results from this article should be used very carefully. The author of the article attributes the disappearance of *C. septempunctata* to the lack of food and not directly as an effect of the insecticide. The EFSA is not convinced that this is the only reason. Given the high toxicity observed in the laboratory data for *C. septempunctata* it is questionable that the disappearance of *C. septempunctata* is only due to lack of food.

In the DAR it is stated that the risk to non-target arthropods from oxydemeton-methyl can be regarded as low. This statement is based on the aged residue studies with *T. dendrolini* and *C. septempunctata* and the field study with *C. septempunctata*. According to the EFSA the study with *T. dendrolini* is not an aged residue study but does show that effects on parasitation were short-lived. The tested concentration in the aged residue study on *C. septempunctata* was too low for the use in orchards. Furthermore given the high toxicity to *C. septempunctata*, this study still leaves some questions open about the recovery/recolonisation after the second application and furthermore only the larval stage was tested. The field study on *C. septempunctata* is not considered sufficient by the EFSA to answer these questions (see above) in the contrary it indicates that time needed for recovery/recolonisation might be much higher. The available semi-field study only gives an idea about rove beetles and web spiders. *C. septempunctata* was not observed in this study. In conclusion the EFSA is of the opinion that further data is needed to address the risk to non-target arthropods for both uses evaluated. The risk to non-target arthropods from the a.s. oxydemeton-methyl was not discussed at the EPCO Experts' meeting.

From extended laboratory studies on *A. rhopalosiphi* and *T. pyri*, M01 appeared to be as toxic as oxydemeton-methyl. A reasoned case regarding the risk from this metabolite was presented in addendum 1. This was discussed at the EPCO meeting. The meeting agreed that non-target arthropods would not be exposed to M01 as non-target arthropods do not eat the plant. It was also considered that as there were semi-field studies these would have assessed any potential exposure to M01.

5.5. RISK TO EARTHWORMS

A study on the acute toxicity of oxydemeton-methyl and the lead formulation Metasystox R 250 EC to earthworms is available. The endpoints were not corrected as the logPow is below 2. The risk assessment was revised as the PEC_{soil} values changed during the EPCO meeting. This revised risk assessment is only available in the list of endpoints. Based on this risk assessment the acute risk to earthworms from oxydemeton-methyl for both the representative uses can be regarded as low.

The DT_{90} for oxydemeton-methyl in field soil dissipation studies was up to 12 days (20°C laboratory value up to 16 days) and the maximum number of applications equals 2. Therefore no chronic study on earthworms is required according to the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002). However a chronic toxicity study with the formulation Metasystox R SL100 Blau is available and therefore a chronic risk assessment was performed. This resulted in a high long term risk to earthworms for both the representative uses evaluated. To address this risk a field study with the lead formulation Metasystox R 250 EC was submitted. During this study Metasystox R 250

EC was applied twice with an interval of 12 weeks at 250 and 1000 g a.s./ha to an old pasture. No effects on tanylobous and epilobous species were observed except for the epilobous species at the highest treatment rate one year after application. This effect was regarded as not biological significant as no effects were observed during previous samplings. Based on this risk assessment also the long term risk to earthworms from both the representative uses of oxydemeton-methyl can be regarded as low.

The metabolites M09, M10 and DMP are regarded as major metabolites in the section on fate and behaviour. Furthermore it is considered necessary that an ecotoxicological risk assessment is performed for the minor metabolite M01 as this metabolite is regarded as a metabolite of concern by the section on fate and behaviour due to its insecticidal properties.
The EFSA considers it not necessary to perform a risk assessment for the metabolite M05 as it is not a major metabolite and does not contain the active moiety anymore. This is confirmed by the available acute toxicity study with M05 on earthworms during which no toxicity was observed. The need for the assessment of the risk to earthworms from M05 might need to be revised after evaluation of the outstanding data on the persistence of this metabolite in the section on fate and behaviour.
Furthermore acute toxicity studies on earthworms with the metabolites M09 and M10 are available. On the basis of these studies the acute risk to earthworms from these metabolites can be regarded as low for both the representative uses evaluated. The maximum DT_{90} values in the laboratory for M09 and M10 are 24.8 and 10.4 days respectively and the maximum number of applications equals 2. Therefore no long term risk assessment is considered necessary for these metabolites.
It was agreed in the EPCO experts' meeting that the metabolite M01 would have been present during the earthworm field study discussed above as it forms very quickly. Therefore the risk from this metabolite is considered addressed.
No studies with DMP are available. The EPCO experts' meeting decided that the applicant should address the risk to earthworms from this metabolite as it is not clear if DMP would have been present during the earthworm field study or in the laboratory studies.
The Log Pow for the metabolites M09, M01, M10 and DMP is not known. Therefore the EFSA proposes that the applicant should make these values available.
It was proposed by the experts from Member States in the experts' meeting on fate and behaviour, that in territories where applied for uses might result in significant periods of anaerobic conditions in soil, national Member State assessments should consider the risk to soil organisms from exposure to M02 and M22.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

The DT_{90} for oxydemeton-methyl in field soil dissipation studies was up to 12 days (20°C laboratory value up to 16 days) and the maximum number of applications equals 2. Therefore no studies on the effects of oxydemeton-methyl on other soil non-target macro-organisms were considered necessary and hence the risk is considered to be low.

Also the DT_{90} for the metabolites M01, M09 and M10 is below 100 days. Therefore no studies on the effects of these metabolites on other soil non-target macro-organisms were considered necessary and hence the risk is considered to be low. This was agreed by the EPCO experts' meeting.
The EFSA considers it not necessary to perform a risk assessment for the metabolite M05 as it is not a major metabolite and does not contain the active moiety anymore. The need for the assessment of the risk to soil macro-organisms from M05 might need to be revised after evaluation of the outstanding data on the persistence of this metabolite in the section on fate and behaviour.
The DT_{90} of the metabolite DMP is not known. In the section on fate and behaviour no degradation of this metabolite is assumed to calculate the PEC_{soil}. If it is assumed that this metabolite does not degradate than consequently also the risk to soil-macro-organisms from DMP needs to be addressed.
It was proposed by the experts from Member States in the experts' meeting on fate and behaviour, that in territories where applied for uses might result in significant periods of anaerobic conditions in soil, national Member State assessments should consider the risk to soil organisms from exposure to M02 and M22.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of oxydemeton-methyl were tested on soil microbial respiration and nitrogen transformation. No deviations of more than 25% after 28 days were observed at up to 5 kg a.s./ha for nitrogen transformation and 6 kg a.s./ha for carbon mineralization (i.e. no breaching of the Annex VI trigger value). These dose rates are higher than the dose rates of the representative uses and hence the risk to soil non-target micro-organisms from oxydemeton-methyl is considered to be low for the representative uses evaluated.

The metabolites M09, M10 and DMP are regarded as major metabolites in the section on fate and behaviour. Furthermore it is considered necessary that an ecotoxicological risk assessment is performed for the minor metabolite M01 as this metabolite is regarded as a metabolite of concern by the section on fate and behaviour due to its insecticidal properties.
The EFSA considers it not necessary to perform a risk assessment for the metabolite M05 as it is not a major metabolite and does not contain the active moiety anymore. The EPCO meeting regarded the risk from this metabolite as addressed.
A study on soil microbial respiration and nitrogen transformation for the metabolites M09 and M10 is available. The final reports of the studies with M09 and M10 on soil microbial processes still need to be submitted. Effects of M09 on soil nitrogen transformation were below 25% at 150 mg/kg soil and effects on carbon mineralization were below 25% at 1.9 mg/kg soil. The risk to soil micro-organisms from M09 is regarded to be low as the tested dose rates are above the PEC_{soil} for M09 (pending on the submission of the final report on the effects on soil microbial processes). No effects of M10 on microbial respiration were observed at 2.05 mg/kg soil. In the study on the effects of M10 on nitrogen transformation an increase of 29% after 28 days was observed at the lowest concentration tested of 30 mg/kg soil. Effects were below 25% at the higher application rate of 150 mg/kg soil. Therefore the risk to soil micro-organisms from the metabolite M10 is regarded as low (pending on the submission of the final report on the effects on soil microbial processes).

No studies with the metabolite M01 are available. It was agreed in the EPCO meeting that the metabolite M01 would have been present during the studies on soil micro-organisms with the parent as it forms very quickly. Therefore the risk from this metabolite is considered addressed.
No studies with DMP are available. The EPCO meeting decided that the applicant should address the risk posed to soil micro-organisms by the soil metabolite DMP.
It was proposed by the experts from Member States in the experts' meeting on fate and behaviour, that in territories where applied for uses might result in significant periods of anaerobic conditions in soil, national Member State assessments should consider the risk to soil organisms from exposure to M02 and M22.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

To address this Annex point a study on the biological activity of oxydemeton-methyl and metabolites M01, M02, M07, M09 and M10 on 5 insect species and one nematode species was submitted. The results show that oxydemeton-methyl and M01, M02 are all insecticides with comparable activity. M09 showed no insecticidal activity.
At the highest concentration tested a comparable activity (less than 50% difference to the parent) was observed against *Spodoptera frugiperda* for M07 and *Meloidogyne incognita* for M07 and M10. According to the EFSA it is not possible to compare the tested concentrations to the application rates of the representative uses as only test concentrations in ppm are available. Therefore the EFSA considers it necessary that the relevance of the tested concentrations is further clarified for the metabolites M07 and M10. Metabolite M07 has a similar structure as metabolite M06 so the biological screening data for M07 could be used to assess the biological activity of M06.

A study on the effects of oxydemeton-methyl on non-target plants was still awaited during the EPCO meeting.

Biological screening data for the ground water metabolites M05 and DMP is considered necessary. The need for these studies was not discussed at the EPCO meeting.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

The EC_{50} (3h) of bacteria in a domestic sewage sludge is 5000 mg a.s./L. Based on this study the risk to biological methods of sewage treatment is considered to be low.

6. Residue definitions

Soil

Definitions for risk assessment: oxydemeton-methyl, M01[31], M09[32], M10[33] and DMP[34]

[31] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate. . Pesticide common name:demeton-S-methylsulphon
[32] M09: 2-ethylsulfinyl ethane sulfonic acid.
[33] M10: 2-ethylsulfonyl ethane sulfonic acid.

Under anaerobic conditions, (pertinent for autumn applications to cereals in some regions): M02[35], M22[36].
Definitions for monitoring: Outstanding ecotoxicology data needs to be provided before the definition can be finalised.

Water

Ground water
Definitions for exposure assessment: oxydemeton-methyl, M01, M05[37], M09, M10 and DMP
Definitions for monitoring: Outstanding mammalian toxicology and ecotoxicology data needs to be provided before the definition can be finalised.

Surface water
Definitions for risk assessment:
surface water: oxydemeton-methyl, M01, M02, M06[38], M07[39], M09, M10, M11[40], M21[41] and DMP
Via drainage and runoff, (Member State level risk assessment) M05
sediment: none
Definitions for monitoring: Outstanding mammalian toxicology and ecotoxicology data needs to be provided before the definition can be finalised.

Air
Definitions for risk assessment: oxydemeton-methyl
Definitions for monitoring: oxydemeton-methyl

Food of plant origin
Definitions for risk assessment: Sum of oxydemeton-methyl, M01, M06 and M07, expressed as oxydemeton-methyl (subject to reconsideration depending on the results of the required metabolism study in cereals)
Definitions for monitoring: Sum of oxydemeton-methyl and M01, expressed as oxydemeton-methyl (subject to reconsideration depending on the results of the required metabolism study in cereals)

Food of animal origin
Definitions for risk assessment: Sum of oxydemeton-methyl, M01 and M07, expressed as oxydemeton-methyl

[34] DMP: dimethyl phosphate.
[35] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate. Pesticide common name: demeton-S-methyl.
[36] M22: 2-ethylthio ethane sulfonic acid.
[37] M05: 1-(ethylsulfonyl)-2-(methylsulfonyl) ethane.
[38] M06: O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate.
[39] M07: O-methyl-S-[2(ethylsulfonyl)ethyl] phoshorothioate.
[40] M11: bis-2-[(ethylsulfinyl)-ethyl]disulfide
[41] M21: 2-ethylsulfinyl-ethyl mercaptan

Definitions for monitoring: Sum of oxydemeton-methyl, M01 and M07, expressed as oxydemeton-methyl

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)*	Persistence	Ecotoxicology
Oxydemeton-methyl	Very low to low persistence ($DT_{50\ lab}$ = 0.5-3.8 d, 20°C, -10kPaWHC); ($DT_{50\ field}$ = 1.5-3.8 d.)	See 5.5, 5.6 and 5.7.
M01	low persistence ($DT_{50\ lab}$ = 1.3 d, 20°C, -10kPaWHC)	Not relevant.
M09	Very low to low persistence ($DT_{50\ lab}$ = 0.9-5 d, 20°C, -10kPaWHC); ($DT_{50\ field}$ = 7.7 d.)	Not relevant.
M10	Very low to low persistence ($DT_{50\ lab}$ = 0.2-2.5 d, 20°C, -10kPaWHC); ($DT_{50\ field}$ = 4.4 d.)	Not relevant.
DMP	No data available, PEC calculated assuming no degradation.	No conclusion possible due to outstanding data gap.
M02 anaerobic conditions	No DT_{50} data available.	No data available.
M22 anaerobic conditions	No DT_{50} data available.	No data available.

* For explanation of codes see appendix 3.

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
Oxydemeton-methyl	Very high, adsorption too low to reliably measure in batch studies	No, but not all representative uses were simulated (data gap)	Yes	Yes	See 5.2
M01	Very high, adsorption too low to reliably measure in batch studies	No, but not all representative uses were simulated (data gap)	Yes	Yes, as toxic as the parent.	No assessment necessary based on the available groundwater modelling.
M05	Very high based on QSAR[42] calculations, No experimental data available	Yes, data gap concentrations are probably even higher than those currently presented as a longer DT_{50} may be appropriate in available simulations, current values at 6/9 scenarios already >0.75µg/L (up to 2.86 µg/L) at remaining 3 scenarios >0.1µg/L	No conclusion possible due to outstanding data gap.	No data available, data gap.	No conclusion possible due to outstanding data gap.

[42] Quantitative structure activity relationship.

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
M09	Very high, adsorption too low to reliably measure in batch studies	No, but not all representative uses were simulated (data gap)	No assessment necessary based on the available groundwater modelling. No data available.	No assessment necessary based on the available groundwater modelling. No data available.	No assessment necessary based on the available groundwater modelling.
M10	Very high, adsorption too low to reliably measure in batch studies	Yes in at least 2 scenarios however all possible application patterns are not yet simulated (data gap) currently the 2 values are in the 0.1-0.75µg/L range(up to 0.23 µg/L)	No conclusion possible due to outstanding data gap.	No data available, data gap.	No conclusion possible due to outstanding data gap.
DMP	No information available	Data gap.	No conclusion possible due to outstanding data gap.	No data available.	No conclusion possible due to outstanding data gap.

* For explanation of codes see appendix 3.

Surface water and sediment

Compound (name and/or code)*	Ecotoxicology
Oxydemeton-methyl	See 5.2
M01	Relevant as M01 has insecticidal activity and based on the available risk assessment for *C. riparius*.
M02	Relevant as M02 has insecticidal activity and poses a comparable risk to aquatic organisms than the parent.
M06	No conclusion possible due to outstanding data gap.
M07	No conclusion possible due to outstanding data gap.
M09	No conclusion possible due to outstanding data gap.
M10	No conclusion possible due to outstanding data gap.
M11	No conclusion possible due to outstanding data gap.
M21	No conclusion possible due to outstanding data gap.
DMP	No conclusion possible due to outstanding data gap.

* For explanation of codes see appendix 3.

Air

Compound (name and/or code)	Toxicology
Oxydemeton-methyl	Toxic by inhalation: LC_{50} (4 h) 0.471 mg/L, 21-day NOAEL 0.00066 mg/L/day

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- Spectra for the relevant impurities in the formulation (data gap identified by rapporteur Member State in the DAR and confirmed by experts' meeting EPCO 35, September 2005; submitted but not evaluated; refer to chapter 1).
- Storage stability study where the relevant impurities in the formulation are analysed for both before and after storage (data requirement identified by the experts' meeting EPCO 35, September 2005; date of submission unknown; refer to chapter 1)
- Data for surface tension at 25 ºC and viscosity at 40 ºC for the undiluted formulation (data requirement identified by the experts' meeting EPCO 35, September 2005; date of submission unknown; refer to chapter 1).
- Method validation data for all impurities in the technical material. If the methods can not be validated then new methods and new 5 batch data will be required (date of submission 31st May 2006, data requirement identified by the rapporteur Member State in the DAR and confirmed by the experts' meeting EPCO 35, September 2005; refer to chapter 1).
- Data to confirm the identity of the impurities revealed by the chemical analysis must be provided to address the requirement of the Directive on the specificity of the methods (data requirement identified by EFSA and confirmed by the evaluation meeting May 2005 and the experts' meeting EPCO 35, September 2005; date of submission unknown; refer to chapter 1).
- Validated method of analysis for the relevant impurities in the formulation (data requirement identified by the experts' meeting EPCO 35; date of submission unknown; September 2005; refer to chapter 1)
- Method of analysis for tissues as the active substance is classified as toxic (data requirement identified by the experts' meeting EPCO 35, September 2005; date of submission unknown; refer to chapter 1).
- Confirmation that the degree of purity of the administered concentrate (pure or 50%) was taken into account in the calculations of the NOAELs in the toxicological studies (particularly in the 90-day rat studies) (data requirement identified by the experts' meeting EPCO 33, September 2005; data of submission unknown; refer to point 2.3).
- Assessment of the toxicological relevance of the groundwater metabolites M05 and M10, pending on the outcome of the FOCUS modelling (data gap identified after the experts' meeting; date of submission unknown; refer to point 2.8).
- A metabolism study in cereals to be conducted in accordance with the supported representative use (relevant for the representative use in cereals; study report submitted in 2006, but not evaluated; refer to point 3.1.1).
- Supervised residue trials in pome fruits and cereals, with analysis of residues according to the residue definition for risk assessment, in all plant parts relevant for human and animal consumption (relevant for all representative uses, data gap resulting from the residue definition proposed for risk assessment by the experts meeting; no submission date proposed; refer to point 3.1.1).

- Storage stability studies, in order to determine the stability of residual compounds according to the residue definition for risk assessment (relevant for all representative uses, data gap resulting from the residue definition proposed for risk assessment by the experts meeting; no submission date proposed; refer to point 3.1.1).
- Data on the rate of degradation of metabolite M05 (1-(ethylsulfonyl)-2(methylsulfonyl) ethane) under aerobic conditions in at least 1 further soil (required to support all uses, data gap identified by the experts' meeting EPCO 31 September 2005; date of submission unknown; refer to point 4.1.2).
- FOCUS groundwater modelling is required for the soil metabolite M05 (1-(ethylsulfonyl)-2(methylsulfonyl) ethane) taking into account the results of the rate of degradation for this metabolite that may be provided as a consequence of the data gap above, a Kfoc of 0mL/g should be used as input unless results from guideline batch adsorption experiments indicate a higher value could be justified (necessary to support all uses, data gap identified by the experts' meeting EPCO 31, September 2005; date of submission unknown; refer to points 4.1.3 and 4.2.2).
- The potential for groundwater exposure from the major soil metabolite DMP (dimethyl phosphate) must be assessed and consequently, if triggered, its relevance may need to be assessed (required to support all uses, data gap identified by the experts' meeting EPCO 31, September 2005; date of submission unknown; refer to point 4.2.2).
- The level of exposure to aquatic systems from the potentially major aquatic metabolite DMP (dimethyl phosphate) must be addressed (required to support all uses, data gap identified by the experts' meeting EPCO 31, September 2005; date of submission unknown; refer to point 4.2.1).
- FOCUS groundwater modelling is required for oxydemeton-methyl, M01 (S-[2-(ethylsulfonyl)ethyl]O,O-dimethylphosphorothioate), M09 (2-ethylsulfinyl ethane sulfonic acid) and M10 (2-ethylsulfonyl ethane sulfonic acid) for a use pattern of 2 autumn applications to winter cereals, or 2 spring applications to both spring and winter cereals. Necessary to support uses on winter and spring cereals when short application intervals are employed, data gap identified by the rapporteur Member State in the addendum to B.8 rev. 2 dated 6 September 2005; date of submission unknown; refer to point 4.2.2).
- A clarification is required whether or not the test material used in the section on ecotoxicology covers the specification of the technical material regarding the impurities and a clarification is required of the composition of the tested premix products (relevant for all representative uses evaluated; data submitted end of March 2006, not evaluated; refer to point 5).
- The relevance of the focal bird species to Southern Europe needs to be addressed (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.1).
- The relevance of the sky lark as a focal species in cereals in northern Member States should be considered (relevant for use in cereals; statement submitted by applicant in March 2006, not evaluated; refer to point 5.1).

- A clarification is needed whether the data on which proportion of diet (PD) for herbivorous birds is based addresses the time and duration of exposure (relevant for use in cereals; statement submitted by applicant in March 2006, not evaluated; refer to point 5.1).
- A further justification for the choice of focal species, PT and PD to refine the risk assessment for birds and mammals should be provided. All data relied upon should be made available (relevant for all representative uses evaluated; data and statement submitted by applicant in October 2005 and March 2006, not evaluated; refer to point 5.1).
- A justification for the woodmouse as a focal species in orchards should be provided (relevant for use in orchards; statement submitted by applicant in March 2006, not evaluated; refer to point 5.1).
- Data to support the refined Fir/bw values for mammals should be submitted (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.1).
- The risk to birds and mammals from the metabolite M01 should be further addressed (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.1).
- A chronic study with oxydemeton-methyl on *Chironomus* sp. (relevant for all representative uses evaluated; proposed by the EFSA; date of submission not known; refer to point 5.2).
- The LogPow values for the metabolites M07, M09, M11, M21, M01, M02, M10 and DMP (relevant for all representative uses evaluated; proposed by the EFSA; date of submission not known; refer to point 5.2 and 5.5).
- A new study with *Daphnia magna* for oxydemeton-methyl 50% premix and the metabolite M02 with measured test concentrations (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.2).
- An acute toxicity study with *Chironomus riparius* with the metabolites M01 and M02 (relevant for all representative uses evaluated; proposed by the EFSA; date of submission not known; refer to point 5.2).
- The long term risk to aquatic invertebrates posed by the metabolites M07, M09 and M011 needs to be addressed (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.2).
- The long term risk to aquatic invertebrates posed by the metabolite M10 needs to be addressed. (relevant for all representative uses evaluated; proposed by the EFSA; date of submission not known; refer to point 5.2).
- The risk to aquatic organisms from the metabolites M05, M21 and DMP needs to be addressed. (relevant for all representative uses evaluated; proposed by the EFSA; date of submission not known; refer to point 5.2).
- The risk to non-target arthropods needs to be further addressed (relevant for all representative uses evaluated; proposed by the EFSA, not peer reviewed; date of submission not known; refer to point 5.4).

- The risk posed to earthworms by the soil metabolite DMP needs to be addressed (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.5).
- The risk posed to soil macro-organisms by the soil metabolite DMP needs to be addressed (relevant for all representative uses evaluated; proposed by the EFSA, not peer reviewed; date of submission unknown; refer to point 5.6).
- The final reports on the effects of the metabolites M09 and M10 on soil microbial processes (relevant for all representative uses evaluated; studies submitted to the RMS, not evaluated; refer to point 5.7).
- The risk posed to soil micro-organisms by the soil metabolite DMP needs to be addressed (relevant for all representative uses evaluated; statement submitted by applicant in March 2006, not evaluated; refer to point 5.7).
- Data to address the risk to plants (relevant for all representative uses evaluated; study submitted, not evaluated; refer to point 5.8).
- Biological screening data for the ground water metabolites M05 and DMP (relevant for all representative uses evaluated; proposed by the EFSA, not peer reviewed; date of submission unknown; refer to point 5.8).
- The relevance of the tested concentrations in comparison to the application rates of the representative uses for the biological screening data for the metabolites M07 and M10 needs to be clarified. (relevant for all representative uses evaluated; proposed by the EFSA, not peer reviewed; date of submission unknown; refer to point 5.8).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as an insecticide as proposed by the applicant which comprises application by orchard air-blast sprayers and by tractor mounted hydraulic sprayers to control aphids in pome fruit and cereals (excluding oats). The maximum total dose for cereals is 0.25 kg oxydemeton-methyl (ODM) per hectare and for pome fruit it is 0.75 kg ODM per hectare.

The representative formulated product for the evaluation was Metasystox 250 EC, an emulsifiable concentrate (EC).

Adequate methods are available to monitor all compounds given in the respective residue definition. Residues in pome fruit can be analysed with a multi-method (The German S16 method has been validated). For the other matrices only single methods are available to determine residues of oxydemeton -methyl.

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.

Oxydemeton-methyl is toxic if swallowed, in contact with skin and by inhalation. It is irritating to eyes and may cause sensitisation by skin contact. The main acute, short-term or long-term toxic effect is an inhibition of blood and brain cholinesterase activities in all tested mammalian species. Another target organ in rodents is the epididymis, but the mode of action is not fully understood and the relevance for humans is unknown. Oxydemeton-methyl is not teratogenic, not oncogenic in rodents, and shows no evidence of delayed neurotoxicity (in hens). The compound has clear mutagenic and clastogenic properties *in vitro* but has no genotoxic potential *in vivo*.

The agreed Acceptable Daily Intake (ADI) is 0.0003 mg/kg bw/day, the agreed Acceptable Operator Exposure Level (AOEL) 0.001 mg/kg bw/day, and the agreed Acute Reference Dose (ARfD) 0.0015 mg/kg bw/day, with the use of a safety factor of 100. The estimated and measured operator exposures are higher than the AOEL for the use on pome fruits and cereals (>70 times the AOEL without PPE in the German model), even with the use of personal protective equipment (>3 times the AOEL in the German model). The worker and bystander exposures exceed the AOEL in the pome fruit scenario.

The metabolism of oxydemeton-methyl has been investigated in apples. Initial reactions are the oxidation of the sulphur in the side chain leading to M01, demethylation of the ester moieties and hydrolysis of the P-S-bond, followed by further oxidation processes. metabolites M01 and M07 have to be considered due to their structural profile as cholinesterase inhibitors. In metabolism studies performed on other crops, another metabolite with the intact organophosphorous structure was identified (metabolite M06). As the metabolic pattern in plant commodities at harvest indicates that metabolites may contribute significantly to the toxicological burden, the residue definition for risk assessment in plant products is proposed to include the parent compound plus metabolites M01, M06 and M07, to allow a reliable assessment of the safety of the consumer to be conducted. The residue definition for monitoring can be restricted to the parent compound and M01, as indicator compounds. A metabolism study on cereals is required for confirmation of the validity of these residue definitions for this crop group.

The conducted supervised residue trials analysed only the parent compound and its metabolite M01and due to deficiencies are not appropriate for MRL setting. A complete data base of supervised residue trials should be submitted with analysis of residues according to the residue definition for risk assessment.

The provided information on processed commodities is very limited and suggests that residues are transferred to apple juice and sauce. However the information is restricted to the levels of the parent compound and metabolite M01, and no balance studies are provided. The need for further information in particular on the effect of processing on the nature of the residues should be examined at Member State level, given the high toxicity of oxydemeton-methyl, and considering the results of the required residue trials.

No residues are expected in following crops and no plant-back interval is needed.

The animal metabolism was investigated in ruminants and poultry, and different metabolic patterns are observed. In ruminants the major constituents of the residues are the parent compound and metabolite M01, while metabolite M07 is clearly the dominant compound in poultry tissues and eggs.

The residue definitions for monitoring and risk assessment in animal commodities are proposed to include the parent compound, metabolite M01 and metabolite M07 in a conservative approach. No MRL proposal for animal commodities can be made given the lack of information on the actual level of exposure of animals to toxicologically relevant compound.
A reliable consumer risk assessment could not be performed at this stage as no reliable information is available on the residue levels in plant commodities.

With the exception of the groundwater exposure assessment and the aquatic exposure assessment for the potential aquatic metabolite DMP, the available information on the fate and behaviour of oxydemeton-methyl in the environment is considered sufficient to complete an appropriate EU level environmental exposure assessment for the applied for uses. Further assessments for metabolites that may be formed in soil under anaerobic conditions have been identified as lacking for autumn applications, in territories where water logged soils may occur. The experts from Member States proposed it would be appropriate for such assessments to be completed when Member States assess product authorisations at the national level, should oxydemeton-methyl be included in Annex 1. The available surface water exposure assessment just considered the spray drift route of entry to surface water. The potential exposure of surface water with the soil metabolites M05, M09 and DMP has not been assessed in the available EU level exposure assessment. Member States should therefore carry out a surface water exposure and consequent aquatic risk assessment for M05, M09 and DMP from the runoff and drainage routes of exposure to surface water at the national level, should oxydemeton-methyl be included in Annex 1. The potential for groundwater exposure could not be concluded. Appropriate FOCUS groundwater modelling is available for oxydemeton-methyl and its soil metabolites: M01, M09 and M10 for some of the potential applied for representative uses on cereals and the use on apples. Modelling was also available for the soil metabolite M05 but data gaps were identified for further substance properties for this metabolite. Consequently the groundwater exposure estimates available for M05 discussed in this conclusion are preliminary. Based on the groundwater modelling results annual average recharge concentrations leaving the top 1m soil column (that do not cover all the possible applied for representative uses on cereals) were < 0.1µg/L for oxydemeton-methyl, M01 and M09 at all 9 FOCUS groundwater scenarios. For 2 of the 9 scenarios concentrations of M10 were predicted to be >0.1 µg/L (up to 0.23 µg/L). Using the available results for M05 that may underestimate leaching potential, the annual average recharge concentrations were >0.1 µg/L at all 9 FOCUS groundwater scenarios. (Preliminary values ranged from 0.17-2.86µg/L). Therefore non relevance assessments were triggered for M05 and M10. Groundwater modelling is not available for the applied for representative uses of 2 autumn applications to winter cereals, or 2 spring applications to both spring and winter cereals. Information is not available to assess the potential for groundwater exposure from the identified major soil metabolite DMP.

A clarification is needed whether or not the test material used in the section on ecotoxicology covers the specification of the technical material regarding the impurities and furthermore the composition of the tested premix products needs to be clarified.

A potential high risk to birds was identified. The experts' meeting accepted the residue data, the residue decline data, the use of a MAF and food in take values (except for yellow wagtail). Further justification of the relevance of focal bird species to southern Member States is required as well as a consideration of the skylark as a focal species in cereals in northern Member States. As regards the other refinements factors, the meeting had reservations and hence further justification is required before these can be incorporated into a refined risk assessment. A PD of 0.764 large insects/0.236 small insects was accepted for yellow wagtail.
Also a potential high risk to mammals was identified. As for birds the meeting accepted the new residue data, the residue decline data and the use of a MAF figure. As regards the other refinement options, the meeting had reservations and hence further justification is required before these can be incorporated in a refined risk assessment.
Furthermore, the risk to birds and mammals from the metabolite M01 needs to be addressed.

Chironomus riparius is the most sensitive aquatic organisms on an acute time-scale when tested with the lead formulation Metasystox R 250 EC. As the EC_{50} for this species is at least 10 times lower than the EC_{50} for *D. magna*, the EFSA considers a chronic study on *Chironomus* sp. necessary. A high risk to aquatic organisms from oxydemeton-methyl was identified for which risk mitigation measures such as bufferzones of 15 m in cereals and 100 m in orchards are considered necessary. The acute studies on *D. magna* with oxydemeton-methyl 50% premix and the metabolite M02 should be repeated as the test concentrations were not analytically verified.
Based on the available assumption for *C. riparius* a high risk was identified for M01 and M02 for both representative uses evaluated. The acute risk from M07, M09, M10 and M11 to aquatic organisms can be regarded as low for both representative uses evaluated. The experts' meeting decided that the long term risk to aquatic invertebrates of the metabolites M07, M09 and M11 needs to be addressed. The EFSA considers such a study also necessary for metabolite M10 as this is a major metabolite in groundwater. Studies to address the risk from the metabolites M05, M21 and DMP are considered necessary.

A high risk to bees was identified which must be managed at Member State level. The available studies were not sufficient to establish a withholding period. Application should be avoided when there are likely to be any bees in the crop.

A high risk to non-target arthropods was observed in the laboratory and extended laboratory studies. Further higher tier studies were submitted to address this risk. The EFSA is of the opinion that further data is needed to address the risk to non-target arthropods for both uses evaluated.

The risk to earthworms and soil-micro-organisms from oxydemeton-methyl, M01, M09 and M10 can be regarded as low. Further studies to address the risk to earthworms and soil-micro-organisms from the metabolite DMP are considered necessary.

M01 and M02 have a comparable insecticidal activity as the parent compound. A further clarification of the tested dose rates in the biological screening data for M07 and M10 is needed to conclude on the biological relevance of these metabolites. A study on the effects of oxydemeton-methyl on non-target plants was still awaited during the EPCO meeting. Biological screening data for the ground water metabolite M05 and DMP are considered necessary.

The risk to soil non-target macro-organisms and biological methods of sewage treatment can be regarded as low.

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

- Risk mitigation measures, such as bufferzones of 15 m in cereals and 100 m in orchards, to address the risk to aquatic organisms are considered necessary (refer to point 5.2).
- Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available (refer to point 5.3).

Critical areas of concern

- No conclusion can be made on the technical specification as the validation data for the methods of analysis for the 5 batch study are not available.
- There is no data to demonstrate that on storage relevant impurities in the technical material are not increasing in the formulation.
- The levels of impurities in the toxicological batch do not support the provisional technical specification.
- Toxic by inhalation, in contact with skin and if swallowed.
- Uncertainty in the conversion of the administered concentrate (50%) to the mean daily intake of the technical material in toxicological studies.
- Estimated operator exposure, although a high degree of PPE is used, is above the AOEL according to model calculations (German model: >7000% of the AOEL without PPE, >300% of the AOEL with PPE). The AOEL is also exceeded in field studies.
- Reproductive effects are observed on epididymis, ovaries and fertility. Possible classification with R62/R63 is forwarded to the ECB.
- A reliable consumer risk assessment could not be performed at this stage as no reliable information is available on the residue levels.
- A definitive conclusion on the potential levels of the metabolites M05 and DMP in groundwater cannot be reached due to identified data gaps.
- Only a limited number of the possible application patterns on cereals that were encompassed by the applied for representative uses on cereals have groundwater exposure assessments. In particular the pattern of two autumn applications to winter cereals, that is likely to represent the worst case for leaching was not simulated. Even for the subset of the cereal use that has been assessed, as noted above there remain deficiencies in the assessment regarding M05 and DMP.

- Mammalian toxicology data required to conclude on the non relevance of the groundwater metabolites M05 and M10 are outstanding, pending on the outcome of the FOCUS modelling.
- A clarification is needed whether or not the test material used in the section on ecotoxicology covers the specification of the technical material regarding the impurities and furthermore the composition of the tested premix products needs to be clarified.
- A potential high risk to birds and mammals was identified. Further justification of several refinement options is requested. The risk to birds and mammals can only be concluded once these data become available.
- A high risk to aquatic organisms from oxydemeton-methyl was identified for which risk mitigation measures such as bufferzones of 15 m in cereals and 100 m in orchards are considered necessary. Several studies to address the risk to aquatic organisms are still outstanding.
- A high risk to bees was identified. Risk mitigation measures to avoid all contact with bees are considered necessary. No data to establish a withholding period is available.
- A high risk to non-target arthropods was identified. Further data to address this risk is considered necessary.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

(Abbreviations used in this list are explained in appendix 2)

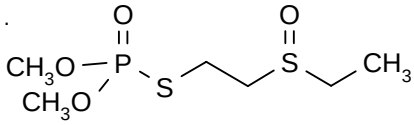
Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Oxydemeton-methyl
Function (e.g. fungicide)	Insecticide
Rapporteur Member State	France
Co-rapporteur Member State	--

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	S-(2-ethanesulfinyl-ethyl) O,O´-dimethylphosphorodithioate
Chemical name (CA) ‡	S-[2-(ethylsulfinyl)ethyl] O,O-dimethylphosphorodithiate
CIPAC No ‡	171
CAS No ‡	301-12-2
EEC No (EINECS or ELINCS) ‡	EU index number:015-046-00-7 EINECS number: 206-110-7
FAO Specification ‡ (including year of publication)	1980 (50-55 % ± 2 % for technical solution) Acidity or Alkalinity [CIPAC 1: MT 31] Max acidity: 0.7% calculated as H_2SO_4. Max alkalinity: 0.01% calculated as NaOH. Acetone Insolubles [CIPAC 1; MT 27]: Max: 0.3% Water [CIPAC 1; MT 30.1]: Max: 0.8%.
Minimum purity of the active substance as manufactured ‡ (g/kg)	Minimum purity = 85%. shipped as a 50% pre-mixture (pre formulation).
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Demeton-S-methyl (≤3.5 %) and demeton-S-methyl sulfone (≤2 %)
Molecular formula ‡	C_6 H_{15} O_4 P S_2
Molecular mass ‡	246.3g/mol

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

Structural formula ‡	

Physical-chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	< –49°C (purity 90 %)
Boiling point (state purity) ‡	Not measurable as decomposition occurs at 65°C.
Temperature of decomposition	The a.s. is not stable. Decomposition occurs at temperatures above 65°C (purity 99.8%)
Appearance (state purity) ‡	Colourless or pale yellow viscous liquid (purity 99%)
Relative density (state purity) ‡	1.31g/mL (density). Purity 99%
Surface tension	66 mN/m at 90% of the concentration of water solubility (purity 99 %)
Vapour pressure (in Pa, state temperature) ‡	$2x10^{-3}$ Pa @ 25^0C results to be confirmed
Henry's law constant (Pa m^3 mol^{-1}) ‡	H<$4x10^{-7}$(Pa x m^3/Mole) at 20-25^0C
Solubility in water ‡ (g/l or mg/l, state temperature)	Completely miscible in water (>1200 g/L) (purity 98%) – not pH dependent
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	(Purity 98.1%) n-hexane - 0.025g/L toluene,2-propanol, dichloromethane,1-octanol, acetone, acetonitrile, dimethylformamide, polyethylene glycol + ethanol all > 250g/L at 20 ^{0}C purity (96%) n-heptane: 0.29 ethyl acetate: >250 g/L (both at 25 °C)
Partition co-efficient (log POW) ‡ (state pH and temperature)	Log P_{ow} = -0.74 at 21^0 C (purity 89%) (pH not given but the active substance has no dissociation constant)
Hydrolytic stability (DT_{50}) ‡ (state pH and temperature)	The half-life in days of the a.s. is as follows pH 50°C 25°C 20°C 4 4.9 182 174 7 3.5 85 73 9 0.2 4.9 4.5

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

Dissociation constant ‡	The a.s. does not show basic or acidic properties in water (purity 99.8%). No pK value can be determined.
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	λ = 213nm – ε= 1356 $l.mol^{-1}/cm^{-1}$ (purity 99%)
Photostability (DT_{50}) ‡ (aqueous, sunlight, state pH)	Half-life = 1.22 hours and a chemical lifetime of 1.77 h.
Quantum yield of direct phototransformation in water at ☒ > 290 nm ‡	Quantum yield = 0.00078 mol/einstein.
Flammability ‡	Flash point = 80.5°C (premix formulation: 53.6 %) Auto ignition temperature of 285^0C (premix formulation: 53.6 %)
Explosive properties ‡	The premix formulation is not explosive (premix formulation: 53.6 %)

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

Summary of representative uses * evaluated (Annex IIA, point 3) as given in the initial EU dossier with no modification of the initially supported uses

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 a.s./hl min max (n)	water l/ha min max	kg a.s./ha min max		
Cereals (except oats)	NE & SE	Metasystox 250 EC	F	Aphids	EC	250	Spray	BBCH 09-18 <BBCH 73	1-2	Not defined by applicant but 10 days was assessed	25-125	100-500	125	21	[1] [2] [3] [4]
Pome fruit	NE & SE	Metasystox 250 EC	F	Aphids	EC	250	Spray	At infestation (pre and/or post blossom)	1-2	10-14	25-37.5	1000-1500	375	90	[1] [2] [3] [4]

[1] The risk assessment has revealed a risk for operators in section 2.
[2] The risk assessment for consumer has revealed data gaps in section 3.
[3] The exposure and risk assessments have revealed data gaps in sections 4 & 5.
[4] The risk assessment has revealed a risk (exceedance of relevant threshold) in section 5.

1: BBCH 09-18 early season 2: Before BBCH 73 3: At infestation 4: Pre-blossom and/or post blossom 5: Pre-blossom until maturity, at infestation
6: At infestation. until meeting in the rows 7: From two leaf-stage until meeting in the rows

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

Remarks:	*	Uses for which risk assessment could not been concluded due to lack of essential data are marked grey	(h)	Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
	(a)	For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)	(i)	g/kg or g/L
	(b)	Outdoor or field use (F), glasshouse application (G) or indoor application (I)	(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
	(c)	*e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds		
	(d)	*e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)	(k)	The minimum and maximum number of application possible under practical conditions of use must be provided
	(e)	GCPF Codes - GIFAP Technical Monograph No 2, 1989		
	(f)	All abbreviations used must be explained	(l)	PHI - minimum pre-harvest interval
	(g)	Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench	(m)	Remarks may include: Extent of use/economic importance/restrictions
			(n)	product concentration of spray liquid

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

Appendix 1.2: Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (principle of method)	HPLC method 2286/1821642/00E. The principle is reverse phase chromatography of sample solutions with an isocratic eluent. Quantitative evaluation is performed after UV detection using external standard.
Impurities in technical as (principle of method)	TLC methods are applicable for the determination of the content of certain by-products. The quantitative evaluation is carried out visually or densiometrically against calibration solutions after colouring with 4-(4-nitrobenzyl)-pyridine and tetraethylene pentamine solution, with nitrobenzyl pyridine/tetraethylene pentamine/hydrobromic/ ammonium molybdate/crystal violet or with palladium chloride solution depending of the compound. The CG-FID method 2201-0222903-97E (headspace technique using the standard addition method). Method 2201-0313201-98E is a general method based on HPLC-MS – An on reverse phase HPLC method is used to determine some impurities in the technical oxydemeton-methyl. Quantification is via UV detection at 200nm. Karl Fischer ‘s method is used to determine water content.
Plant protection product (principle of method)	Method 2001-002051-90 for the determination of the oxydemeton-methyl content in formulations is based on reverse phase chromatography of sample solutions with an isocratic eluent. Quantitative evaluation is performed after UV detection using external standardization.

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	**DFG method S 19, 1982; Bayer method no.00086 plus modification 00086/MO 12.** **DFG method S 16, 1979; Bayer method no.00085** Samples are extracted with acetone/water, partitioned with sodium chloride and

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

	dichloromethane, cleaned up via gel chromatography and eluted with cyclohexane/ethyl acetate, oxidised with potassium permanganate to convert the residue of concern to demeton-S-methyl sulphon (M01[1]), dried over sodium sulfate, re dissolved in acetone prior to analysis and quantification via GC-FID. LOQ - 0.01mg/kg in acid high content commodities and water high content commodities. **Alternative methods** (method 00009, method 00015, method 00255, ...) are given consisting in three steps (extraction, oxidation and quantification using GC/FID or NPD). The main area of variation between methods is in the extraction phase. LOQ = 0.05 mg/kg in cereals (grain, straw and green plants), =0.01 mg/kg in peas, potatoes or sugar beet method 00585: same principle but extraction with a microwave LOQ = 0.005 mg/kg for apple, grape and potatoes and 0.01 mg/kg in Brussels sprout and sugar beet
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	***As no MRLs are set, no method is required. However, a method was provided and it is detailed below, this method has not been peer reviewed***. Animal tissues are dried with sodium sulphate (except milk), extracted with acetonitrile then with hexane. The acetonitrile phase is evaporated. Fat is extracted with hexane followed by an acetonitrile extraction, then partitioned as with other animal tissues. Eggs are extracted with acetone. Following filtration, the filter cake is washed with dichloromethane. The combined extracts are partitioned; the lower phase is evaporated, dissolved in hexane and extracted with acetonitrile, evaporated, re dissolved in hexane and partitioned against water; the water phase is extracted with dichloromethane. The organic phase is evaporated and dissolved in acetone prior to oxidation with magnesium sulphate and potassium permanganate. After oxidation, the mixture is partitioned against dichloromethane, dried with anhydrous sodium sulphate, re dissolved in acetone and determined by GC/FID. LOQ - 0.01mg/kg.

[1] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate

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

Soil (principle of method and LOQ)	Extraction with solvent, clean up, oxidization and quantification using GC/MS with 3 ions (1 for routine analysis and 2 for verification). This method is acceptable and fully validated at 0.05 and 0.5 mg/kg. LOQ can be given to be 0.05 mg/kg soil. As the determination is acceptable for the 3 ions, no confirmatory method is required.
Water (principle of method and LOQ)	LC/MS/MS (parent ion: 263 ; daughter ion: 169 and 121) this method is fully validated (0.05 and 0.5 µg/L) for the determination of ODM[2] and M01 and demeton-S-methyl (M02[3]) in drinking water and for ODM and M02 in surface water and the LOQ can be given to be of 0.05 µg/L in drinking and surface water.
Air (principle of method and LOQ)	The Tenax or XAD2 air sampling tubes are extracted with ethyl acetate. The oxydemeton-methyl content is quantified by GC-NPD. LOQ= 0.0005 mg/m^3 or = 1.01 ug/tube
Body fluids and tissues (principle of method and LOQ)	**In urine**: Method 520 developed for analysis of urine samples. Residues are first extracted with a suitable solvent, oxidised using 2-methyl-2-propanol/potassium permanganate prior to extraction and qualification via GC-MS detection. LOQ - 0.0101mg/L **In blood**: An analytical method was developed and validated for the determination of ODM and M01 in human blood. The method involves an extraction of EDTA-blood with methylene chloride followed by centrifugation and separation of the organic and aqueous phase. Residues are quantified using GC/MS (m/z: 109 for oxydemeton methyl and 169 for M01). External standardisation. This method is fully validated at 50 µg/L and 500 µg/L for the determination of ODM and M01 in human blood with LOQ = 50 µg/L **In tissues:** *method required*

[2] ODM: oxydemeton-methyl
[3] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate

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

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

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

Appendix 1.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism in mammals (Annex IIA, point 5.1)

Rate and extent of absorption ‡	Rapid, > 90 % in rats based on urine excretion.
Distribution ‡	Widely distributed, highest level in blood.
Potential for accumulation ‡	No potential for accumulation in organs
Rate and extent of excretion ‡	Almost complete in 72 hours, mainly via the urine
Metabolism in animals ‡	Moderately metabolised (27-67%) by oxidation, hydrolysis
Toxicologically significant compounds ‡ (animals, plants and environment)	Parent compound, Impurities/metabolites: demeton-S-methylsulphon (M01[4]), demeton S methyl (M02[5]) Plant metabolites: M06[6] and M07[7]

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	48 mg/kg bw	**T, R25**
Rat LD_{50} dermal ‡	112 mg/kg bw	**T, R24**
Rat LC_{50} inhalation ‡	0.471 mg/L	**T, R23**
Skin irritation ‡	Non irritant	
Eye irritation ‡	Irritant	**R36**
Skin sensitization ‡ (test method used and result)	Skin sensitiser (M&K, Buehler)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Inhibition of brain and blood cholinesterase activities
Lowest relevant oral NOAEL / NOEL ‡	Overall NOAEL = 0.1 mg/kg bw/d (90-d rat, 1-y dog) NOAEL 14-day rat: 0.15 mg/kg bw/d
Lowest relevant dermal NOAEL / NOEL ‡	0.5 mg/kg bw/d (21 days rabbit)
Lowest relevant inhalation NOAEL / NOEL ‡	0.00066 mg/L/d (21 days rat)

[4] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate
[5] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate
[6] M06: O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate
[7] M07: O-methyl-S-[2-(ethylsulfonyl)-ethyl]phoshorothioate

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	Positive *in vitro*, negative *in vivo*. Weight of evidence indicates no genotoxic potential.

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

Target/critical effect ‡	Inhibition of brain and blood cholinesterase activities, vacuolisation of epididymis
Lowest relevant NOAEL / NOEL ‡	0.03 mg/kg/d (2-year study in rat)
Carcinogenicity ‡	No oncogenic potential in rodents

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Parental: AChE inhibition, vacuolisation of epididymis Reproduction: reduced fertility index and litter size Offspring: reduced pup viability and body weight **R62 ?; R63 ?**	
Lowest relevant reproductive NOAEL / NOEL ‡	Parental: Reproduction: Offspring:	0.15 mg/kg bw/d 0.45 mg/kg bw/d 0.45 mg/kg bw/d
Developmental target / critical effect ‡	No teratogenic potential	
Lowest relevant developmental NOAEL / NOEL ‡	Maternal: Developmental:	<0.5 mg/kg bw/d (rat), 0.4 mg/kg bw/d (rabbit) ≥4.5 mg/kg bw/d (rat); ≥1.6 mg/kg bw/d (rabbit) (highest doses tested)

Neurotoxicity / Delayed neurotoxicity ‡ (Annex IIA, point 5.7)

.....	No delayed neurotoxicity in hens after acute or sub- chronic exposure

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

Other toxicological studies ‡ (Annex IIA, point 5.8)

M01: demeton-S-methylsulphon	Anti cholinesterase activity Genotoxicity: Positive *in vitro*, negative *in vivo* Found in rat metabolism Considered toxicologically equivalent to the parent.
M02: demeton-S-methyl	Anti cholinesterase activity LD_{50} oral route: 30 mg/kg bw Genotoxicity: positive in vitro, negative in vivo Considered toxicologically equivalent to the parent.
M06: desmethyl oxydemeton-methyl	Assessment using QSAR. Mutagenic activity *in vitro* in bacteria expected (presence of an alkyl ester of phosphoric or phosphonic acid group). Mild/moderate skin sensitizer, severe ocular irritant. Considered toxicologically equivalent to the parent.
M07: desmethyl oxydemeton-methyl sulfone	Assessment using QSAR. Mutagenic activity *in vitro* in bacteria expected (presence of an alkyl ester of phosphoric or phosphonic acid group. Possible severe skin sensitizer. Considered toxicologically equivalent to the parent.

Medical data ‡ (Annex IIA, point 5.9)

.....	No adverse effects reported in plant personel workers. Findings in poisoning cases are typical of AChE inhibition.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.0003 mg/kg bw/d	2 year study in rat	100
AOEL (systemic)‡	0.001 mg/kg bw/d	90 day study in rat 1 year study in dog	100
ARfD ‡ (acute reference dose)	0.0015 mg/kg bw	14 day study in rat	100

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

Dermal absorption (Annex IIIA, point 7.3)

Metasystox 250 EC	20 % (concentrate and in-use dilutions), based on the *in vivo* monkey study (20% after 9h of exposure) and the *in vitro* assays on human epidermis (18-19%)

Acceptable exposure scenarios (including method of calculation)

Operator (with PPE)	**Pome fruits**:	with PPE / without PPE
	POEM:	12,713% / 34,088% of AOEL
	BBA:	2,899% / 22,489% of AOEL
	Cereals:	with PPE / without PPE
	POEM:	1,823% / 12,885% of AOEL
	BBA:	314% / 7,943% of AOEL
	Field study performed for both uses: with some deficiencies, but showed exceedence of the AOEL.	
Workers	Pome fruit:	3000% of AOEL immediately after application
	Cereals:	83% of AOEL
Bystanders	Pome fruit:	464% of AOEL
	Cereals:	27% of AOEL

Classification and proposed labelling (Annex IIA, point 10)

with regard to toxicological data	T; Toxic
	R 23/24/25, Toxic by inhalation, in contact with skin and when swallowed
	R36, Irritating to eyes
	R43, May cause sensitization by skin contact
	R62 ? Possible risk of impaired fertility
	R63 ? Possible risk to the unborn child

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

Appendix 1.4: Residues

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

Plant groups covered	Apple (fruits), sugar beet (root vegetables)
Rotational crops	Red beet, kale and wheat
Plant residue definition for monitoring	Sum of oxydemeton-methyl and demeton-S-methylsulphon (M01[8]) expressed as oxydemeton-methyl
Plant residue definition for risk assessment	Sum of oxydemeton-methyl, demeton-S-methylsulphon (M01), metabolite M06[9] and metabolite M07[10] expressed as oxydemeton-methyl
Conversion factor (monitoring to risk assessment)	To be determined on the basis of supervised residue trials with analysis of metabolites M06 and M07

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

Animals covered	Goat and laying hens
Animal residue definition for monitoring	Sum of oxydemeton-methyl, demeton-S-methylsulphon (M01) and metabolite M07 expressed as oxydemeton-methyl
Animal residue definition for risk assessment	Sum of oxydemeton-methyl demeton-S-methylsulphon (M01) and metabolite M07 expressed as oxydemeton-methyl
Conversion factor (monitoring to risk assessment)	No
Metabolism in rat and ruminant similar (yes/no)	Difficult to assess as only one metabolite was identified in ruminants (demeton-S-methylsulphon (M01))
Fat soluble residue: (yes/no)	No

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

.....	No residues are expected

[8] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate
[9] M06: O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate
[10] M07: O-methyl-S-[2-(ethylsulfonyl)-ethyl]phoshorothioate

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

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

.....	Not possible to conclude. A decline of the residues seems to occur in some plant matrices, but it is unclear whether this is due to a real degradation, or to analytical or methodological problems.

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)	Expected intakes of toxicologically relevant residues not possible to determine due to missing information on metabolites M06 and M07.		
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Unclear, but metabolism studies were conducted at exposure rates probably largely in excees of the expected actual exposure, making any extrapolation doubtful.		
	Feeding studies in dairy cattle and laying hens (up to 30 ppm parent compound in the diet) Only residue of oxydemeton-methyl and its demeton-S-methylsulphon (M01) metabolite were analysed		
Muscle	< 0.01	< 0.01	Not required
Liver	< 0.01	< 0.01	Not required
Kidney	< 0.01	< 0.01	Not required
Fat	< 0.01	< 0.01	Not required
Milk	< 0.01		
Eggs		< 0.01	

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

Summary of critical residues data (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	Proposed MRL mg/kg	STMR mg/kg
Pome fruits	N/S	Data base unclear		No proposal is possible	
Cereals	N/S	Data base unclear			

(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 critical GAP

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

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

ADI	0.0003 mg/kg
TMDI (European Diet) (% ADI)	Exposure assessment cannot be performed due to missing information on residue levels in plant commodities
NEDI (% ADI)	Exposure assessment cannot be performed due to missing information on residue levels in plant commodities
Factors included in NEDI	Not applicable
ARfD	0.0015 mg /kg
Acute exposure (% ARfD)	Exposure assessment cannot be performed due to missing information on residue levels in plant commodities

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

Crop/processed crop	Number of studies	Transfer factor	% Transference *
Apple / Apple sauce Apple / Apple Juice	2 2	0.3 - <0.6 0.9 - 1.0	Balance data not available
Note that these transfer factors are related to the sum of parent compound and demeton-S-methylsulphon (M01). Metabolites M06 and M07 are not included			

* Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies

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

Pome fruit	No proposal due to unclear/incomplete data base
Wheat, rye, triticale	
Barley, oats	
Animal products	

*) LOQ

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

Appendix 1.5: Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	6.6-38%AR after ca. 90 days ethane-^{14}C-radiolabel (n=2) 79%AR after ca. 49 days methoxy-^{14}C-radiolabel (n=1)
Non-extractable residues after 100 days ‡	17-20%AR after ca. 90 days ethane-^{14}C-radiolabel (n=2) 20%AR after ca. 49 days methoxy-^{14}C-radiolabel (n=1)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	M01[11] max. 6.3 % (3d) M05[12] max. 9.5 % (4 d) M09[13] max. 39 % (2 d) M10[14] max. 26.5 % (365 d) DMP[15] 45.8 % (1d, indicative)

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

Anaerobic degradation ‡	Information required for autumn application Metabolite M02[16] expected (see anaerobic water-sediment system) Additional information Puhl, 1978 (temperature ? indicative) (M02 confirmed max. 6.2 % (day 13, indicative) M09 max. 32 % (day 3, indicative) M22[17] max. 22.4 % (day 13, indicative) Mineralization around 8 % (57 days, indicative) Non-extractable residues 68 % (57 days, indicative)
Soil photolysis ‡	Not significant, DT_{50} = 74 d (light), 65 d (dark) (first order kinetics) Metabolites: M09 1.6 %, M10 18.3 %, M07[18] 2.1 %. Bound residues: 3.8 %. No mineralization. (Values under irradiation, similar values in dark controls)

[11] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate. or demeton-S-methylsulphon
[12] M05: 1-(ethylsulfonyl)-2-(methylsulfonyl) ethane.
[13] M09: 2-ethylsulfinyl ethane sulfonic acid.
[14] M10: 2-ethylsulfonyl ethane sulfonic acid.
[15] DMP: dimethyl phosphate.
[16] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate. or demeton-S-methyl
[17] M22: 2-ethylthio ethane sulfonic acid.
[18] M07: O-methyl-S-[2-(ethylsulfonyl)-ethyl]phoshorothioate

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

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

Method of calculation	Single first order kinetics
Laboratory studies ‡ (range or median, with n value, with r^2 value)	DT_{50lab} (aerobic) : ODM[19]: (25°C) 0.4-3.2 d (n=2) (20°C) <1 d (n=3) Same data, normalised to 20°C and -10kPa soil moisture 0.51-3.79 d (geometric mean for FOCUS modelling 0.76 d, n=5,) M01 1.08 d (n=1, 25°C) 20°C and -10kPa for FOCUS modelling 1.28 d, M05 14.1-31.6 d (n=2, 20°C) Normalised to -10kPa 9.4 & 25.2 d (n=2), not estimated in a third soil with lower degradation more information required M09 0.9-7.46 d (n=3, 20°C) Normalised to -10kPa 0.86-4.97 d (geometric mean for FOCUS modelling 1.32 d n=3), M10 0.27-3.12 d (n=3, , 20°C)) Normalised to -10kPa 0.18-2.49 d (geometric mean for FOCUS modelling 0.92d n=3) DMP not provided data gap identified
	DT_{90lab} (aerobic) : ODM 25°C 1.3-10.6 d, 20°C <3.32 d Data at 20-25°C used for DT_{50}, calculation at 20°C 2.0-≤15.7 d (n=5, pH 5.3-7.5) M01 25°C 3.6 d (n=1) M05 20°C 46.8-105 d (n=2) M09 20°C 3-24.8 d (n=3) M10 20°C 0.9-10.4 d (n=3)
	DT_{50lab} (10°C, aerobic): not provided, not required (fast aerobic degradation) Data at 20-25°C, calculation at 10°C 1.3-10.4 d (mean around 3.7 d, n=5, pH 5.3-7.5, first order kinetics)
	DT_{50lab} (20°C, anaerobic): rapid, precise value not provided, required for autumn application
	degradation in the saturated zone: not provided

[19] ODM: oxydemeton-methyl

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

Field studies ‡ (state location, range or median with n value)	$DT_{50f:}$ 2 US sites (California), not a usual field dissipation study design. ODM: 1.49-3.82 d (outdoor experiment in vessels, summer application, 2 soils, first order kinetics) Metabolites: M01: maximum evaluated to 7 %, transient M09: max. 28.5 %, DT_{50} 18 d (1 soil, apparent, could be overestimated) * Same data, recalculated 7.72 d (n=1) SFO M10: max. 14.0 %, DT_{50} 14 d (1 soil, apparent, could be overestimated) * Same data, recalculated 4.44 d (n=1) SFO * DT_{50} values for ODM, M09 and M10 recalculated by notifier by using the same data with compartment model and Single First Order.
	$DT_{90f:}$ ODM: 4.9-12.7 d
Soil accumulation and plateau concentration ‡	No data, not required for ODM (no accumulation expected)

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	ODM: very low adsorption. No reliable experimental value, Koc value of zero assumed for PECgw modelling. M01: Very low adsorption, no reliable experimental value, Koc value of zero assumed for PECgw modelling. M05: not provided, required No experimental study, low adsorption assumed, Koc value of zero assumed for PECgw modelling. M09: not adsorbed. Koc value of zero assumed for PECgw modelling. M10: not adsorbed. Koc value of zero assumed for PECgw modelling. M02: Very low adsorption, no reliable experimental value, Koc value of zero assumed for PECgw modelling. DMP not provided, assessment of groundwater leaching potential required

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

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

Column leaching ‡	No data
Aged residues leaching ‡	Indicative study: 30 d incubation, mineralization 50 %, bound residues 40 %. Elution 562 mm (12.5 mm for 45 d). Radioactivity in leachate around 5 % (ODM, M01, M09, M10, M21[20], < 1 % each).
Lysimeter/ field leaching studies ‡	No data, not required

PEC (soil) (Annex IIIA, point 9.1.3)

Parent and metabolites

PECsoil after 1 application of ODM or 2 applications with an interval of 10 days
to cereals (125 g ODM / ha / application) or to apple orchards (375 g ODM / ha / application) 5cm soil layer 1.5g cm^{-3}

Crop						Cereals		Apple orchards	
Rate (g/ha)						125		375	
Interception (worst case assumptions)						0-(25) %		50 %	
Period (worst case assumptions)						autumn BBCH 09-18		spring BBCH 54-59	
Number of applications						1	2	1	2
Compound		Conditions	Molar mass	Maximum fraction of parent	DT_{50} soil	Initial PECsoil (mg/kg) (depth of top soil 5 cm density 1.5 g/cm^3)			
ODM		**aerobic**	**246.3**	**1**	**3.82 days**	**0.167 (0.125)**	**0.194 (0.145)**	**0.25**	**0.291**
M01	demeton-S-methylsulphon	aerobic	262.3	0.063	2.82 days	0.011 (0.008)	0.012 (0.009)	0.017	0.019
M05	ESOMSOE	aerobic	200.3	0.098	*	0.013 (0.010)	0.027 (0.020)	0.020	0.040
M09	ESES	aerobic	186.24	0.305	7.72 days	0.038 (0.029)	0.054 (0.041)	0.058	0.082
				or 0.389		0.049 (0.037)	0.069 (0.052)	0.074	0.104

[20] M21; 2-ethylsulfinyl-ethyl mercaptan

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

Crop						Cereals		Apple orchards	
Rate (g/ha)						125		375	
Interception (worst case assumptions)						0-(25) %		50 %	
Period (worst case assumptions)						autumn BBCH 09-18		spring BBCH 54-59	
Number of applications						1	2	1	2
Compound		Conditions	Molar mass	Maximum fraction of parent	DT_{50} soil	Initial PECsoil (mg/kg) (depth of top soil 5 cm density 1.5 g/cm^3)			
M10	ESOES	aerobic	202.25	0.265	4.44 days	0.036 (0.027)	0.044 (0.033)	0.054	0.065
DMP	dimethyl phosphate	aerobic	126 ?	0.458	*	0.039 (0.029)	0.078 (0.059)	0.059	0.117
M02	*ODM-sulfide*	*anaerobic*	*230*	*0.062***	*	*0.01 (0.007)*	*0.019 (0.015)*	*0.015*	*0.029*
M22	*ETES*	*anaerobic*	*170*	*0.224***	*	*0.026 (0.019)*	*0.052 (0.039)*	*0.039*	*0.077*

* No degradation of metabolites assumed (DT_{50} in soil not determined): PECsoil 2 applications = PECsoil 1 application x 2.
** Indicative values.

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

Hydrolysis of active substance and relevant metabolites (DT_{50}) ‡ (state pH and temperature)	pH 5: DT_{50} 96.3 d (25°C) Metabolite: M06[21] max. 24.5 %
	pH 7: DT_{50} 39.6-42.3 d (25°C) (73 d at 20°C, extrapolated by calculation) Metabolites: M06 max. 20.4-37.1 %, M21 max. 0.4 %, M11[22] max. 13.4-16.5 % (M11 + M21 max. 13.4-16.9 %) formation of M11 could have occurred by dimerization of M21 under analytical conditions, in this case the sum M11 + M21 should be considered

[21] M06: O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate.
[22] M11: bis-2-[(ethylsulfinyl)-ethyl]disulfide

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

	pH 9: DT_{50} 2.3-2.5 d (25°C) (4.5 d at 20°C, extrapolated by calculation) Metabolites: M21 max. 9.0 %, M11 max. 74.2-84.9 % (M11 + M21 max. 74.7-84.9 %) formation of M11 could have occurred by dimerization of M21 under analytical conditions, in this case the sum M11 + M21 should be considered Equilibrium M21/ M11 possible in water.
Photolytic degradation of active substance and relevant metabolites ‡	pH 5: not significant, DT_{50} 187 d (light 38°N, April, day length not reported), 257 d (dark) (first order kinetics)
Readily biodegradable (yes/no)	No
Degradation in water/sediment DT_{50} water ‡ DT_{90} water ‡ DT_{50} whole system ‡ DT_{90} whole system ‡	2.3-3.4 d (first order kinetics) in water phase 22°C whole system: same as in water (low amount of ODM in sediment) 5.4-12.1 d (first order kinetics) indicative values in sediment
Mineralization	29-31 % (91 d)
Non-extractable residues	45-66 % (91 d)
Distribution in water / sediment systems (active substance) ‡	maximum 48.5 % in water and 3.5 % in sediment (after 1 day)
Distribution in water / sediment systems (metabolites) ‡	Aerobic conditions : M01: max. 0.9 % in water and 0.2 % in sediment M02: max. 3.4 % in water and 3.1 % in sediment M07: max. 18.0 % (major) in water and 1.6 % in sediment (DT_{50} 8.9 days in one system, slow degradation with plateau around 10 % and no estimation of DT_{50} possible in another system. No degradation assumed for PECsw calculation). M06:: max <9.4 % in water and < 1.6 % in sediment M09: max. 9.9 % in water and < 1.7 % in sediment M10: max. 5.1 % in water and 1.9 % in sediment M11: max. 22.3 % (major) in water and 1.3 % in sediment (DT_{50} 6.4-10.0 d in water) M21/ M11 possible in water. M11 and M21 both considered to be potentially major in water.

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

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

Parent

Method of calculation	Spray drift (90th or overall 90th percentile value) into a 30 cm depth water body. ODM: DT_{50} 3.4 d (aerobic) M01: 1 %, molar ratio MR 262/246=1.065 M02: 3.4 % (aerobic) MR 230/246 = 0.93 M07: 18 %, MR 248/246 =1.01 M09: around 9 %, MR 186/246 = 0.76 M11: 22 %, MR 274/246 =1.11
Application rate	Cereals: 125 g/ha, 2 applications (interval 10 days) Orchard: 375 g/ha, 2 applications (interval 10 days or interval 8 days)
Main routes of entry	Spray drift

Initial PECsw for ODM

Crop	Cereals	Orchard					
Rate (g/ha)	125	375					
Distance (m)	1	3	5	10	15	20	30
Drift (%)	2.77	15.7 [1]	8.4 [1]	3.6 [1]	1.81 [1]	1.09 [1]	0.54 [1]
PECsw (µg/L) [2]	**1.15**	**19.6** [1]	**10.5** [1]	**4.5** [1]	**2.3** [1]	**1.4** [1]	**0.67** [1]
Drift (%) [4]	2.4	12.1 [1]	-	-	-	-	-
PECsw (µg/L) [5]	1.13	17.1 [1] 18.1 [1])	-	-	-	-	-

[1] late application (BBCH 54-59 and/or 63-71 for orchards)
[2] for single application (90th percentile)
[4] overall 90th percentile
[5] for two applications, 10 d interval (overall 90th percentile)

Decrease in concentration of ODM in water (as % of initial PECsw)

Time (d)	Actual	TWA
Initial	100	100
1	81.6	90.5
2	66.5	82.1
4	44.2	68.4

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

Time (d)	Actual	TWA
7	24.0	53.3
14	5.7	33.0
21	0.3	23.0
28	-	17.5
42	-	11.7

PECsw for metabolites for 2 applications of ODM

As a first approach, because no reliable DT_{50} are available for the different metabolites, concentrations are estimated to be multiplied by a factor of 2 for 2 applications (no degradation assumed).

Revised PECsw resulting from drift (90th percentile drift values)
after 1 application of ODM or 2 applications with an interval of 10 days
to cereals (125 g ODM / ha / application) or to apple orchards (375 g ODM / ha / application)

Crop			Cereals		Apple orchards	
Rate (g/ha)			125		375	
Distance (m)			1		3	
Drift (%)			2.77		15.72	
Number of applications			1	2	1	2
Compound		Conditions	Molar mass	Maximum fraction of parent	DT_{50} water	Initial PECsw (µg/L)			
ODM		**aerobic**	**246.3**	**1**	**3.4 d**	**1.15**	**1.15**	**19.65**	**19.65**
M01	demeton-S-methylsulphon	aerobic	262.3	0.01	*	0.012	0.025	0.21	0.42
M02	demeton-S-methyl	aerobic	230	0.034	*	0.037	0.073	0.62	1.25
M07	ODM-desmethyl-sulfone	aerobic	248.3	0.18	*	0.21	0.42	3.57	7.13
M07 (Na-alt)	ODM-desmethyl-sulfone Na-salt	aerobic	270	0.18	*	0.23	0.46	3.88	7.75
M09	ESES	aerobic	186.24	0.099	*	0.086	0.173	1.47	2.94
M11	ODM-disulfide-disulfoxide	aerobic	274	0.223	*	0.29	0.57	4.87	9.75
M21	ODM-thiol	aerobic	138x2=276	0.223	*	0.29	0.58	4.91	9.82

* No degradation of metabolites assumed.

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

Crop		Cereals											
Rate (g/ha)		125											
Distance (m)		1		5		10		15		20		30	
Drift (%)		2.77		0.57		0.29		0.20		0.15		0.10	
Number of applications		1	2	1	2	1	2	1	2	1	2	1	2
Compound		Initial PECsw (µg/L)											
ODM		1.15	1.15	0.24	0.24	0.12	0.12	0.083	0.083	0.063	0.063	0.042	0.042
M01	demeton-S-methyl-sulphon	0.012	0.025	0.0025	0.005	0.0013	0.0026	0.0009	0.0018	0.0007	0.0013	0.0004	0.0009
M02	demeton-S-methyl	0.037	0.073	0.0075	0.015	0.0038	0.0077	0.0026	0.0053	0.002	0.004	0.0013	0.0026

Crop		Apple orchards									
Rate (g/ha)		375									
Distance (m)		3		5		10		15		20	
Drift (%)		15.72		8.41		3.60		1.81		1.09	
Number of applications		1	2	1	2	1	2	1	2	1	2
Compound		Initial PECsw (µg/L)									
ODM		19.65	19.65	10.51	10.51	4.5	4.5	2.26	2.26	1.36	1.36
M01	demeton-S-methylsulphon	0.21	0.42	0.112	0.224	0.048	0.096	0.024	0.048	0.015	0.029
M02	demeton-S-methyl	0.62	1.25	0.334	0.668	0.143	0.286	0.072	0.144	0.043	0.087

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

Crop		Apple orchards									
Rate (g/ha)		375									
Distance (m)		30		40		50		75		100	
Drift (%)		0.54		0.32		0.22		0.11		0.06	
Number of applications		1	2	1	2	1	2	1	2	1	2
Compound		Initial PECsw (µg/L)									
ODM		0.68	0.68	0.4	0.4	0.28	0.28	0.14	0.14	0.075	0.075
M01	demeton-S-methylsulphon	0.007	0.014	0.004	0.009	0.003	0.006	0.0015	0.003	0.0008	0.0016
M02	demeton-S-methyl	0.021	0.043	0.013	0.025	0.009	0.018	0.004	0.009	0.002	0.005

PEC (sediment)

Parent

Method of calculation	No data, not required (negligible amounts in sediment)
Application rate	Not applicable

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS PEARL 2.2.2
Application rate	Cereals (wheat) 125 g/ha x 2 applications 1 in autumn 25% crop interception with a second in spring 70% crop interception. Orchards (apples) 375 g/ha x 2 applications, 60% & 70% crop interception

PEC$_{(gw)}$

Maximum concentration	Output not provided by FOCUS models, not required
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Not relevant

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

Input parameters for PECgw simulations

Substance	Molar mass (g/mole)	Kom (cm^3/g) assumption	1/n	DT_{50} (days)	Kinetic fraction (ODM to metabolite)	Water solubility * (g/L)	Vapour pressure * (Pa)	Plant uptake factor
ODM	246.3	0	0.93	0.84	--	1000 (20°C)	$3.9\ 10^{-3}$ (20°C)	0
M01	262.3	0	0.9	1.09	0.23	122 (25°C)	$2.37\ 10^{-3}$ (25°C)	0
M05	200.3	0	0.9	25.23 **	0.09	68.9 (25°C)	$1.4\ 10^{-2}$ (25°C)	0
M09	186.2	0	0.9	1.67	0.29	100 (25°C)	$4.93\ 10^{-5}$ (25°C)	0
M10	202.2	0	0.9	1.22	0.10	100 (25°C)	$2.25\ 10^{-5}$ (25°C)	0

* Estimated water solubility and vapour pressure should be justified.
** More information required about M05 DT_{50} in soil: if more persistent, higher PECgw possible.

PECgw following use on winter cereals, 2 applications of ODM, 1 in autumn and 1 in spring, interception 25-70 %

FOCUSgw scenario	80^{th} percentile annual average concentration at 1 m (µg/L)				
	ODM	M01	M05	M09	M10
Châteaudun	0.000	0.000	**0.568**	0.001	0.030
Hamburg	0.005	0.020	**1.222**	0.068	**0.189**
Jokioinen	0.002	0.015	**2.145**	0.071	**0.228**
Kremsmünster	0.000	0.001	**0.634**	0.005	0.048
Okehampton	0.001	0.002	**0.820**	0.008	0.062
Piacenza	0.002	0.006	**0.525**	0.016	0.067
Porto	0.001	0.003	**0.463**	0.011	0.050
Sevilla	0.000	0.000	**0.168**	0.001	0.010
Thiva	0.000	0.000	**0.278**	0.001	0.016

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

PECgw following use on apple orchards, 2 applications of ODM in spring, interception 60-70 %

FOCUSgw scenario	80th percentile annual average concentration at 1 m (µg/L)				
	ODM	M01	M05	M09	M10
Châteaudun	0.000	0.000	**0.939**	0.000	0.048
Hamburg	0.000	0.000	**1.372**	0.000	0.071
Jokioinen	0.000	0.000	**2.857**	0.000	**0.208**
Kremsmünster	0.000	0.000	**0.962**	0.000	0.050
Okehampton	0.000	0.001	**0.919**	0.003	0.051
Piacenza	0.000	0.001	**1.031**	0.004	0.061
Porto	0.000	0.000	**0.341**	0.000	0.017
Sevilla	0.000	0.000	**0.663**	0.000	0.034
Thiva	0.000	0.000	**0.315**	0.000	0.016

Additional estimation of the risk of groundwater contamination required for M05 and DMP.

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

Direct photolysis in air ‡	Data not submitted, not required
Quantum yield of direct phototransformation	0.00078 (aqueous)
Photochemical oxidative degradation in air ‡	Latitude: ..... Season: ..... DT_{50} 1.22 h (Atkinson)
Volatilization ‡	From plant surfaces: total volatilization from plants and soil could be about 6 % within 24 h (outdoor experiment in vessels, indicative)
	from soil: total volatilization from plants and soil could be about 6 % within 24 h (outdoor experiment in vessels, indicative)

PEC (air)

Method of calculation	Not calculated

$PEC_{(a)}$

Maximum concentration	Expected to be low due to low Henry law constant, and short DT_{50} in air (photochemical oxidation).

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

Definition of the Residue (Annex IIA, point 7.3)

Relevant to the environment	**Metabolites requiring risk assessment or groundwater exposure assessment** **Soil**: ODM and demeton-S-methylsulphon (M01). ESES (M09) and ESOES (M10) DMP **Groundwater**: ODM and demeton-S-methylsulphon (M01). ESOMSOE (M05), ESES (M09) and ESOES (M10) DMP **Surface water**: ODM, demeton-S-methylsulphon (M01) and demeton-S-methyl (M02). ODM-desmethyl (M06) ODM-desmethyl-sulfone (M07), ESES (M09), ESOES (M10) ODM-thiol (M21) and ODM-disulfide-disulfoxide (M11) (equilibrium M21/M11 possible) DMP. **Sediment**: none **Air**: ODM.

Under anaerobic conditions, other metabolites may require a risk assessment at Member States level. Additional residue in soil under anaerobic conditions: M02 (active), M22.

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

Soil (indicate location and type of study)	No data
Surface water (indicate location and type of study)	No data
Ground water (indicate location and type of study)	No precise data
Air (indicate location and type of study)	No data

Classification and proposed labelling (Annex IIA, point 10)

with regard to fate and behaviour data	Candidate for R 53 – May cause long-term adverse effects in the aquatic environment

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

Appendix 1.6: Effects on non-target Species

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

Toxicity to mammals ‡	LD_{50} = 48 mg a.s./kg b.w. (acute test) NOEL = 3 mg a.s./kg food (0.15 mg a.s./kg bw, effects on reproduction)
Acute toxicity to birds ‡	LD_{50} = 34 mg a.s./kg b.w. (Bobwhite quail, males) LD_{50} = 29 mg a.s./kg b.w. (Japanese quail) LD_{50} = 61 mg Metasystox R 250 EC/kg b.w. (Bobwhite quail, corresponding to 16.24 mg a.s./kg bw)
Dietary toxicity to birds ‡	LD_{50} = 2003 mg/kg food (Mallard duck), NOEC = 602 mg/kg food *i.e.* NOEL (mortality) = 119 mg a.s./kg b.w./day LD_{50} = 361 mg/kg food (Bobwhite quail), NOEC = 132 mg/kg food *i.e.* NOEL (mortality) = 56.6 mg a.s./kg b.w./day
Reproductive toxicity to birds ‡	NOEC = 54 mg/kg food *i.e.* 7.65 mg a.s./kg b.w./day (Mallard duck) NOEC = 6.9 mg/kg food *i.e.* 0.97 mg a.s./kg b.w./day (Bobwhite quail)

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

Birds: risk assessment in cereals (2 x 0.125 kg a.s./ha, 10 days interval) and orchards (2 x 0.375 kg a.s./ha, 10 days interval), according to Sanco 4145/2000

Crop	Category *(feed item)*	Time-scale	FIR	RUD*	Ftwa**	MAF **	endpoint	ETE	TER	Annex VI Trigger
cereals	Short grass	Acute	0.44	30.02	1	1.30	16.24	2.15	7.57	10
		Short-term		19.13	1	1.13	56.6	1.19	47.00	10
		Long-term		19.13	0.23	1.13	0.97	0.27	3.60	5
cereals	Insects	Acute	1.04	52	No	No	16.24	6.76	2.40	10
		Short-term		29			56.6	3.77	14.77	10
		Long-term		29			0.97	3.77	0.26	5
orchards	Insects	Acute	1.04	52	No	No	16.24	20.28	0.80	10
		Short-term		29			56.6	11.31	4.925	10
		Long-term		29			0.97	11.31	0.09	5

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

* mean measured residues in winter cereals in order to estimate residues in short grass (90th percentile = 30.02 mg/kg, median = 19.13 mg/kg)
** refined DT_{50} of 3.35 days.

Terrestrial vertebrates: risk assessment in cereals (2 x 0.125 kg a.s./ha, 10 days interval) and orchards (2 x 0.375 kg a.s./ha, 10 days interval)

Crop	Category *(feed item)*	Time-scale	FIR	RUD*	Ftwa**	MAF**	endpoint	ETE	TER	Annex VI Trigger
cereals	Short grass	Acute Long term	1.39 1.39	30.02 19.13	1 0.23	1.3 1.13	48 0.15	6.78 0.85	7.08 0.18	10 5
cereals	Insects	Acute Long-term	0.63	14 5.1	No	No	48 0.15	1.1 0.4	43.5 0.37	10 5
orchards	Short grass	Acute Long term	1.39 1.39	30.02 19.13	1 0.23	1.3 1.13	48 0.15	6.78 0.85	7.08 0.18	10 5

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	Endpoint	Toxicity (mg a.s./L)
Laboratory tests ‡				
Fish (*Onchorhynchus mykiss*)	Oxydemeton-methyl	96 h	LC_{50}	17*
Fish (*Onchorhynchus mykiss*)		98 d	NOEC	1.8
Invertebrates (*Daphnia magna*)		48 h	EC_{50}	0.11*
Invertebrates (*Daphnia magna*)		21 d	NOEC	0.027
Algae (*Scenedesmus subpsicatus*)		96 h	$E_{b/r}C_{50}$	> 100
Fish (*Onchorhynchus mykiss*)	Demeton-S-methylsulphon (M01[23])	96 h	LC_{50}	49
Invertebrates (*Daphnia magna*)		48 h	EC_{50}	35.4*
Invertebrates (*Daphnia magna*)		21 d	NOEC	0.01
Fish (*Onchorhynchus mykiss*)	Demeton-S-methyl (M02[24])	96 h	LC_{50}	4.5
Invertebrates (*Daphnia magna*)		48 h	EC_{50}	0.023*
Invertebrates (*Daphnia magna*)		21 d	NOEC	0.0056
Fish (*Onchorhynchus mykiss*)	Desmethyl-oxydemeton-methylsulfone (M07[25])	96 h	LC_{50}	> 100
Invertebrates (*Daphnia magna*)		48 h	EC_{50}	> 100

[23] M01: S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate
[24] M02: S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate
[25] M07: O-methyl-S-[2-(ethylsulfonyl)-ethyl]phoshorothioate

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg a.s./L)
Fish (*Onchorhynchus mykiss*) Invertebrates (*Daphnia magna*)	2-ethylsulfinyl-ethane sulfonic acid (M09[26])	96 h 48 h	LC_{50} EC_{50}	> 100 > 100
Fish (*Onchorhynchus mykiss*) Invertebrates (*Daphnia magna*)	2-ethylsulfonyl-ethane sulfonic acid (M10[27])	96 h 48 h	LC_{50} EC_{50}	> 100 > 100
Fish *(Onchorhynchus mykiss)* Invertebrates *(Daphnia magna)*	Bis-2-[(ethylsulfinyl)ethyl]disulfide (M11[28])	96 h 48 h	LC_{50} EC_{50}	> 100 33
Fish *(Leuciscus idus melanotus)* Fish *(Onchorhynchus mykiss)* Invertebrates *(Daphnia magna)* Sediment dwelling organisms *(Chironomus riparius)* Algae *(Scenedesmus subpsicatus)*	Metasystox R 250 EC	96 h 21 d 48 h 48 h 72 h	LC_{50} NOEC EC_{50} EC_{50} $E_{b/r}C_{50}$	1.88 0.39 0.34 0.011 4.37/13.36
Invertebrates *(Daphnia magna)*	Metasystox R 250 EC blue	21 d	NOEC	0.057

Microcosm or mesocosm tests
No data

* Additional information as the test concentrations were not analytically verified. A new study is requested on *D. magna* for ODM 50% premix and M02.

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

PECsw were calculated using Rautman *et al* (2001) drift values, for a 30 cm depth water column. The maximum of single or multiple application was used (DT_{50} in water is 3.4 d so that highest PEC may correspond to a single application). All toxicity endpoints were compared to initial PECsw.

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER	Annex VI Trigger
Cereals	**Oxydemeton-methyl**						
	Fish	Acute-96h	1	17	1.15	14 780	100
	Daphnids	Acute-48h	1 5	0.11	1.15 0.24	**95.7** **458**	100
	Algae	Chronic-72h	1	> 100	1.15	> 86 900	10
	Fish	Chronic-98d	1	1.8	1.15	1 565	10
	Daphnids	Chronic-21d	1	0.027	1.15	23.5	10

[26] M09: 2-ethylsulfinyl ethane sulfonic acid.
[27] M10: 2-ethylsulfonyl ethane sulfonic acid
[28] M11: bis-2-[(ethylsulfinyl)-ethyl]disulfide

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

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER	Annex VI Trigger
	M01						
	Fish	Acute-96h	1	49	0.025	1 960 000	100
	Daphnids	Acute-48h	1	35.4	0.025	1 416 000	100
	Daphnids	Chronic-21d	1	0.01	0.025	400	10
	M02						
	Fish	Acute-96h	1	4.5	0.073	61 644	100
	Daphnids	Acute-48h	1	0.023	0.073	315	100
	Daphnids	Chronic-21d	1	0.0056	0.073	76.7	10
	Chironomids	Acute-48 h	1 10	0.0011*	0.073 0.0077	**15** **143**	100

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER	Annex VI Trigger
Cereals	**M07**						
	Fish	Acute-96h	1	> 100	0.42	> 238 095	100
	Daphnids	Acute-48h	1	> 100	0.42	> 238 095	100
	M09						
	Fish	Acute-96h	1	> 100	0.173	> 578 035	100
	Daphnids	Acute-48h	1	> 100	0.173	> 578 035	100
	M11						
	Fish	Acute-96h	1	> 100	0.57	> 175 439	100
	Daphnids	Acute-48h	1	33	0.57	> 57 895	100
	Metasystox R 250 EC						
	Fish	Acute-96h	1	1.88	1.15	1635	100
	Daphnids	Acute-48h	1	0.34	1.15	295	100
	Algae	Chronic-72h	1	4.37	1.15	3800	10
	Fish	Chronic-21d	1	0.39	1.15	339	10
	Daphnids	Chronic-21d	1	0.057	1.15	49.6	10
	Chironomids	Acute-48 h	1 15	0.011	1.15 0.083	**9.57** **132**	100

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

Appendix 1 – list of endpoints

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER	Annex VI Trigger
Orchards	**Oxydemeton-methyl**						
	Fish	Acute-96h	3	17	19.65	865	100
	Daphnids	Acute-48h	3 30	0.11	19.65 0.68	**5.59** **161**	100
	Algae	Chronic-72h	3	> 100	19.65	> 5 089	10
	Fish	Chronic-98d	3	1.8	19.65	91.6	10
	Daphnids	Chronic-21d	3 15	0.027	19.65 2.26	**1.37** **11.94**	10
	M01						
	Fish	Acute-96h	3	49	0.42	116 667	100
	Daphnids	Acute-48h	3	35.4	0.42	84 286	100
	Daphnids	Chronic-21d	3	0.01	0.42	23.8	10
	M02						
	Fish	Acute-96h	3	4.5	1.25	3600	100
	Daphnids	Acute-48h	3 15	0.023	1.25 0.144	**18.4** **159.7**	100
	Daphnids	Chronic-21d	3 10	0.0056	1.25 0.286	**4.48** **19.58**	10
	Chironomids	Acute-48 h	3 75	0.0011*	1.25 0.009	**0.88** **122**	100
	M07						
	Fish	Acute-96h	3	> 100	7.13	> 14 025	100
	Daphnids	Acute-48h	3	> 100	7.13	> 14 025	100

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER	Annex VI Trigger
Orchards	**M09**						
	Fish	Acute-96h	3	> 100	2.94	> 34 014	100
	Daphnids	Acute-48h	3	> 100	2.94	> 34 014	100
	M11						
	Fish	Acute-96h	3	> 100	9.75	> 10 256	100
	Daphnids	Acute-48h	3	33	9.75	> 3 385	100

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

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER	Annex VI Trigger
	Metasystox R 250 EC						
	Fish	Acute-96h	3 5	1.88	19.65 10.51	**95.7** **178.9**	100
	Daphnids	Acute-48h	3	0.34	19.65	17.30	100
	Algae	Chronic-72h	3	4.37	19.65	222.4	10
	Fish	Chronic-21d	3	0.39	19.65	19.85	10
	Daphnids	Chronic-21d	3 10	0.057	19.65 4.5	**2.90** **12.66**	10
	Chironomids	Acute-48 h	3 100	0.011	19.65 0.075	**0.56** **146.7**	100

* no test with M02, EC50 assumed to be ten times lower than that of the parent (tested as Metasystox R 250 EC), according to guidance document Sanco/3268/2001.

Bioconcentration

Bioconcentration factor (BCF) ‡	Data not required. (log Pow = –0.74 at 21 °C)
Annex VI Trigger:for the bioconcentration factor	Not required.
Clearance time (CT_{50}) (CT_{90})	Not required.
Level of residues (%) in organisms after the 14 day depuration phase	Not required.

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

Acute oral toxicity ‡	Metasystox R 250 EC: 0.8 microg /bee (48 h, corresponding to 0.2 microg a.s./bee)
Acute contact toxicity ‡	Metasystox R 250 EC: 0.7 microg /bee (72 h, corresponding to 0.175 microg a.s./bee)

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

Application rate (kg a.s./ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
0.125	cereals	Oral	625	50
	cereals	Contact	714	50

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

Application rate (kg a.s./ha)	Crop	Route	Hazard quotient	Annex VI Trigger
0.375	orchards	Oral	1875	50
	orchards	Contact	2142	50

Field or semi-field tests
Succinct data confirm oxydemeton-methyl toxicity to bees. Residue toxicity tests: - low effects of Metasystox R 250 EC in adult bees exposed to woody parts of apple trees for 24 hours to 2 days aged residues, and for 48 hours to > 10 days aged residues. - low effects of Metasystox R 250 EC in adult bees exposed to stems of *Phacelia tanacetifolia* for 24 hours or 48 hours to fresh residues.

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

Risk assessment for oxydemeton-methyl R 250 EC

First tier risk assessment (according to ESCORT 2)					
Species	Crop	Application rate (g a.s./ha)	LR_{50} (g a.s./ha)	In-field HQ	Off-field HQ
Aphidius rhopalosiphi	Cereals	125	> 0.375	**< 333**	**< 9.23**
	Apple orchards	375		**<1000**	**< 292**
Typhlodromus pyri	Cereals	125	11	**11.36**	0.3
	Apple orchards	375		**34.1**	**9.95**
Second tier risk assessment (according to ESCORT 2)*					
Species	Crop	Application rate (g a.s./ha)	LR_{50} (g a.s./ha)	In-field HQ	Off-field HQ
Aphidius rhopalosiphi	Cereals	125	42.5	**2.94**	0.04
	Apple orchards	375		**8.8**	1.29
Typhlodromus pyri	Cereals	125	142.6	0.87	0.01
	Apple orchards	375		**2.63**	0.38

* The EFSA does not agree to calculate HQ values based on LR50 values from extended laboratory studies.

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

Species and stage	Test type	Dose rate (g a.s./ha) or test type	Value (g a.s./ha or %)
Parasitoid			
Aphidius rhopalosiphi (adults)	Ext. Lab.	48 h LR_{50} Reproduction	42.5 70% reduction at 31.24 g/ha
Trichogramma dendrolini (adults)	Semi field	5 day parasitisation 500 g/ha	Sign. affected for 2 days
Predatory mite			
Typhlodromus pyri (protonymphs)	Ext. Lab.	48 h LR_{50} Reproduction	142.6 28% and 89% reduction at 150 and 300 g/ha respectively
Foliage dwelling predator			
Adalia bipunctata (larvae)	Lab.	Mortality at 12.5 g/ha	100%
Coccinella septempuncata (larvae)	Ext. Lab.	48 h LR_{50}	< 37.5
Coccinella septempuncata (larvae)	Ext. Lab.	48 h LR_{50}	4.3
Coccinella septempuncata (larvae)	Aged residues	Mortality at 375 g a.s./ha	54 % at day 2, -3% at day 8
Coccinella septempuncata (larvae)	Semi field	Mortality at 75, 300 and 500 g a.s./ha	Over 80%
Chrysoperla carnea (larvae)	Ext. Lab.	48 h LR_{50}	< 37.5
Chrysoperla carnea (larvae)	Ext. Lab.	48 h LR_{50}	13.4
Poecilus cupreus (adults)	Lab.	Mortality at 37.5 g a.s./ha Feeding at 37.5 g a.s./ha	36.7 % 45% decrease
Poecilus cupreus (adults)	Semi field	Mortality at 125 g a.s./ha Feeding at 125 g a.s./ha	2 % 20% decrease
Poecilus cupreus (adults)	Semi field	Mortality at 300 g a.s./ha Feeding at 300 g a.s./ha	6 % 33% decrease
Rove beetles Web spiders Other invertebrate species	Semi field	Nb of insects trapped from 4 to 38 day after treatment at 125 g a.s./ha	No effect -30% up to 10 days No effect

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

Field or semi-field tests
A field study with *C. septempunctata* is available. The product was applied at 200 g a.s./ha. The RMS concluded that there is a tendency for recovery. The EFSA does not agree and considers further data necessary.

Risk assessment for demeton-S-methylsulphon (M01)

First tier risk assessment (according to ESCORT 2)					
Species	Crop	Application rate (g a.s./ha)	LR_{50} (g a.s./ha)	In-field HQ	Off-field HQ
Aphidius rhopalosiphi	Cereals	125	0.547 g a.s./ha	**228**	0.08
	Apple orchards	375		**8.82**	**2.6**
Typhlodromus pyri	Cereals	125	12.8 g a.s./ha	**9.76**	0.27
	Apple orchards	375		**29.3**	**8.56**
Second tier risk assessment (according to ESCORT 2)*					
Species	Crop	Application rate (g a.s./ha)	LR_{50} (g a.s./ha)	In-field HQ	Off-field HQ
Aphidius rhopalosiphi	Cereals	125	30	4.16	0.06
	Apple orchards	375		12.5	1.825
Typhlodromus pyri	Cereals	125	186	0.67	0.009
	Apple orchards	375		2.01	0.29
Coccinella 7-punctata	Cereals	125	< 37.5	-	-
	Apple orchards	375		-	-
Chrysoperla carnea	Cereals	125	< 37.5	-	-
	Apple orchards	375		-	-

Species and stage	Test type	Dose rate (g a.s./ha) or test type	Value (g a.s./ha)
Parasitoid			
Aphidius rhopalosiphi (adults)	Ext. Lab.	48 h LR_{50} determination Reproduction	30 49% reduction at 20 g/ha
Predatory mite			
Typhlodromus pyri (protonymphs)	Ext. Lab.	48 h LR_{50} Reproduction	186 42% reduction at 160 g/ha
Foliage dwelling predator			
Coccinella septempuncata (larvae)	Ext. Lab.	48 h LR_{50}	< 37.5

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

Species and stage	Test type	Dose rate (g a.s./ha) or test type	Value (g a.s./ha)
Chrysoperla carnea (larvae)	Ext. Lab.	48 h LR_{50}	< 37.5

Effects on earthworms (Annex IIA, point 8.4, Annex IIIA, point 10.6)

Acute toxicity ‡	Oxydemeton-methyl LC_{50} 14 d =115 mg a.s./kg soil M09 LC_{50} 14 d > 1 000 mg/kg soil M10: LC_{50} 14 d > 1 000 mg/kg soil M05[29]: LC_{50} 14 d > 1 000 mg/kg soil Metasystox R 250 EC: LC50 14 d 333 mg/kg soil corresponding to 80 mg a.s./kg soil
Reproductive toxicity ‡	Oxydemeton-methyl: NOEC 56 d = 3.75 kg/ha, corresponding to 412 g a.s./ha, calculated to be 0.55 mg a.s./kg soil in 5-cm depth
Field study	Metasystox R 250 EC: no effect on *Tanylobous* sp. and *Epilobous* sp. in an old pasture treated at 250 and 1000 g a.s./ha.

Toxicity/exposure ratios for earthworms (Annex IIIA, point 10.6)

PECsoil are calculated for two applications in a 5 cm depth soil of d = 1500 g/cm^3.

Crop	Group	Time scale	Distance (m)	Endpoint (mg/L)	PEC (microg/L)	TER
cereals	Oxydemeton-methyl	Acute	115 mg a.s./kg soil	0.194	592	10
		Chronic	0.55 mg a.s./kg soil	0.194	2.83	5
	M09	Acute	> 1000 mg a.s./kg soil	0.069	> 14493	10
	M10	Acute	> 1000 mg a.s./kg soil	0.044	> 22727	10
	Metasystox R 250 EC	Acute	80 mg a.s./kg soil	0.194	412	10
orchards	Oxydemeton-methyl	Acute	115 mg a.s./kg soil	0.291	395	10
		Chronic	0.55 mg a.s./kg soil	0.291	1.89	5
	M09	Acute	> 1000 mg a.s./kg soil	0.104	> 9615	10
	M10	Acute	> 1000 mg a.s./kg soil	0.065	> 15385	10
	Metasystox R 250 EC	Acute	80 mg a.s./kg soil	0.291	275	10

Effects on soil micro-organisms (Annex IIA, point 8.5, Annex IIIA, point 10.7)

Test substance	Parameter measured	observations
Oxydemeton-	Nitrogen transformation	Deviation of less than 25 % at 28 DAT for application rate up to 5 kg a.s./ha (6.67 mg a.s./kg

[29] M05: 1-(ethylsulfonyl)-2-(methylsulfonyl) ethane

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

Test substance	Parameter measured	observations
methyl-R 250 EC		soil)
	Carbon mineralisation	Deviation of less than 25 % at 28 DAT for application rate up to 6 kg a.s./ha (8 mg a.s./kg soil)
M09	Nitrogen transformation	Deviation of less than 25 % at 28 DAT for application rate up to 112.5 kg/ha (150 mg/kg soil)
	Carbon mineralisation	Deviation of less than 25 % at 28 DAT for application rate up to 1.9 mg test substance/kg soil
M10	Nitrogen transformation	Deviation of less than 25 % at 28 DAT for application rate 112.5 kg/ha (150 mg/kg soil)
	Carbon mineralisation	Deviation of less than 25 % at 28 DAT for application rate up to 2.05 test substance/kg soil

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	N; Harmful R50/53 Very toxic to fish, may cause long-term adverse effects in the aquatic environment (no information on biodegradation available)

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

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

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 Pesticide 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)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	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
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
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)
µg	microgram
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
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
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPUND CODES

Code	ISO common name	Systematic chemical name
ODM	oxydemeton-methyl	*S*-[2-(ethylsulfinyl)ethyl] *O*,*O*-dimethyl phosphorothioate
M01	demeton-S-methylsulphon	S-[2(ethylsulfonyl)ethyl]O,O-dimethylphoshorothioate
M02	demeton-S-methyl	S-[2(ethylthio)ethyl]O,O-dimethylphoshorothioate
M05	-	1-(ethylsulfonyl)-2-(methylsulfonyl) ethane
M06	-	O-methyl-S-[2(ethylsulfinyl)ethyl] phoshorothioate
M07	-	O-methyl-S-[2(ethylsulfonyl)ethyl] phoshorothioate
M09	-	2-ethylsulfinyl ethane sulfonic acid
M10	-	2-ethylsulfonyl ethane sulfonic acid
M11	-	bis-2-[(ethylsulfinyl)-ethyl]disulfide
M12	-	2-hydroxy-3-[(2-ethylsulfinyl-2-ethyl)-thio]propionic acid
M13	-	2-hydroxy-3-[(2-ethylsulfonyl-2-ethyl)-thio]propionic acid
M14	-	2-hydroxy-3-[(2-ethylsulfonyl-2-ethyl)-sulfinyl]propionic acid
M21	-	2-ethylsulfinyl-ethyl mercaptan
M22	-	2-ethylthio ethane sulfonic acid
DMP	-	dimethyl phosphate