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

malathion

finalised: 13 January 2006

SUMMARY

Malathion 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.

Finland being the designated rapporteur Member State submitted the DAR on malathion in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 2 February 2004. Following a quality check on the DAR, the peer review was initiated on 16 April 2004 by dispatching the DAR for consultation of the Member States and the sole applicant Cheminova A/S. There was also another notifier (Cequisa) according to Commission Regulation (EC) No. 703/2001 but it was not possible to reach an agreement and to provide a collective dossier. 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 in September 2004. 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 January – March 2005.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 30 November 2005 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 acaricide and insecticide as proposed by the applicant, which comprises foliar spraying to control various harmful organisms in apples, strawberries, alfalfa and ornamentals at application rate up 1.8 kg malathion per hectare. Malathion can be used as acaricide and insecticide.
The representative formulated product for the evaluation was "CHA 3110" ("Fyfanon 440"), an oil in water emulsion (EW), registered under different trade names in some EU Member States.

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

Adequate methods are available only for ground water and air to monitor all compounds given in the respective residue definition, i.e. malathion. In case of food of plant origin only methods for the determination of malathion and malaoxon are available. No method for the determination of malathion in food of animal origin was submitted. In case of soil and surface water no enforcement method for the determination of malathion is needed due to the fact that the DT_{90} values are less than 3 days.

Only single methods for the determination of residues are available. However, malathion and malaoxon can be determined by a multi-residue method (the applicability of the so-called extent S19 method has been demonstrated).

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.

The concentration of isomalathion in the batches of technical malathion tested in the toxicological studies is lower than in the specification (between 0.018%-0.44%, if mentioned at all, of the current specification.) The currently supported specification of malathion allows a maximum concentration of 0.2 % (w/w) isomalathion in the technical active substance and according to the FAO specification, it is 0.4 % (w/w).

Based on the available studies in the toxicological data package, only the 0.03% isomalathion content can be said to be covered. As for the level of 0.2% isomalathion, an additional safety factor of 10 was added to the ADI and the AOEL in order to be able to conclude on the risk assessment due to uncertainties in studies relevant for the setting of reference values. Furthermore, a data requirement for further genotoxicity studies to be performed has to be fulfilled and a non genotoxic potential demonstrated in order to be able to cover (from a toxicological point of view) the specification of 0.2% of isomalathion in the technical material.

The level of isomalathion in the current 5-batch analysis showed a mean content of 0.048-0.076%. This implies that the limit of 0.03% regarding the toxicological data package would not be feasible. Thus, the toxicological assumptions have to be based on the 0.2% limit. Furthermore, it is shown in the FAO specification that the amount of isomalathion even increases during storage both in relation to time and temperature by a factor of 2-10. Thus, the reference values have to be based on the 0.2% level.

Malathion is rapidly absorbed and excreted. There is no evidence of accumulation. The highest concentration was found in the liver, followed by skin, fat, bone and gastrointestinal tract. The metabolites excreted in urine and faeces were primarily the mono and dicarboxylic acids of malathion. Malathion was moderately toxic by the oral route in rat (a classification as Xn; R22 "Harmful if swallowed" is proposed). Malathion is not acutely toxic via the dermal route or through inhalation; it is not irritant to skin and eyes but it is a skin sensitizer (Xi; R43 "May cause sensitisation by skin contact "is proposed).

The target effect in short and long term studies is the decrease of acetyl cholinesterase activities. Overall, malathion does not show genotoxic potential *in vivo*. The occurrence of nasal tumours was due to a local mechanism of irritancy and cytotoxicity and no classification with regard to

carcinogenicity is proposed. Malathion induced a decrease in pup weights; but no classification is proposed. No neurotoxic potential was identified.
The reference values were all based on the specification on the content of 0.2% of the impurity isomalathion. Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 0.03 mg/kg bw/day, with a safety factor of 1000. Two Acute Reference Dose (ARfD) values are set. The first ARfD is 0.3 mg/kg bw/day based on available animal data with a safety factor of 100. The second ARfD is based on human data (isomalathion content 0.24%), is 1.5 mg/kg bw, with a safety factor of 10 added. The AOEL is exceeded for high crops (apples) but is below the AOEL for low crops (strawberry and alfalfa), with German model and PPE applied. The estimated exposure is below the AOEL for hand held application as well as indoor applications.
Re-entry exposure does not exceed the AOEL except for ornamentals in greenhouse; the exposure of bystanders is below the AOEL only strawberry application. Re-entry exposure does not exceed the AOEL for ornamentals in greenhouse. The estimated exposure is below the AOEL for strawberries and apples after a re-entry interval and when PPE is used. The estimated exposure during use of amateurs exceeds the AOEL. However, until isomalathion is proven non genotoxic, the operator risk assessment cannot be regarded as conclusive.

The metabolism of malathion in plants was studied in different crops. Results of those studies indicate that, even though the metabolic pattern appeared being comparable, significant differences in quantity of the formed metabolites, and therewith its relevance regarding consumer exposure, exist. The metabolism of malathion yields the major metabolites malathion mono- and dicarboxylic acid, and desmethyl-malathion; but also, even though at lower levels, malaoxon was identified.
Further information to address the toxicological relevance of malathion metabolites are required. With regard to consumer exposure, a number of data gaps have been identified in the expert meeting on residues. It is noted, that there may be additional data gaps resulting from conclusions drawn by experts in other sections, which have an impact on the residue section, but weren't considered by the residues experts at that time. Since there is a lack of data sufficiently addressing the hazard and/or the consumer exposure with regard to residues resulting from malathion use on food/feed crops, the consumer risk assessment cannot be concluded.

The available data demonstrate that in soil malathion degrades to the major (>10% applied radioactivity (AR)) metabolites malathion monocarboxylic acid (MMCA) malathion dicarboxylic acid (MDCA). Mineralization of the α carbon radiolabels in each ester moiety accounted for 50-67%AR after 92-162 days incubation at 20-22°C. The values for residues not extracted by acidified acetonitrile:water followed by methylenene chloride and a methanol Soxhlet extraction or 1N hydrochloric acid followed by acidified acetonitrile and an acetone Soxhlet extraction were 26-41% AR after 92-120 days. In soil malathion and MMCA exhibited very low persistence and MDCA exhibited low persistence.

In guideline batch soil adsorption studies malathion exhibited medium mobility. There was no evidence of pH dependant adsorption. MDCA exhibited very high to high mobility with adsorption

being pH dependent with lower adsorption at higher soil pH. The adsorption of MMCA could not be measured in batch adsorption studies due to its very rapid degradation. However it is considered it will have high to very high mobility depending on soil pH, based on extrapolation of the results from MDCA.

In sediment water systems malathion exhibited very low persistence breaking down to the major metabolites MMCA (which exhibited low persistence) and MDCA (which exhibited medium persistence). All the compounds remained primarily in the water phase of the test sediment water systems. Mineralization of the α carbon radiolabels in each ester moiety accounted for 58-69 % AR after 120 days at 20°C. Residues not extracted from sediment by acidified acetonitrile followed by Soxhlet extraction with acetone were also a sink for radioactivity representing 25-36%AR at 120 days. Levels of extractable radioactivity in sediment were relatively low (<15%AR) at all sampling times. MDCA was the largest proportion of this sediment extractable radioactivity but it accounted for a maximum of only 7.5%AR.

The available aquatic exposure assessment is appropriate for addressing the spray drift route of entry to surface water for malathion and its metabolites and the runoff and drainage routes of entry for malathion and it's MMCA metabolite. However MS should carry out a surface water exposure and consequent aquatic risk assessment for MDCA from the runoff and drainage routes of exposure at the national level, as the EU level assessment did not cover this situation, (although the risk is expected to be low as MDCA has low toxicity to the aquatic organisms tested).

The available FOCUS groundwater modelling indicates that the potential for groundwater contamination as a consequence of the representative field uses applied for, for annex 1 listing for malathion and its major soil metabolites MMCA and MDCA is minimal. (This may not be the case for other field uses especially if applications are possible over the late autumn and winter period. The available modelling indicated that in this situation contamination of vulnerable shallow groundwater by MDCA might be expected). A groundwater assessment is not available for the applied for intended use for glasshouse ornamentals.

Data are not available to conclude on the risk to birds and mammals following early application in apple orchards. For the late application in apples, and the use in strawberry and alfalafa, the risk to birds and mammals is considered low based on actual residue data, except the long-term risk for a small herbivorous mammal eating short grass in apple orchards. The TER obtained by assuming 30% deposition is 3.9 and the TER obtained based on actual residues in ground vegetation in the residue trial is 3.6, indicating a potential risk. Proposals for refinement have not been peer reviewed and need to be further justified. No exposure of birds and mammals from the use in glasshouses is expected.

Risk mitigation measures comparable to at least 50 m are required for the use in apples to protect the aquatic environment following late application in apples. For the early application even larger buffer

zones are needed. For strawberry and alfalfa 10 m buffer zones are required. The risk to aquatic organisms from the use on ornamentals in glasshouses is considered low.

The toxicity to bees is high and risk mitigation measures should be set at Member State level. For apples and alfalfa no application should be done during flowering. Risk mitigations measures are also needed to protect other non-target arthropods off field.

The risk to earthworms, other soil macro- and micro-organisms, non-target flora and biological methods of sewage treatment is considered low.

Key words: malathion, isomalathion, peer review, risk assessment, pesticide, acaricide, 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. Malathion is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Finland as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Finland submitted the report of its initial evaluation of the dossier on malathion, hereafter referred to as the draft assessment report, to the EFSA on 2 February 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 16 April 2004 to the Member States and the main applicant Cheminova A/S. 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 27 September 2004 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 was attending 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 expert meetings organised on behalf of the EFSA by the EPCO-Team at the Federal Office for Consumer Protection and Food Safety (BVL) in Braunschweig in January – March 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 30 November 2005 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 14 October 2004)
- 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. 1-2 of 1 December 2005)

Given the importance of the draft assessment report including its addendum (compiled version of November 2005 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.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Malathion is the ISO common name for diethyl (dimethoxythiophosphorylthio)succinate or *S*-1,2-bis(ethoxycarbonyl)ethyl *O,O*-dimethyl phosphorodithioate (both, IUPAC).

Malathion belongs to the class of organothiophosphate acaricides such as diazinon, phosalone and phosmet and to the class of aliphatic organothiophosphate insecticides such as cadusafos and ethoprophos. Malathion is located either in the waxy plant cuticle or in the leaf apoplast, but is not exposed to phloem transport and is acting as a cholinesterase inhibitor.

The representative formulated product for the evaluation was "CHA 3110" ("Fyfanon 440"), an oil in water emulsion (EW), registered under different trade names in some EU Member States as acaricide and insecticide as proposed by the applicant, which comprises foliar spraying to control various harmful organisms in apples, strawberries, alfalfa and ornamentals at application rate up to 1.8 kg malathion per hectare. Malathion can be used as acaricide and insecticide.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of malathion as manufactured should not be less than 950 g/kg which is in compliance with the FAO Specification 12/TC (December 2004). It should be noted that the technical material is a racematic mixture. The technical material contains four impurities that have to be regarded as relevant. The proposed maximum levels are 1 g/kg for malaoxon[3], 15 g/kg for the MeOOSPS-triester[4], 5 g/kg for the MeOOOPS-triester[5] and 2 g/kg for isomalathion[6]. The value for isomalathion should be regarded as provisional and is lower than the value set in the FAO specification (4 g/kg), due to the fact that the submitted data package for toxicology does not support a higher the value than of 2 g/kg (see section 2).
Moreover, it should be noted that the FAO specification is based on an evaluation of data submitted by the manufacturer Cheminova and applicable to products of this manufacturer. The FAO specification may not be appropriate for the products of other manufacturers.

The content of malathion in the representative formulation is 440 g/L (pure).

According to the FAO specification (12/EW, December 2004), the maximum content of the four relevant impurities in the formulation should not be higher than 0.8% of the malathion content for malaoxon, 0.6% for isomalathion, 1.6% for the MeOOSPS-triester and 0.5% for the MeOOOPS-triester. However, the submitted data package for toxicology does not support a higher value than 2 g/kg of isomalathion in the technical material at the moment. Thus, the maximum content of isomalathion in the representative formulation ("CHA 3110", "Fyfanon 440") should not be higher than 0.88 g/L taken into account the application rate of 1.8 kg/ha as well as the content of malathion in the representative formulation.
According to the results of the shelf-life studies all amounts were in compliance with these limits.

Beside the lower value for one relevant impurity, the assessment of the data package revealed no particular area of concern in respect of the identity, physical, chemical and technical properties of malathion or the respective formulation.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of malathion in the technical

[3] Malaoxon: butanedioic acid, (dimethoxyphosphinothioyl)-, diethyl ester; CAS No. 1634-78-2
[4] MeOOSPS-triester: phosphorodithioic acid, *O*,*O*,*S* trimethyl ester; CAS No. 2953-29-9
[5] MeOOOPS-triester: phosphorothioic acid, *O*,*O*,*O* trimethyl ester; CAS No. 152-18-1
[6] isomalathion: succinic acid, mercaptodiethylester, *S* ester with *O*,*S*-dimethyl phosphorodithioate; CAS No. 3344-12-5

material and in the representative formulation. Also for the determination of the significant and relevant impurities in the technical material as well as for the relevant impurities in the formulation sufficient analytical methods are available.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available only for ground water and air to monitor all compounds given in the respective residue definition, i.e. malathion for both matrices. In case of food of plant origin no method for the determination of desmethyl malathion would be available. A validated method would be necessary, in case the residue definition will be amended to malathion, malaoxon and desmethyl malathion expressed as malathion (see 3.1 and 3.4).
In contrast to what is stated in the DAR, an analytical method for the determination of residues in food of animal origin is needed, because in the meantime a residue definition (malathion, only) as well as MRLs are proposed (see 3.2 and 3.4).
In case of soil and surface water no enforcement method for the determination of malathion is needed due to the fact that the DT_{90} values are less than 3 days (being aware that the DT_{90} value in soil depends on the soil characteristics). However, validated methods for the determination of malathion in soil and surface water would be available. In case the metabolite MDCA[7] would be the target analyte for monitoring purposes, only a validated method for the determination of MDCA in surface water would be available (LOQ 0.5 mg/kg).

The methodology used is GC with FP detection and HPLC with MS/MS detection. None of them is enantio selective. Residues of malathion and malaoxon in food of plant origin can be determined according to the so-called "extended S19 method" (method L.00.00.34, Collection of Official Methods under Article 35 of the German Federal Food Act). However, the limit of quantification is not for all tested crop types in compliance with the criteria of Annex VI and SANCO/825/00, where is stated that the LOQ should be ≤ 0.1 mg/kg in cases where the MRL is > 0.1 mg/kg. The applicability for desmethyl malathion is not reported

The discussion in the expert meeting (EPCO 20, March 2005) on identity, physical and chemical properties and analytical methods was limited to the specification of the technical material, certain physical and chemical properties of malathion and to the analytical methods.

2. Mammalian toxicology

Malathion was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 18) in February 2005.

[7] MDCA: malathion monocarboxylic acid

The purity of the technical malathion used in the studies submitted in the dossier ranged from 92.1 % to 98 % active substance (minimum purity > 95%). Four impurities are regarded as relevant of which isomalathion is of a toxicological concern. One of the major problems is related to the toxicological impact of isomalathion on the toxicological profile of malathion.

The concentration of isomalathion in the batches of technical malathion tested in the toxicological studies is lower than in the specification (between 0.018%-0.44%, if mentioned at all, of the current specification). The currently supported specification of malathion allows a maximum concentration of 0.2% (w/w) isomalathion in the technical active substance and according to the FAO specification, it is 0.4% (w/w).

Based on the available studies in the toxicological data package, only the 0.03% isomalathion content can be said to be covered. As for the level of 0.2% isomalathion, an additional safety factor of 10 was added to the ADI and the AOEL in order to be able to conclude on the risk assessment due to uncertainties in studies relevant for the setting of reference values. Furthermore a data requirement for genotoxicity studies to be performed has been proposed during the experts´ meeting (see 2.4).

In a post meeting at EFSA between co-chairs of physical chemistry and mammalian toxicology the level of isomalathion in the current 5-batch analysis was reviewed and discussed. It showed a mean content of 0.048-0.076%. This implies that the limit of 0.03% regarding the toxicological data package would not be feasible and that the toxicological assumptions have to be based on the 0.2% limit. Furthermore, it is shown in the FAO specification that the amount of isomalathion even increases during storage both in relation to time and temperature by a factor of 2-10. Thus, the reference values have to be based on the 0.2% level.

2.1 ABSORPTION, DISTRIBUTION, EXCRETION AND METABOLISM (TOXICOKINETICS)

Malathion is rapidly absorbed (90% within 72 hours, based on urinary excretion data), biotransformed and excreted mainly in urine (76-88 % of the dose in urine and 6-14% in faeces). There is no evidence of accumulation. The highest concentration was found in the liver, followed by skin, fat, bone and gastrointestinal tract. The metabolites excreted in urine and faeces were primarily the mono and dicarboxylic acids of malathion.

2.2 ACUTE TOXICITY

Malathion was moderately toxic by the oral route in rat (LD_{50} 1778 mg/kg bw) based on a recent study (Moore, 2002), therefore, a classification as **Xn; R22 "Harmful if swallowed**" is proposed. Malathion is not toxic via the dermal route (LD_{50} > 2000 mg/kg bw in the rat) or through inhalation (LC_{50}>5 mg/L). Malathion is not an irritant to skin and eyes but it is a skin sensitizer. Therefore, **Xi; R43 "May cause sensitisation by skin contact "** is proposed. The isomalathion content in the acute studies referred to was 0.4%.

2.3 SHORT TERM TOXICITY

The target effect in short term studies is the decrease of acetyl cholinesterase activities. The information on the isomalathion content in the dog studies is not known and the studies are thus

considered as of limited evidence. However, it was concluded by the experts that the NOAEL in the 28 day study is < 125 mg/kg bw/day and in the 1 year study < 62.5 mg/kg bw/day.
The 90-day feeding study in rat, was discussed at the experts´ meting and it was agreed to increase the NOAEL from 6.6 mg/kg bw/day (as originally proposed by the RMS in the DAR) to 34.4 mg/kg bw/day. The acetyl cholinesterase inhibition in brain was considered to be the relevant toxicological end point, 9% in males and 10% in females. The isomalathion content in this study was 0.03%. This was considered to be the relevant short term NOAEL.
The toxicity of malathion by dermal route was tested in a 21-day study in rabbit (isomalathion content, 0.2%) and the NOAEL was 300 mg/kg bw/day based on (decreased brain acetyl cholinesterase activities). The toxicity of malathion by inhalation was tested in a 14-day and a 90-day study in rat. In the 14-day study, the NOAEL for cholinesterase inhibition could not be determined. In the 90-day study, the NOAEL for (brain acetyl cholinesterase inhibition was 0.45 mg/L.)

2.4. GENOTOXICITY

Malathion was tested in a number of *in vivo* and *in vitro* studies.
The chromosomal aberration test with human lymphocytes as well as a mouse lymphoma test (both studies are from 2001) gave positive results, the isomalathion content was 0.14%. An *in vitro* UDS test was negative (0.2 % isomalathion). Although the Ames test was negative, a concern was raised on the quality since no information on the isomalathion content was provided.

Increased frequency of metaphases with chromosomal aberrations was observed in the absence of metabolic activation in a chromosome aberration test with human lymphocytes but the increased frequency was not seen later in a second test which was performed at lower concentrations. Both of the *in vivo* tests with assays of somatic cells were negative (isomalathion content was 0.2%).

It was considered by the experts that the positive results observed in the *in vitro* tests may be due to isomalathion and other impurities, as reported also in the open literature. However, the positive effects reported in the open literature were discussed during the meeting: all the available data support the conclusion that there is no genotoxic potential *in vivo*. No information on the genotoxic potential on isomalathion is provided in the DAR. For an isomalathion content of 0.03%, the experts agreed on that there was not a genotoxic potential. However, if the request on the 0.2% isomalathion content in the specification is maintained, the EPCO 20 meeting concluded that a new Ames test (with the isomalathion content of 0.2%) would be required or identified as a data gap. If this study would demonstrate a positive result it is not possible to set limit values and a secondary test, an UDS test would be required. A new Ames test with 0.2% isomalathion was submitted in August 2005 and assessed by the RMS, but not peer reviewed.

2.5 LONG TERM TOXICITY

Long term toxicity of malathion was assessed in 2 chronic toxicity/carcinogenicity studies in rat and in a 18-month study in mouse. The target effect was the inhibition of acetyl cholinesterase activity.

The occurrence of nasal tumours in the rat was discussed in the addendum and during the meeting. Nasal tumours were observed at the highest dose levels and were found to be related to an irritation mechanism caused by a prolonged high level exposure of nasal epithelium to malathion from food as a vapour or absorbed to inhaled food particles. Exposure to acids produced with malathion metabolism would lead to irritancy and cytotoxicity. This condition produces a state of reactive hyperplasia, one of the major causative factors in tumours. Liver tumours were also observed in the mouse, but only at high dose levels, the NOAEL for tumours is 143 mg/kg bw/day. No classification with regard to carcinogenicity was proposed by the experts.

The overall NOAEL for long term toxicity and carcinogenicity is 29 mg/kg bw/day, from the 2-year rat study based on inhibition of acetyl cholinesterase activity in brain. The isomalathion content in the studies are 0.03% and 0.018%.

2.6. REPRODUCTIVE TOXICITY

In the two-generation toxicity studies, the parental NOAEL was 595/655 (M/F) mg/kg bw/day and the reproductive and offspring NOAEL is 132/152 (M/F) mg/kg bw/day based on the decreased pup weights.

In teratogenicity studies in rabbits, there was an increased incidence of resorptions not attributable to decreased body weight in dams, suggesting that resorptions were not related to maternal toxicity. Although not dose-related, the number of resorptions at the two highest dose levels was about twice higher than in controls. Thus, the experts agreed on a parental and teratogenicity NOAEL of 25 mg/kg bw/day. The isomalathion content in the batch used is not reported in the study.

2.7. NEUROTOXICITY

Malathion did not induce delayed neurotoxicity in hens. Due to clinical signs, no NOAEL in an acute neurotoxicity study with rats could be determined. In a 13-week neurotoxicity study in rat, the lowest relevant NOAEL for acetyl cholinesterase inhibition is 4 mg/kg bw/day, based on brain cholinesterase inhibition.

The developmental neurotoxicity of malathion was investigated with rats in one developmental neurotoxicity and one supplementary study addressing effects on cholinesterase activities. A NOAEL of 50 mg/kg bw/day (based on clinical signs and behavioural assessment in a developmental toxicity study and brain acetyl cholinesterase esterase inhibition in pups in a supplementary study) was agreed on by the experts.

2.8. FURTHER STUDIES

Metabolites

Malaoxon

The NOAEL of malathion metabolite, malaoxon, for acetyl cholinesterase inhibition in brain was 1 mg/kg bw/day in rats in a 24-month study. There was evidence of leukaemia at 114 mg/kg bw/day in males a dose level where marked toxicity was observed including increased mortality.

Isomalathion

No studies have been provided from the notifier.

According to the review by Litchfield (2003 and 2004) presented in the addendum it is evident that isomalathion increases the toxicity of malathion. In acute studies, malathion spiked with 2% of isomalathion is approximately 10-fold more toxic than pure malathion without any isomalathion. It has a high to moderate toxicity. Furthermore, it is shown in the FAO specification that the amount of isomalathion increases during storage both in relation to time and temperature by a factor of 2-10.

In the DAR several acute toxicity studies in the rat are reported, where it is demonstrated that increasing the amount of isomalathion such as the Fischer, 1991b where the isomalathion content is 0.018% the LD_{50} is 5000 mg/kg bw, the in two other studies with 0.3% and 0.44% of isomalathion, the LD_{50} is 1649 and 1778 mg/kg bw, the recent study from 2002 (which is reported in the list of endpoints).

Malathion dicarboxylic acid

No studies have been provided by the notifier on malathion dicarboxylic acid (MDCA). However, MDCA has been identified in rat metabolism studies (in urine in low dose males) to a level of 13% and it was concluded by the experts that it should be considered as of equivalent toxicity as malathion.

EFSA note: This might apply also to malathion monocarboxylic acid (MMCA).

Desmethyl-malathion

No studies have been provided by the notifier on desmethyl-malathion (DMM). However, DMM has been identified in rat metabolism studies (in urine in low dose males) and it was concluded by the experts that without experimental data DMM cannot be considered as less toxic than malathion.

Human study

In humans, metabolism and excretion of malathion appears to be very rapid with the majority of the metabolites formed and excreted within the first 12 hours after ingestion (Gilles and Dickinson, 2000). However, there seems to be considerable variation in the metabolic pathways between different persons.

Oral administration of malathion to human volunteers as a single dose up 15 mg/kg bw did not cause any significant changes in vital signs, ECGs, haematology, clinical chemistry, urinalysis or physical examination in any of the 48 of which 14 with placebo subjects during the study. Malathion did not cause any inhibition of plasma or RBC cholinesterase in either male or female subjects even at the highest dose. The average dermal absorption of malathion in a human voluntary study ranged from 5.5 % to 15 %, depending on the formulation.

The scientific acceptability of the single oral dose study in humans was discussed during the meeting. Although, the study shows some weaknesses it was agreed that the study has been performed on basis of scientific knowledge and the (NOAEL) of 15 mg/kg bw was confirmed. The meeting discussed the

possibility to use it for setting of ARfD and discussed the possible safety factor. The experts agreed that in the case the isomalathion content in this study is 0.2% or above a safety factor of 10 would be appropriate. In the case the isomalathion content would be less than 0.2% or unknown a safety factor of 100 would be applied. The human oral study was performed with malathion containing 0.24% isomalathion. The safety factor of 10 for the specification with 0.2% isomalathion in malathion is proposed.

2.9. MEDICAL DATA

There have been no proven poisoning incidents caused by malathion during normal production in the period from the middle of the 70's until 1994. No reliable differences were found in the observed mortality or incidence of cancer in relation to that expected among the staff who had been employed for at least one year in a manufacturing plant of malathion in the period of 1953-1993. The survey was, however, not large enough to exclude occupationally-related reasons for the more rare causes of death or cancer illnesses.

Fifty six published studies of human poisoning incidents to malathion were reported. A total of 8 cases with accidental ingestion are reported. Occupational or residential exposure is described in 18 publications. The most severe poisonings have occurred when malathion has been broken down to products such as isomalathion which are more toxic than the parent compound.

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

ADI and AOEL

The experts considered the NOAEL from the long term rat study to be the most appropriate basis for the ADI (29 mg/kg bw/day) and the NOAEL of 34 mg/kg bw/day in the 90-day rat for the AOEL.

In the current short term long term study the content of the impurity isomalathion is 0.03% and in the long term it is 0.03% and 0.018%. The content of isomalathion in the specification for Annex I inclusion is 0.2% and for the FAO specification 0.4%.

The experts agreed that the ADI and AOEL would only cover a technical material of malathion with an isomalathion content of 0.03%. In that case, the ADI and AOEL was agreed to be 0.3 mg/kg bw (rounded value) with the safety factor of 100 added. However, according to the current 5-batch analysis this would not be feasible (see introductory part of section 2)**.**

Therefore, considering the level of 0.2% of isomalathion concerns were raised in relation to a) that the end point measurements of effects on acetyl cholinesterase was only determined at the level of 0.03% of isomalathion as well as b) the inconclusive genotoxic potential of malathion and the impact of isomalathion (see 2.4).

Thus, an additional safety factor of 10 was agreed in the case the specification would be 0.2% of isomalathion and a new Ames test with malathion containing 0.2% isomalathion was required.

The resulting ADI as well as AOEL is 0.03 mg/kg bw/day (rounded value) for the test material containing 0.2% isomalathion with a safety factor of 1000.

ARfD

The ARfD should be based on the developmental toxicity rabbit study. A NOAEL of 25 mg/kg bw/day and a LOAEL of 50 mg/kg bw/day have been reported in this study (isomalathion content not reported). The experts concluded this study to be the appropriate one to derive the ARfD.

The proposed ARfD based on animal data is therefore 0.3 mg/kg bw based on the developmental rabbit study with a safety factor of 100.

The safety factor applied for the ARfD was not increased since the end point was increased incidence of resorptions not acetyl cholinesterase inhibition. The ARfD is it is supported by the data from the rat studies were inhibition on acetyl cholinesterase inhibition was observed and the isomalathion content was 0.14%,

The human oral study was performed with malathion containing 0.24% isomalathion and was considered as scientific valid and was considered for setting a second ARfD. The safety factor of 10 for the specification with 0.2% isomalathion in malathion is proposed and the resulting **ARfD proposed based on a human study is 1.5 mg/kg bw.**

2.10 DERMAL ABSORPTION

A human voluntary study was presented in the DAR, showing average dermal absorption of malathion in the study ranging from 5.5% to 15%, depending on the formulation. Some MS commented on the reliability of the study due to major weaknesses (total duration of exposure, low recovery of radioactivity).

New studies were submitted in the addendum and discussed during the experts´ meeting.

In an *in vivo* study in rats, the total absorption of malathion after 24 h was 1.53% for the undiluted suspension concentrate and 12.7 % for the field spray dilution. (excluding tape strips). The experts, however, agreed on a value of 1.9% after 168 h (instead of 1.53% after 24 h) for the concentrate taking into account that adsorption from the stratum corneum will continue.

Based on an *in vitro* rat/human data, dermal absorption values of 2% for the concentrate and 5% for the dilution were established.

However, based on the outcomes of the *in vivo* human study, the experts proposed a worst case assumption for human risk assessment and proposed to use a dermal absorption value of 5% for the concentrate and 15% for the dilution.

2.11 EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

Operator exposure

The representative product is formulated as a liquid oil in water emulsion (EW) containing 440 g/L malathion. The formulation also contains 9% of emulsifiers and adjuvants, and water (ad 100% by weight). Malathion is used for controlling harmful pest organisms in apples, strawberries, alfalfa and glasshouse ornamentals. The crops may be treated both with tractor mounted equipment (field crop and orchard sprayers) and with hand-held application methods directed downwards or upwards.

The intended application rates vary between 0.114 to 1.80 kg malathion/ha.

The operator exposure in different scenarios was estimated by the German model, the UKPOEM model and EUROPOEM. Greenhouse exposure was estimated by the modified Dutch model. As the dermal absorption value was revised during the experts´ meeting, 5% for a concentrate and 15% for a spray solution as well as the AOEL, 0.03 mg/kg bw/day new calculations were provided in the addendum and is summarised in the table below.

Scenario	Model	No PPE	With PPE*
High crops (apples)	German	4791	262
	UK POEM	2871	1185
Low crops (alfalafa, strawberries)	German	1525	71
	UK POEM	2240	163
Hand held, apples	German	1424	59
Hand held strawberries	UK POEM	1804	245
Ornamentals, indoor	Dutch	20	7

*UK-POEM: gloves during mixing/loading and application; in hand held application on strawberries, an impermeable coverall is considered

German model: gloves during M/L and application, coverall and sturdy footwear during application

Dutch model: long trousers, short-sleeved shirt and gloves

According to estimations with the EUROPOEM model, results showed that the AOEL was exceeded in all field application methods when personal protective equipment was not used (range: 366-19,000% of AOEL). When personal protection equipment (gloves, coverall) is taken into account the operator's exposure for apple broadcast and for strawberry hand held applications is still exceeding the AOEL.

Strawberry and alfalfa ground boom applications (with PPE) were found to be below the AOEL with German model. Exposures below the AOEL are apple hand held application with German model as well as indoor applications (ornamentals) with Dutch model.

Worker exposure

The worker exposure was re-calculated using new dermal absorption rate of 15% (spray solution). The dermal, as well as inhalation, re-entry exposure estimations are calculated using updated recommendations of the EUROPOEM II final, December 2002.

Re-entry exposure after a single application as well after consecutive applications for both apples and strawberries exceeded the AOEL (170-660%) even when personal protection equipment is worn (coverall and gloves). For roses (glass house) the re-entry exposure is below AOEL (96% without PPE, 25% with gloves).

Bystander exposure

In tractor mounted applications a bystander is assumed to stand at the distance of 8 m from the source. When using hand held methods or static equipment the distance is assumed to be shorter, 1- 2 m from the source.

The potential exposure of a bystander was estimated by using the dossier's parameters for arable spraying (strawberries) and orchards (apples) when using tractor mounted and hand held methods. The strawberry exposure scenario covers also the bystander exposure in alfalfa applications (strawberry has higher dose than alfalfa). Exposure time was considered to be one hour, which is a conservative assumption. Absorption via inhalation is assumed to be 100 % and 15 % via dermal route (spray solution). The bystander is assumed to weigh 60 kg.

The exposure of bystanders represents 13-80 % of the AOEL for the strawberry application scenario and 157-470 % for orchard spraying scenario, with and without the use of PPE.

Amateur exposure

Malathion 440 g/l EW product can be used besides of agricultural applications also by amateurs in strawberry, apple and ornamental cultivations in home gardens. Amateur exposure was estimated in an addendum. The exposure scenario in amateur uses differs significantly from the professional uses. Amateurs are not assumed to use PPE. The spraying areas as well as spraying durations are considered to be clearly smaller in home garden applications than in professional applications.

The German model and the UK-POEM predictions indicated that the amateur´s exposure during strawberry, ornamentals and apple spraying exceeds the AOEL. There might also be a concern for bystander and re-entry situations, especially in the case of children.

3. Residues

Malathion was discussed at EPCO experts' meeting for residues (EPCO 19) in Braunschweig (Germany) in February 2005. A number of data gaps have been identified during this meeting. It is noted, that there may be additional data gaps resulting from conclusions drawn by experts in other sections, which have an impact on the residue section, but couldn't considered by the residues experts at the time of their meeting.

Shortly before the second discussion of malathion in the evaluation meeting the applicant provided EFSA with a position paper, indicating that apparently further data and information have been generated and submitted to the RMS in October 2005. It is noted, that in that position paper the applicant also questions the results reported in a metabolism study formerly considered valid and indicates the reassessment of that study. However, due to the very late submission this data was neither assessed nor peer reviewed and its acceptability is unclear. Thus, it is not referred to in the conclusion on the section of residues presented below.

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of ^{14}C-malathion was initially studied in four different crops: alfalfa, cotton, lettuce and wheat. Later in the process a metabolism study on apples was submitted and evaluated in addendum 1 to the DAR. Malathion was applied to apples at N rate, and to alfalfa and wheat forage at *ca* 2.5 N rate, with regard to the representative uses evaluated. Uses on the other tested crops, such as oilseeds or leafy crops, are currently not part of the peer review process.

The majority of the radioactive residues was identified or characterised in those studies. Unchanged malathion was found in each crop matrix tested and was, with the exception of apples, the major residue, amounting to 10 – 42 % of TRR. Main metabolites were malathion monocarboxylic acid (up to 12.8 % TRR in lettuce), malathion dicarboxylic acid (up to 4.9 % TRR in wheat forage), and desmethyl malathion (up to 48.8 % TRR in apples). It is noted that percentage TRR of desmethyl-malathion was much lower in the other crops (0.1-0.5% TRR); however, the expert meeting on residues concluded that the high level of desmethyl-malathion in apples may give rise to concern in terms of consumer exposure, and hence clarification on its toxicological properties was needed. The experts' meeting for toxicology (EPCO 18) advised that without experimental data it was not possible to conclude that desmethyl-malathion was less toxic than malathion. (refer to 2.8) Thereupon a data gap was identified by the experts, namely, data addressing the toxicological properties of desmethyl-malathion need to be submitted. Another outcome of EPCO 18 was that malathion dicarboxylic acid (MDCA) should be considered as of equivalent toxicity as malathion. This might also apply to malathion monocarboxylic acid (MMCA). However, this information was made available after the residues experts' meeting, and thus, it couldn't be considered by the residues experts anymore.
Malaoxon, already proven as a toxicologically significant metabolite (refer to 2.8), was found in all tested crops; determined levels were 0.8 % TRR (1.8 mg/kg) in alfalfa hay, 0.4 % of TRR (0.04 mg/kg) in wheat grain, 0.1 % of TRR (0.20 mg/kg) in wheat straw, 1.2 % of TRR (5.3 mg/kg) in lettuce, 0.2 % of TRR (0.30 mg/kg) in cotton seed and up to 7.7 % TRR (0.20 mg/kg) in apples (PHI 7). The experts noted that the results for malaoxon found in the metabolism studies, in particular in the study on apples, seem not to correspond with the results gained from the supervised residue trials, in which residues of malaoxon were rarely above LOQ (0.01 mg/kg). The meeting agreed that this discrepancy needs to be further elaborated and explained by the applicant, before a conclusion can be drawn whether or not consumer exposure to malaoxon residues in apples might be significant.
Low levels of isomalathion, a known significant impurity of malathion, was found in alfalfa hay (0.2 % of TRR, 0.43 mg/kg). In the metabolic study on apples non-radioactive isomalathion was found qualitatively by HPLC MS/MS in all samples, indicating that isomalathion may contribute to residue levels as an impurity.
Other metabolites were identified but they were present each at amounts less than 1% TRR. Among these metabolites were diethyl maleate, monoethyl maleate, diethyl mercaptosuccinate, diethyl methylthiosuccinate, diethyl fumarate and tetraethyl dithiodisuccinate. Radioactivity was also found in endogenous plant constituents such as cell wall fractions including starch, protein, pectin, lignin, hemicellulose and cellulose.

In alfalfa, cotton, lettuce and wheat the main metabolic pathway proceeded via de-esterification of malathion to form malathion monocarboxylic and dicarboxylic acids and then succinic acid. The succinate was apparently incorporated into small organic acids and sugars via the citric acid cycle. In apples a main route of metabolism seems to be the transformation of malathion to desmethyl-malathion. However, the presence of malathion dicarboxylic acid indicates that, on another route, malathion metabolites also enter the pool of endogenous components.
Though the metabolism of malathion appeared to be qualitatively the same in all five tested crops, differences in quantity of metabolites became obvious, and therewith their relevance with regard to consumer exposure. This refers in particular to desmethyl malathion, but also to malaoxon.

A study simulating normal processing practice by applying representative hydrolytic conditions indicated that with increasing temperature malathion becomes increasing labile and degrades rapidly to desmethyl-malathion.

Taking into account the observation in the apple metabolism and the simulated processing study with regard to desmethyl malathion, EPCO 19 concluded that the residue of concern for risk assessment in plants should be the sum of malathion, malaoxon and also desmethyl malathion, expressed as malathion. It is noted, that this proposal was made by the experts without being aware of the latest EPCO 18 conclusion concerning the toxicological relevance of MDCA, and also MMCA.
For monitoring purposes the residue should be defined as sum of malathion and malaoxon, expressed as malathion, unless it turns out to be desmethyl-malathion even more toxic than malathion. In that case desmethyl-malathion should be included in the residue definition for monitoring, too.

A total of 20 supervised residue trials have been conducted with malathion in open field conditions on apples, strawberries and alfalfa. The trials were reported in sufficiently detail and were supported by acceptable analytical information. The residues were analysed and expressed as malathion and malaoxon. Desmethyl-malathion was not analysed for in any of the submitted supervised field trials. Thus, the available data don't correspond to the proposed residue definition for risk assessment, but might be suitable to propose MRLs subject to whether or not desmethyl-malathion will be included in the residue definition for monitoring.
In processing studies in apples and tomatoes the effects of processing on residue levels of malathion and malaoxon have been investigated, but again, desmethyl-malathion was not considered. In the apple processing study residues of malathion and malaoxon concentrated in wet pomace, but not in juice. The pasteurisation procedure applied for processing tomatoes to puree and ketchup was considered adequate to reflect also the preparation of canned fruit (e.g. strawberries). A marked decrease of malathion and malaoxon residue levels was observed. According to these results it was concluded by the RMS that residues of malathion and malaoxon will not concentrate in processed foods consumed by humans. However, the conclusion on processing studies will need to be reconsidered in the light of the relevance of desmethyl-malathion.

Consequently, the expert meeting phrased a data gap for the applicant to present data on the level of desmethyl-malathion on raw agricultural commodities (RAC) and processed products, unless it can be proven that desmethyl-malathion is not of toxicological relevance. Furthermore data demonstrating the stability of desmethyl malathion under storage conditions is needed.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Malathion is rapidly degraded in soil. Basically, in such cases a rotational crop study is not required. Nevertheless such a study was submitted and evaluated in the DAR. The study indicated, that the degradation of malathion in the soil and formation of bound residues in soil probably leaves applied radioactivity only partly available for uptake for rotational crops. Radioactivity taken up from soil into plants was degraded in a similar manner as observed in plant metabolism studies. However, the expert meeting on residues proposed a data gap in order to clarify the residue situation of desmethyl-malathion in rotational crops, which was not addressed by the information currently available.
EFSA note: Potential uptake of MMCA and DCMA into rotational crops might also need to be considered. (see also 3.1.1 and 4.1.1)

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Livestock metabolism was studied in dairy goats and laying hens by orally dosing the animals with ^{14}C-malathion for 5 and 4 consecutive days, respectively. Radioactivity was rapidly excreted and hence mainly found in goat urine (55% of total dose) and faeces (11%); and in hen excreta (29%), respectively. Excretion in milk was minor (0.5-2% total dose) and TRR in milk plateaued from day 2 through day 5 of treatment. Residue levels in eggs were not reported; and TRR in egg yolk didn't reach a plateau within the 4 days dosing period. Other excretory routes (i.e. volatiles) were not investigated but may represent a significant route of elimination. The overall accountabilities of the studies were not reported.
In organs and edible tissues of both species TRR were highest in the excretory and metabolising organs liver and kidney. Chromatographic profile analysis showed that neither malathion nor its immediate metabolites were present at levels exceeding the LOQ in edible tissues, milk and eggs, with the exception of goat kidney were metabolites MDCA and MMCA were found at levels about LOQ. MDCA and MMCA were present at high levels in urine samples.
Results from these studies suggest that malathion is rapidly and completely metabolised and incorporated into naturally occurring biochemical compounds such as intermediates in the TCA cycle (citrate cycle), proteins, triglycerides, and lactose. Neither malathion nor any toxicologically significant products arising from its immediate metabolism is expected to occur in edible animal matrices. Thus, no residue definition was proposed for ruminants and hens in a first place.

It is noted that besides malathion (and malaoxon) the metabolite desmethyl-malathion is part of the plant residue definition and may form a major residue component in livestock feed. As such, the metabolism studies with malathion might be considered less relevant in the light of the proposed residue definition for plants. In addendum 3 to the DAR, which was neither peer reviewed nor discussed by experts, RMS has elaborated aspects regarding the potential dietary intake of desmethyl-

malathion by livestock. Based on evidence from open literature desmethyl-malathion is formed within animal metabolism, but is found only in urine and not in tissue. Further on, desmethyl-malathion is more polar than malathion. According to those data RMS suggests that also desmethyl-malathion has a high elimination rate and thus a low accumulative potential. It is therefore hypothesised by RMS that any intake level of desmethyl-malathion, yielding from the representative uses, would most likely not lead to significant residue levels in animal tissues. However, RMS emphasised that more data is needed to allow firm conclusions. Estimates of desmethyl-malathion intake levels by livestock animals are based on plant metabolism studies only and not on residue trials, and furthermore, test animals in livestock metabolism studies were dosed with malathion only. Consequently, it is currently not possible to be assured whether residue levels in food of animal origin will be indeed not detectable, i.e. $\leq$ 0.01 mg eq/kg (per single compound), as observed in the submitted livestock metabolism studies with malathion. Currently residue levels at the limit of detection for animal products have been proposed by RMS in the listing of endpoints, based on a residue defined as malathion and desmethyl-malathion, expressed as malathion. It is noted that neither the proposed residue definition for livestock nor the proposed residue levels for food of animal origin have been peer reviewed or discussed by experts and need to be re-evaluated upon receipt of the outstanding data related to desmethyl-malathion residues. A reassessment may also need to consider potential residues of MMCA and MDCA in animal products.

It is currently not possible to conclude whether or not MRLs for food of animal origin need to be proposed.

3.3. CONSUMER RISK ASSESSMENT

Currently, the acute and chronic dietary risk assessment for consumers **cannot be concluded** as long as the toxicological relevance of desmethyl-malathion is not clarified and further residue data on desmethyl-malathion are not made available. Furthermore the relevance of the metabolites MMCA and MDCA for consumer exposure is currently unclear. No assessment and discussion took place in the light of the decision of the toxicology experts' meeting. Lastly for the uses in apples, further information is needed to conclude whether or not consumer exposure to residues of malaoxon (more toxic than malathion) in apples might be significant.

A provisional risk assessment would need to include a combination of a number of assumptions on the toxicological properties and/or on the residue behaviour of desmethyl-malathion, MMCA, MDCA and malaoxon. A sound risk assessment is only possible upon receipt of data addressing the identified data gaps.

3.4. PROPOSED MRLS

As already elucidated in paragraph 3.1.1., the available data might be suitable to propose MRLs. The proposal is based on the currently suggested residue definition for monitoring. However, it is noticed that the proposal is not conclusive, unless the relevance of desmethyl-malathion has been clarified. Therefore, the currently proposed MRLs are **provisional**.

Apples	0.5 mg/kg
Strawberries	0.5 mg/kg

Due to lacking data it is currently not possible to conclude whether or not MRLs for food of animal origin need to be proposed. (refer to 3.2)

It is noted that there are several established or proposed Codex Alimentarius Commission (CAC) MRLs for malathion which are not comparable with the above proposed MRLs due to differences in the underlying GAP and residue definition.

4. Environmental fate and behaviour

In January-February 2005 malathion was discussed in the EPCO expert meeting on Environmental fate and behaviour (EPCO 16).

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

In soil experiments carried out under aerobic conditions in the laboratory (20-22°C 75% field capacity (FC) or 45% maximum water holding capacity (MWHC) in the dark, the predominant pathway of malathion degradation was microbially intermediated hydrolysis of the ester bond to malathion monocarboxylic acid (MMCA) (max. 25% of applied radioactivity (AR)) and subsequently to malathion dicarboxylic acid (MDCA) (max. 62%AR). Small amounts (< 10 %AR) of malic acid, lactic acid, glycolic acid, succinic acid and tartaric acid were also produced before final mineralization to carbon dioxide (50-67 % AR after 92-162 days). The formation of residues not extracted by acidified acetonitrile:water followed by methylenene chloride and a methanol Soxhlet extraction or 1N hydrochloric acid followed by acidified acetonitrile and an acetone Soxhlet extraction was also a significant sink for the applied radiolabel (26-41% AR after 92-120 days). Malaoxon was detected in one study at trace levels, however it was at its maximum level (1%) at 0 hours, indicating it was probably introduced as a contaminant in the radiolabelled material used to dose the soil.

Under anaerobic conditions in soil, the route of degradation identified was essentially the same degradation pathway as described above for aerobic conditions. In a laboratory soil photolysis study, the rate of degradation on light exposed dry soil was very slow compared to that observed in the moist dark soil degradation experiments. No photodegradation products were identified as a consequence of the limited degradation of parent malathion.

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

The rate of degradation of malathion has been investigated under aerobic conditions at a range of temperatures and moisture contents in six soils (pH 6.1-8.1, organic carbon 0.3–2.07%, texture sand –

silty clay). Malathion degraded rapidly in soil. On the basis of the six available study results the single first order DT_{50} were 0.1 days (22°C at 75% of 0.33 bar, DT_{90} 0.3 days), 1.2 days (24-26°C, at 75% of 0.33 bar, DT_{90} 4 days) and 0.17-0.25 days (20°C and 45% MWHC, DT_{90} 0.55 – 0.84 days).

Under anaerobic conditions the DT_{50} of malathion was determined to be <30 days, however approximately 57 % of the parent material had degraded during the 1.08 day aerobic period prior to the initiation of anaerobic conditions.

The major degradation products (> 10 %AR), MMCA and MDCA also degraded rapidly in soil with estimated single first-order DT_{50} values of 0.12-0.72 days (DT90 0.38-2.4 d) and 1.2-5.3 days (DT90 4.1 – 17.8 d) respectively. These first order DT_{50} were estimated from the 20°C studies where parent malathion was dosed and represent the decline from the peak measured metabolite amounts in each soil. Therefore true degradation rates calculated with a kinetic model that also accounted for the concurrent formation rate from the precursor would have lower values than these. These values are however acceptable for use in exposure assessment as they represent a worst case.

Two field dissipation studies where malathion was dosed were provided. These studies were conducted in the United States, (Georgia and California). In both studies, malathion was applied 6 times over a six-week period at 1.3 kg a.s./ha (7.8 kg a.i/ha total which is higher than the EU intended uses) to cotton and to a bare soil plot. At both locations malathion dissipated rapidly with no build up of residues between applications. MDCA formed rapidly. Malathion dissipation was too rapid (<1 day) to determine a DT_{50}. Single first order DT_{50} of 1.7 to 2.7 days were estimated for MDCA. The malaoxon moiety was not detected in either study, although the limit of quantification for the method of analysis (0.01mg/kg) was high relative to the maximum malathion residue levels determined in the studies (0.1-0.41mg/kg). Although these studies were not conducted in Europe the results confirm the rapid degradation of malathion and its metabolites seen in laboratory studies.

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

The adsorption / desorption of malathion was investigated in five soils, all with quite low levels of organic carbon. Calculated adsorption K_foc values varied from 151 to 308 mL/g, (mean 217 mL/g) indicating that malathion is moderately mobile in soil (1/n 0.9 – 0.98, mean 0.94). The adsorption / desorption properties of MDCA have been studied in four soils with a range of pH and organic carbon contents. Adsorption K_foc values were in the range of 6 – 64 mL/g (1/n 0.72-1.07, mean 0.98). Adsorption was pH dependant with lower adsorption observed at higher soil pH. This was discussed at the experts' meeting where it was agreed appropriate to use the correlation:
logKoc = -0.4158soilpH+3.7382, when selecting K_foc values for MDCA to use as input to groundwater modelling. The derivation of the correlation is outlined in detail in the addendum to the DAR dated January 2005.

The adsorption / desorption properties of MMCA were investigated in four soils. However, the compound was extremely unstable in the test soils and degraded rapidly to malathion dicarboxylic acid before reaching the adsorption equilibrium. As a result the definitive adsorption / desorption test could not be completed. Member state experts' agreed that for leaching modelling purposes it was appropriate to use the same adsorption values that had been determined for MDCA (including the pH correlation).

The mobility of malathion and its metabolites was assessed in four different soil types in an aged laboratory column leaching study. After ageing of 0.5-14 hours the soils contained approximately 38 – 60 %AR malathion, 7 – 20 % MDCA and 16 – 34 % MMCA. The column were leached with 51 cm of water in one day. Following the leaching process, 48 – 62 % of column AR was found in the leachate in three of the soils but in the final soil (silty clay) only 5 % was found. The radioactivity in the three leachates consisted primarily of MDCA (18 – 69 %) with smaller amounts of MMCA acid (5 – 14 %). Parent malathion was only found in the leachate from the sandy soil, and at trace amounts (1.9 %).

The two acid metabolites of malathion (MDCA and MMCA) are expected to be more mobile than malathion due to their chemical properties. The detection of significant proportions in the leachate under these extreme conditions confirms this expectation. A less extreme situation was examined in a sandy loam soil where 1 cm of water per day was applied for a period of 45 days. During the study, a significant proportion of mineralisation of malathion occurred (CO_2 evolution was in the region of 45 %AR) and levels of radioactivity in the leachate were lower than in the saturated leaching experiment, however dicarboxylic acid was found in the leachate in an amount of 11.8 % AR.

Additionally, on the basis of in the United States performed field dissipation studies malathion and MDCA showed some movement below the 0-15 cm soil layer. Although no trace of either compound was detectable after 14 days at any depth in either the cotton planted or the bare soil plots the limit of quantification in the study (0.01mg/kg) was high relative to the maximum malathion residue levels determined in the studies (0.1-0.41mg/kg). This therefore simply confirms there is potential for movement of malathion and MDCA out of the top soil layers under field conditions. Note the study was not designed to assess field leaching potential, as only soil and not soil water was sampled.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

The aqueous hydrolysis of malathion under sterile conditions was base-catalysed. At pH 7, (the value tested closest to natural conditions), malathion was more stable than when microorganisms are present (the single first order DT_{50} was 6.2 days). The main hydrolysis products in these sterile conditions were malathion MMCA, ethyl hydrogen fumarate and diethyl thiosuccinate. This route of degradation is not expected to be a significant route of dissipation of malathion in the natural environment where microorganisms are present.

Aqueous photolysis of malathion was slow (single first order laboratory DT_{50} 156 days, the DAR summary did not equate the light energy of the test system to natural sunlight). Photolysis is not expected to be a significant route of dissipation of malathion in the environment as biodegradation is rapid.

A ready biodegradability test (OECD 301D) indicated that malathion is 'not readily biodegradeable' using the criteria defined by the test. (This study is summarised in the addendum to the DAR dated January 2005).

The water-sediment study (2 systems studied at 20°C in the laboratory sediment pH 7.5 and 8, water pH in both systems 8) demonstrated rapid degradation of malathion in both the water phase (single first order DT_{50} 8-10 hours) and in the total system (single first order DT_{50} were the same estimated for water alone). The MMCA acid (max. 47.7 % AR) and MDCA (max. 34.9 % AR) metabolites were detected in the water phase and both of the substances had disappeared completely after 61 days. The single first order DT_{50} estimated for MMCA and MDCA in the water phases were 3-4 days and 15-17 days respectively. Single first order DT_{50} estimated for the total test systems were the same as for the water phases. A number of minor degradates (<10 % AR) were identified including oxalic acid, lactic acid, glycolic acid, succinic acid, malic acid and tartaric acid. These are assumed to be next steps in the degradation of malathion, MMCA and MDCA. Malaoxon was not detected in the study. The terminal metabolite, CO_2, was the most significant degradation product accounting for 57.7-68.6 % AR by the end of the study (120 days). Residues not extracted from sediment by acidified acetonitrile followed by Soxhlet extraction with acetone were also a sink for radioactivity representing 25.5-36.4%AR at study end. There was no single major (>10%AR) residue in sediment extracts (largest identified component MDCA accounting for a maximum 7.5%AR). The member state experts' discussed whether degradation rates might be slower in acidic natural water systems than in the systems tested (neither was acidic). They concluded that taking all the available evidence together (including that from degradation studies in soil) that for this active ingredient it was probable that degradation was primarily catalysed by microbial enzymes and malathion was unlikely to be significantly more persistent in acidic natural water systems. Experts were happy that further data was not necessary to address this issue. The EFSA agrees with this conclusion for this active substance.

The available surface water exposure assessment just considered the spray drift route of entry to surface water. However due to the very rapid degradation rate of malathion and its MMCA metabolite in soil, the potential exposure of surface water via the drainage and runoff routes of entry are considered negligible by the EFSA for these two compounds. Surface water exposure from the soil metabolite MDCA could not be completely excluded on this basis, as it has a DT90 in soil of up to 18 days. Member states should therefore carry out a surface water exposure and consequent aquatic risk assessment for MDCA from the runoff and drainage routes of exposure at the national level. However MDCA has low toxicity to aquatic organisms (see section 5.2) so risk, at least for the representative uses applied for at the EU level, is likely to be low.

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

The notifier provided and rapporteur assessed three separate sets of groundwater simulations of malathion and its metabolites MMCA and MDCA conducted with the FOCUS scenarios using the FOCUS PRZM model (v 2.4.1).

1. In section B.8.6.1 of the DAR, simulations were carried out assuming there was no PH dependence of the adsorption of MMCA and MDCA (mean $K_f$oc value of 26mL/g, 1/n 0.98 was used as metabolite adsorption input at all scenarios). For strawberries a good agricultural practice (GAP) of 6 applications were simulated each of 2.16 kg/ha (0.864kg/ha accounting for 60% crop interception), with applications being made in July and August for all scenarios except Jokioinen where the last 2 applications were in September. (Note the applied for intended use being supported through the review is a lower GAP at only 4 applications per year each at 1.5 kg/ha). For apples 3 applications were simulated each of 1.8 kg/ha (0.36kg/ha accounting for 80% crop interception) with applications being made between mid August and the 24th October (last application being 7 days before leaf fall, which would be after the last apples were harvested, i.e. later than the intended GAP). In these simulations annual average concentrations in leachate leaving the top 1m soil column were estimated to be less than the parametric drinking water limit of 0.1µg/L at all scenarios except for the apple simulation at Piacenza where the metabolite MDCA was predicted to have a concentration of *ca.* 0.3 µg/L (malathion and MMCA were <0.1 µg/L).

2. In section B.8.6.1 no. 2 of addendum to the DAR dated January 2005 the simulations were carried out as described at 1 above except the potential for the adsorption of MMCA and MDCA to change with pH was incorporated into simulation for the scenarios with neutral or basic soil descriptions (Chateaudun, Kremsmunster, Okehampton, Piacenza, Sevilla and Thiva). These are the scenarios where the soil pH adsorption correlation described at 4.1.3 above predicted $K_f$oc values would be lower than the 26mL/g value used in the simulation described at 1 above. The $K_f$oc values used as modelling input were 4.2, 10.9, 25.7, 19.3, 7.4 and 6.1mL/g for each scenario respectively. In these simulations annual average concentrations in leachate leaving the top 1m soil column were estimated to be less than the parametric drinking water limit of 0.1µg/L at all scenarios except for the apple simulation at Kremsmunster and Piacenza where the metabolite MDCA was predicted to have concentrations of *ca.* 0.33 and 0.56µg/L respectively (malathion and MMCA were <0.1 µg/L).

3. In section B.8.6.1 of the addendum to the DAR dated January 2005, the first modelling described was the same as outlined at 1. above for apples except an earlier application window was simulated (April-June applications) and crop interception values were consequently reduced (0.9kg/ha first application 0.54kg/ha 2nd and 3rd applications accounting for 50% and 70% crop interception respectively). In these simulations annual average concentrations in leachate leaving

the top 1m soil column were estimated to be less than the parametric drinking water limit of 0.1µg/L at all scenarios.

The EFSA carried out additional simulations for the earlier application pattern described at 3 above using FOCUSPRZM 2.4.1 and FOCUSPEARL 2.2.2. at the Kremsmuster scenario using the $K_f$oc of 10.9mL/g and at the Piacenza scenario using the $K_f$oc of 19.3mL/g to account for pH dependant adsorption. Predicted concentrations were less than the parametric drinking water limit of 0.1µg/L. (See EFSA addendum dated 9 September 2005 for a summary of the input and output files.)

Based on this modelling, leaching to groundwater from the applied for intended uses on Strawberry and Alfalfa above the parametric drinking water limit (0.1µg/l) would not be expected. For earlier applications to Apples (last application before 13 June at Kremsmunster) leaching to groundwater above the 0.1µg/l limit would not be expected. When very late applications are made to apples (later than the notified GAP of last application 7 days before harvest) leaching to groundwater above the 0.1µg/l limit would not be expected in geoclimatic situations represented by the Chateudun, Hamburg, Jokioinen, Okehampton, Porto, Sevilla and Thiva FOCUS groundwater scenarios. This pattern of use on apples could however result in the exposure of groundwater above the 0.1µg/l limit for the metabolite MDCA (but not parent malathion or metabolite MMCA) in geoclimatic situations represented by the northern European Kremsmunster and southern European Piacenza scenarios.

The available modelling identifies a potential concern for groundwater contamination by MDCA from the use on apples. However the available modelling does not represent the notified representative use (applications were simulated late in the season after all apples would have been harvested but there is a specified pre-harvest interval of 7 days). Therefore exceptionally the EFSA carried out further simulations using more realistic application timings at the Kremsmunster and Piacenza scenarios using FOCUSPRZM 2.4.1 and FOCUSPEARL 2.2.2. All other inputs except the date of application were identical to the modelling described at 2 above (see EFSA addendum dated September 2005 for a summary of the input and output files). The application dates simulated at Piacenza were 29 July, 12 August and 26 August (assuming a late last harvest date of 1 September). These dates at Kremsmunster were 25 August, 9 September and 23 September (assuming a late last harvest date of 1 October). In these simulations annual average concentrations in leachate leaving the top 1m soil column were estimated to be less than the parametric drinking water limit of 0.1µg/L at both scenarios (the model predicted values were 0.014-0.046µg MDCA/L Piacenza, 0.026-0.034µg MDCA/L Kremsmunster).

In conclusion, for the applied for intended outdoor uses, the EFSA considers the potential for groundwater exposure by malathion or its soil metabolites MMCA and MDCA above the parametric drinking water limit of 0.1µg/L, is low.

A groundwater exposure assessment from the intended use on ornamentals grown in glasshouses is not available.

4.3. FATE AND BEHAVIOUR IN AIR

Volatilisation of malathion from soil was very low (< 6% over 16 days). A further study indicated that malathion underwent minimal volatilisation (<1% in the vapour phase) with no direct photolytic degradation in the vapour phase. The vapour pressure of malathion (0.00045 Pa at 25°C) means that malathion would be classified under the national scheme of The Netherlands as slightly volatile, indicating limited losses due to volatilisation would be expected. Therefore the PECair is 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 0.414 days indicating the small proportion of applied malathion that did volatilise would be unlikely to be subject to long range atmospheric transport.

5. Ecotoxicology

Malathion was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 17) in January - February 2005.

5.1. RISK TO TERRESTRIAL VERTEBRATES

Toxicity studies with birds were performed with technical malathion and the formulated product containing different amounts of the toxicologically relevant impurity isomalathion. In the bird acute toxicity study the isomalathion content was 0.14%. A lower acute endpoint value was derived in a study with the formulated product with an isomalathion concentration below the specification. In the short-term study the isomalathion content was equal to the specification. In the three bird reproduction studies the isomalathion content varied from 0.03% in one study to 0.2% in two studies. The study with the lowest isomalathion content gave the lowest NOEC value with the same bird species. The acute toxicity study with rats that was used for the assessment was performed with spiked isomalathion material (0.44 %). The end point was also the lowest LD_{50} value from acceptable studies. The teratology study with rabbits was used for risk assessment since lowest relevant NOAEL for population biology purposes was observed in this study (increased number of resorptions used as endpoint). However, the isomalathion content of the technical malathion is not available.

The risk to birds and mammals was calculated for the standard indicator species proposed in the Guidance Document on Birds and Mammals (SANCO/4145/2000). The use on ornamentals in glasshouses is not considered relevant for birds and mammals since no exposure is assumed. For the use in alfalfa, strawberry and apple orchards the actual residue concentrations from available field studies were used to calculate ETE instead of the generic values provided in the guidance document. These field trials were conducted according to the proposed GAP except for apple orchards where application was done at a post-flowering stage and hence application to apples pre-flowering is not covered by the assessment.

Based on 90th percentile RUD values from the field trials for the acute assessment and mean RUD values for the short- and long-term assessment, including a f_{twa} factor based on dissipation half life for the long term, TER values were calculated for a herbivorous and a fructivorous bird respectively in alfalfa and strawberry, and for an insectivorous bird in all three crops. All TER values except the acute one for an herbivorous bird in alfalfa are above the relevant Annex IV trigger indicating a low risk. The residue data and calculations are provided in the DAR, supplemented with addendum 1 and 3. The final assessment has however not been peer reviewed. The acute TER value for herbivorous birds in alfalfa is 8.8. The RMS supports the applicants' argumentation that based on the food intake rate the daily dose for a medium herbivorous bird would be one tenth of the NOEC for lethal and sublethal effects obtained in the acute study with the technical malathion and the risk is therefore considered to be low. The EFSA agrees with this opinion. However this argumentation has not been peer reviewed by Member States.

For mammals all acute TER values were above the Annex VI trigger without considering refinements based on actual residue concentration in the crops. For apple orchards a deposition factor of 0.3 (foliage development) was taken into account to estimate the residue in short grass below the trees. For the long-term actual concentrations of residues and dissipation rates determined in the residue trials were used to refine the assessment. All TER values are above the trigger except for a small herbivorous mammal eating short grass in apple orchards. The TER obtained by assuming 30% deposition is 3.9 and the TER obtained based on actual residues in ground vegetation in the residue trial is 3.6, hence indicating a potential long-term risk. A proposal on how to refine the risk assessment by considering residues in different food items (based on the residue trials presented in the DAR and addenda), proportion of different food types (PD) in the diet of bank voles[8] and portion of diet obtained in the treated are[9] (PT) from the applicant is presented in addendum 3. The RMS has calculated a TER value based on the assumptions but without considering refinement of PT and obtained a value of 7.6, which is above the trigger. If the PT factor of 0.8 presented in addendum 3 would be taken into account a TER value of 4.5 would be obtained if the refinement in PD is ignored. However, this refined assessment has not been peer reviewed and it could be questioned to what extent data on proportion of different food types from a study in a mixed farmland area can be used to refine the assessment for the use in apple orchards. The EFSA is therefore of the opinion that the long-term risk to herbivorous mammals in apple orchards needs to be further addressed.

The risk to birds and mammals from exposure to contaminated drinking water is based on the PEC_{sw} since it was considered that exposure from spray solution would be negligible for the evaluated uses. The acute TER values indicate a low risk. The long-term risk is considered low based on the rapid dissipation of malathion from natural water bodies.

[8] Abt, K.F. and Bock, W.F., 1998. Seasonal variation of diet composition in farmland field mice *Apodemus* spp. and bank voles *Clethrionomys glareolus*. Acta Theriologica 43 (4): 379-389.
[9] DEFRA Project PN0915 Improving estimates of wildlife exposure to pesticides in arable crops.

The metabolites malathion mono- and dicarboxylic acid are not considered to be of ecotoxicological concern. All TER values for the toxicologically relevant metabolite malaoxon are above the Annex VI trigger indicating a low risk.

Malathion has a log P_{ow} value of 2.7 and a fish BCF of 103 and depurates rapidly. Consequently, the risk of secondary poisoning for birds and mammals arising from malathion applications is considered to be low.

5.2. RISK TO AQUATIC ORGANISMS

Acute toxicity test with fish were performed with technical material that contained 0.14% isomalathion in five out of six cases. One study had an isomalathion content of 0.2%. The sensitivity of four species was in the same range while two species were less sensitive. The lowest LC_{50} value is from a study with three-spined stickleback with 0.14% isomalathion. The chronic fish study had isomalathion content equal to the specification. Both acute and chronic toxicity studies with *Daphnia* were performed with technical malathion that contained isomalathion at the 0.2% specification. However the final risk assessment is based on a mesocosm study that was performed with a formulation batch that contained 0.014% isomalathion (should be compared with the "formulation specification" of 0.088%, since technical malathion has specification of 0.2 % and the formulation contains 440 g of technical malathion = isomalathion 0.088 %).

Malathion is very toxic to fish and aquatic invertebrates. The most sensitive organism tested was *Daphnia magna* with an EC_{50} of 0.72 µg/L and a NOEC for reproduction of 0.6 µg/L. The first tier risk assessment, based on 90th percentile spray drift values to a 30 cm static water body at different distances, indicates a high risk even with large buffer zones to reduce the exposure. The acute trigger for fish was reduced from 100 to 10 based on available values for six different species. This was discussed in the experts' meeting and not all Member States agreed. It was decided to forward the question on the lowering of safety factors to the scientific panel. The EFSA proposes to revisit the assessment when the opinion of the panel has been adopted.

For aquatic invertebrates the assessment was refined based on results from an available mesocosm study. Since only one application was used in the study it was agreed in the experts' meeting to base the assessment on the NOEC as recovery from multiple applications is not known. The meeting could not agree on which safety factor should be used. It was however decided that a safety factor of 3-5 should be applied to cover different habitats and since no static single species laboratory studies are available to compare with. Additionally, higher crustaceans that are known to be sensitive to organophosphates were not abundant in the mesocosm. For the early application in apple orchards a 50 m buffer zone is required to obtain TER values for fish that are above the trigger of 10. For the late application a buffer zone of 40 m is required. With safety factors of 3 or 5 from the mesocosm study, buffer zones of 50 or 75 m respectively are required to protect aquatic invertebrates in the case of late application in apple orchards, while for the early application these buffer zones are not enough. For

the use in alfalfa and strawberry 10-20 m buffer zones are required. The risk to aquatic organisms from the use on ornamentals in glasshouses is considered low.

Based on toxicity data, no further concern is required for any of the major metabolites for the representative uses evaluated.

It should be noted that the refined aquatic risk assessment is based on the mesocosm study where the formulated malathion contained only 0.014% isomalathion which is lower than the specification of technical malathion of 0.2% (formulation isomalathion concentration at highest 0.088 %).

5.3. RISK TO BEES

The available studies with the formulated product indicate a high oral and contact toxicity to honeybees and the calculated HQ values are 4500 and 11250, which is 90-225 times the Annex VI trigger indicating a high risk. No field- or semi field studies are available that covers the dosage for the use in apple orchards and alfalfa. For strawberry a study from Spain is available where formulated malathion was applied at 2.16 kg/ha in greenhouse tunnels where bee colonies had been placed. No significant effect of the treatment was seen. The risk to bees was discussed in the experts' meeting and it was agreed that risk mitigation measures should be set at Member State level. For apples and alfalfa no application should be done during flowering.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The HQ values calculated according to ESCORT 2 and based on the first tier studies with the two standard species *Aphidius rhopalosiphi* and *Typhlodromus pyri* indicate a high in-field risk for non-target arthropods, except for *T. pyri* for the glasshouse use on ornamentals. The off-field HQ values also indicate a high risk. Extended laboratory studies are available with the standard species and larvae of the foliar dwelling *Crysoperla carnea* and *Orius laevigatus* at dose rates of 2.6 and 6.3 kg a.s/ha. The results with fresh residues indicate a high in-field risk. The most sensitive species tested is *A. rhopalosiphi* for which the 50% threshold for mortality was exceeded up to and on 28 and 63-day aged residues at the two application rates respectively.

Little or no effects were seen on predatory mites following field application of up to 2.28 kg a.s./ha to strawberry crop in the UK. Additional results from field trials on apple in France (drift rate at 10 and 20 m from 3×1.8 kg a.s./ha) and on alfalfa in Italy (drift rate at 1 m from 1×1.5 and 6×2.16 kg a.s./ha) showed no long-term effects indicating that rapid recolonisation from off-field areas would be possible. It can therefore be concluded that recovery of in-field populations should be possible within a year using 1 m buffer zone with field crops and 10 m buffer zone for late application in apples. However, the RMS points out that the assessment only covers late application in apples, and that for early application risk mitigation measures comparable to 20 m buffer zones are considered necessary.

It should be noted that extended laboratory studies with arthropods were performed with a formulation that contained lower amounts of isomalathion than the specification (isomalathion

content of the formulation 0.088 %). The isomalathion content of the formulation used in the field studies is not known and analytical results should be provided by the applicant.

5.5. RISK TO EARTHWORMS

Studies on the acute toxicity to earthworms from malathion and the metabolites dimethyl thiophosphate and dimethyl phosphate indicate a low acute toxicity. No studies are available with the monocarboxylic and dicarboxylic acid metabolites. However TER values were calculated assuming 10-times higher toxicity compared to the parent. Since malathion degrades rapidly no long term studies are required. All acute TER values are above the Annex VI trigger and therefore the risk to earthworms is considered to be low.

5.6. RISK TO OTHER SOIL NON-TARGET ORGANISMS

No data on other soil non-target macro-organisms are available since DT_{90} <365 days and no adverse effects were observed in the tests with earthworms or soil micro-organisms.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

The effects of malathion on soil carbon and nitrogen conversion were tested up to 6.3 kg a.s./ha. No deviations of more than 25% after 28 days were observed. Hence the Annex VI trigger was met, and since malathion is degraded rapidly and no carry over of residues is expected from multiple applications, the risk is considered low.

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

A limit test on vegetative vigour with six plant species at an application rate of 1.8 kg a.s./ha is presented in Addendum 3 dated September 2005, but has not been peer reviewed. No effects on biomass were seen for any of the tested plants and only minor (<10%) phytotoxic effects were observed on two species. The TER values calculated for drift rates at 3 and 10 m for late application in apples are above the Annex VI trigger of 5 indicating a low risk to non-target plants outside the treated field. Since the spray drift is lower for field crops even with 1 m buffer zone than for apples with 3 m, the risk is also considered as low for these uses.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

Data from a test with activated sludge are available and indicate that the risk to biological methods of sewage treatment plants is low.

6. Residue definitions

Soil

Definitions for risk assessment: malathion; [10]malathion monocarboxylic acid and [11]malathion dicarboxylic

Definitions for monitoring: malathion (However as in some soils the DT_{90} of malathion was < 3 days, malathion dicarboxylic acid may be a more appropriate marker compound to monitor).

Water

Ground water

Definitions for risk assessment: malathion; malathion monocarboxylic acid and malathion dicarboxylic

Definitions for monitoring: malathion

Surface water

Definitions for risk assessment: surface water: malathion; malathion monocarboxylic acid and malathion dicarboxylic

sediment: none

Definitions for monitoring: malathion (However as the DT_{90} of malathion in sediment water systems was < 3 days, malathion dicarboxylic acid may be a more appropriate marker compound to monitor).

Air

Definitions for risk assessment: malathion

Definitions for monitoring: malathion

Food of plant origin

Definitions for risk assessment: sum of malathion, malaoxon and desmethyl-malathion, expressed as malathion

Definitions for monitoring: sum of malathion and malaoxon, expressed as malathion; pending confirmation that desmethyl-malathion is not more toxic than malathion (refer to 3.1.1.)

Food of animal origin

Definitions for risk assessment: cannot be concluded based on currently available data; provisional RMS proposal: malathion and desmethyl-malathion, expressed as malathion (not peer reviewed)

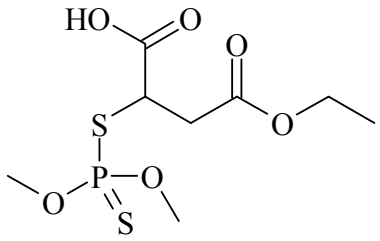
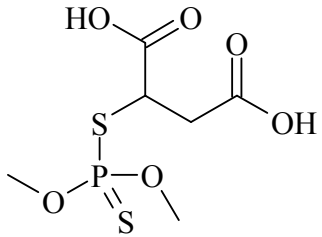
Definitions for monitoring: cannot be concluded based on currently available data; provisional RMS proposal: malathion and desmethyl-malathion, expressed as malathion (not peer reviewed)

[10] Butanedioic acid [(dimethoxyphosphinothioyl)thio]-ethyl ester carboxylic acid

[11] Butanedioic acid [(dimethoxyphosphinothioyl)thio]-di carboxylic acid

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
malathion	Very low to low persistence ($DT_{50\ lab}$ = 0.1-1.2 d, 20°C, 45% MWHC or 22-26°C, 75%FC); ($DT_{50\ field}$ = <1 d)	See 5.5
malathion monocarboxylic acid 	Very low persistence ($DT_{50\ lab}$ = 0.12-0.72 d, 20°C, 45% MWHC)	No study available. Risk considered low based on the assumption of 10-fold increase in toxicity compared to malathion.
malathion dicarboxylic acid 	low persistence ($DT_{50\ lab}$ = 1.2-5.3 d, 20°C, 45% MWHC)	No study available. Risk considered low based on the assumption of 10-fold increase in toxicity compared to malathion.

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 activity	Ecotoxicological activity
malathion	medium mobility (Koc = 151-308 mL/g)	FOCUS modelling: No	Yes	Yes	See 5.2
malathion monocarboxylic acid	Very high to high mobility pH dependent classification extrapolated from malathion dicarboxylic acid	FOCUS modelling: No based on adsorption extrapolated from malathion dicarboxylic acid including taking account of pH dependant adsorption	No exposure No assessment necessary	No exposure, no assessment necessary	No exposure, no assessment necessary. >2 orders of magnitude less toxic than malathion
malathion dicarboxylic acid	Very high to high mobility (Koc = 6-64 mL/g) pH dependent	FOCUS modelling: No pH dependant adsorption taken account of in modelling.	No exposure No assessment necessary	No exposure, no assessment necessary	No exposure, no assessment necessary. >2 orders of magnitude less toxic than malathion

Surface water

Compound (name and/or code)	Ecotoxicology
malathion	See 5.2
malathion monocarboxylic acid	>2 orders of magnitude less toxic than malathion
malathion dicarboxylic acid	>2 orders of magnitude less toxic than malathion

Air

Compound (name and/or code)	Toxicology
malathion	Not acutely toxic via inhalation; short term NOAEL (90-day rat study) 0.1 mg/L

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

- Depending on the final residue definition for monitoring purposes, an analytical method for the determination of residues in food of plant origin, which is in compliance with the proposed residue definition could be required (date of submission unknown, data gap under discussion, refer to chapter 1, 3.1 and 3.4)
- An analytical method for the determination of residues in food of animal origin (date of submission unknown, data gap identified after the experts' meeting for residues, refer to chapter 1, 3.2 and 3.4)
- Depending on the final residue definition for monitoring purposes for soil further data (method for MDCA) could be required (refer to chapter 1 and 6)
- A new Ames test (with the isomalathion content of 0.2%) is required (see 2.4).
- If the Ames test would demonstrate a positive result it is not possible to set limit values and a secondary test, an UDS test would be required (see 2.4). The study is available (submitted in August, 2005), assessed by the RMS but not peer reviewed
- Data addressing the toxicological properties of desmethyl-malathion need to be submitted (relevant for use in apples, strawberries; date of submission unknown, data gap identified after the experts' meetings for toxicology and for residues, refer to chapter 2.8 and 3.1.1).
- The discrepancy of results for malaoxon obtained in the apple metabolism study vs. the supervised residue trials needs to be further elaborated and explained by the applicant. (relevant for use in apples; date of submission unknown, data gap identified in the experts' meeting for residues, refer to chapter 3.1.1)
- Data on the level of desmethyl-malathion on RAC and processed products need to be submitted, unless it can be proven that desmethyl-malathion is of no toxicological relevance. (relevant for use in apples, alfalfa, strawberries; date of submission unknown, data gap identified in the experts' meeting for residues, refer to chapter 3.1.1)
- Data demonstrating the stability of desmethyl-malathion under storage conditions is needed. (relevant for use in apples, alfalfa, strawberries; date of submission unknown, data gap identified in the experts' meeting for residues, refer to chapter 3.1.1)
- The residue situation of desmethyl-malathion in rotational crops needs to be clarified. (relevant for use in alfalfa, strawberries; date of submission unknown, data gap identified in the experts' meeting for residues, refer to chapter 3.1.2)
- The long-term risk to mammals needs to be further addressed (relevant for use in apple orchards; proposals for refinement submitted by the applicant but not peer reviewed; refer to point 5.1)
- The assessment of acute risk to fish should be revisited when the opinion of the Scientific Panel on lowering of safety factors based on additional toxicity data from several species is available (relevant for all uses; refer to point 5.2)

- Analytical results of isomalathion content in the formulation used in non-target arthropod field trials (relevant for use in apple, strawberry and alfalfa; no submission date proposed by the notifier; refer to point 5.4)
- The risk to non-target organisms needs to be addressed (relevant for use in apples, alfalfa, strawberries; study submitted before 21 June 2005, evaluated and included in Addendum 3 but not peer reviewed; refer to point5.8)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as acaricide and insecticide as proposed by the applicant, which comprises foliar spraying to control various harmful organisms in apples, strawberries, alfalfa and ornamentals at application rate up 1.8 kg malathion per hectare. Malathion can be used as acaricide and insecticide.

The representative formulated product for the evaluation was "CHA 3110" ("Fyfanon 440"), an oil in water emulsion (EW), registered under different trade names in some EU Member States.

Adequate methods are available only for ground water and air to monitor all compounds given in the respective residue definition, i.e. malathion. In case of food of plant origin only methods for the determination of malathion and malaoxon are available. No method for the determination of malathion in food of animal origin was submitted. In case of soil and surface water no enforcement method for the determination of malathion is needed due to the fact that the DT_{90} values are less than 3 days.

Only single methods for the determination of residues are available. However, malathion and malaoxon can be determined by a multi-residue method (the applicability of the so-called extent S19 method has been demonstrated).

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.

The concentration of isomalathion in the batches of technical malathion tested in the toxicological studies were approximately one tenth, if mentioned at all, of the current specification. The currently supported specification of malathion allows a maximum concentration of 0.2 % (w/w) isomalathion in the technical active substance and according to the FAO specification, it is 0.4 % (w/w).

Based on the available studies in the toxicological data package, only the 0.03% isomalathion content can be said to be covered. As for the level of 0.2% isomalathion, an additional safety factor of 10 was added to the ADI and the AOEL in order to be able to conclude on the risk assessment due to uncertainties in studies relevant for the setting of reference values. Furthermore, a data requirement for further genotoxicity studies to be performed has to be fulfilled and a non genotoxic potential

demonstrated in order to be able to cover (from a toxicological point of view) the specification of 0.2% of isomalathion in the technical material.

The level of isomalathion in the current 5-batch analysis showed a mean content of 0.048-0.076%. This implies that the limit of 0.03% regarding the toxicological data package would not be feasible. Thus, the toxicological assumptions have to be based on the 0.2% limit. Furthermore, it is shown in the FAO specification that the amount of isomalathion even increases during storage both in relation to time and temperature by a factor of 2-10. Thus, the reference values have to be based on the 0.2% level.

Malathion is rapidly absorbed and excreted. There is no evidence of accumulation. The highest concentration was found in the liver, followed by skin, fat, bone and gastrointestinal tract. The metabolites excreted in urine and faeces were primarily the mono and dicarboxylic acids of malathion. Malathion was moderately toxic by the oral route in rat (a classification as **Xn; R22 "Harmful if swallowed**" is proposed). Malathion is not acutely toxic via the dermal route or through inhalation; it is not irritant to skin and eyes but it is a skin sensitiser (**Xi; R43 "May cause sensitisation by skin contact "**is proposed).

The target effect in short and long term studies is the decrease of acetyl cholinesterase activities. Overall, malathion does not show genotoxic potential *in vivo*. The occurrence of nasal tumours was due to a local mechanism of irritancy and cytotoxicity and no classification with regard to carcinogenicity is proposed. Malathion induced a decrease in pup weights; but no classification is proposed. No neurotoxic potential was identified.

The reference values were all base on the specification on content of 0.2% of the impurity isomalathion. Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 0.03 mg/kg bw/day, with a safety factor of 1000. The Acute Reference Dose (ARfD) is 0.3 mg/kg bw/day, safety factor of 100. Based on human data, two other ARfD values were proposed in relation to the isomalathion content i.e. a) in the case the isomalathion content is 0.14-0.2% or above a safety factor of 10 would be appropriate. The resulting ARfD would be 1.5 mg/kg bw b) In the case the isomalathion content would be less than 0.14% or unknown a safety factor of 100 would be applied. The resulting ARfD would be 0.15 mg/kg bw.

The AOEL is exceeded for high crops (apples) but is below the AOEL for low crops (strawberry and alfalfa), with German model and PPE applied. The estimated exposure is below the AOEL for hand held application as well as indoor applications.

Re-entry exposure does not exceed the AOEL except for ornamentals in greenhouse; the exposure of bystanders is below the AOEL only strawberry application. **However, until isomalathion is proven non genotoxic, the operator risk assessment cannot be regarded as conclusive.**

The metabolism of malathion in plants was studied in different crops. Results of those studies indicate that, even though the metabolic pattern appeared being comparable, significant differences in quantity of the formed metabolites, and therewith its relevance regarding consumer exposure, exist. The metabolism of malathion yields the major metabolites malathion mono- and dicarboxylic acid, and desmethyl-malathion; but also, even though at lower levels, malaoxon was identified.

Further information to address the toxicological relevance of malathion metabolites are required. With regard to consumer exposure, a number of data gaps have been identified in the expert meeting on residues. It is noted, that there may be additional data gaps resulting from conclusions drawn by experts in other sections, which have an impact on the residue section, but weren't considered by the residues experts at that time. Since there is a lack of data sufficiently addressing the hazard and/or the consumer exposure with regard to residues resulting from malathion use on food/feed crops, **the consumer risk assessment cannot be concluded.**

The information available on the fate and behaviour in the environment is sufficient to carry out an appropriate environmental exposure assessment at the EU level. The drainage and runoff routes of exposure to surface water have not been covered for the soil metabolite malathion dicarboxylic acid in the available EU level assessment. This exposure assessment and the associated risk assessment to aquatic organisms from malathion dicarboxylic acid should be completed in national assessments made by the member states. For the notified intended field uses, the potential for groundwater exposure by malathion or its soil metabolites MMCA and MDCA above the parametric drinking water limit of 0.1µg/L, is low.

Data are not available to conclude on the risk to birds and mammals following early application in apple orchards. For the late application in apples, and the use in strawberry and alfalafa, the risk to birds and mammals is considered low based on actual residue data, except the long-term risk for a small herbivorous mammal eating short grass in apple orchards. Proposals for refinement have not been peer reviewed and need to be further justified. No exposure of birds and mammals from the use in glasshouses is expected. Risk mitigation measures comparable to at least 50 m are required for the use in apples to protect the aquatic environment following late application in apples. For the early application even larger buffer zones are needed. For strawberry and alfalfa 10 m buffer zones are required. The risk to aquatic organisms from the use on ornamentals in glasshouses is considered low. The toxicity to bees is high and risk mitigation measures should be set at Member State level. For apples and alfalfa no application should be done during flowering. Risk mitigations measures are also needed to protect other non-target arthropods off field. The risk to earthworms, other soil macro- and micro-organisms, non-target flora and biological methods of sewage treatment is considered low.

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

- The maximum content of isomalathion in the representative formulation ("CHA 3110", "Fyfanon 440") should not be higher than 0.88 g/L (provisional limit).
- PPE have to be worn in order to have n operator exposure below the AOEL.
- Risk mitigation measures comparable to 50 m buffer zones are required for the use in apple orchards (late application) to protect the aquatic environment, for early application >50 m is required (refer to point 5.2).
- Risk mitigation measures comparable to 10 m buffer zones are required for the use in strawberry and alfalfa to protect the aquatic environment (refer to point 5.2).

- Risk mitigation measures to protect bees should be set by Member States (refer to point 5.3).
- Risk mitigation measures comparable to 20 m (early application) and 10 m (late application) buffer zones are required for the use in apple orchards to protect off-field non-target arthropods (refer to point 5.4).

Critical areas of concern

- The content of isomalathion in the technical material (2 g/kg) as well as in the representative formulation (0.88 g/L) should be regarded as provisional (refer to chapter 1 and 2).
- The concentration of isomalathion in the batches of technical malathion tested in the toxicological studies were approximately one tenth, of the current specification (0.2 % (w/w)). Based on the available studies in the toxicological data package, only the 0.03% isomalathion content can be said to be covered. As for the level of 0.2% isomalathion, an additional safety factor of 10 was added to the ADI and the AOEL in order to be able to conclude on the risk assessment due to uncertainties in studies relevant for the setting of reference values. Furthermore, further genotoxicity studies have to be provided and a non genotoxic potential demonstrated in order to be able to cover the specification of 0.2% of isomalathion in the technical material. **Thus, until isomalathion is proven non genotoxic the operator risk assessment (AOEL) cannot be regarded as conclusive**.
- The estimated operator exposure is above the AOEL for high crop (apples) although PPE is applied, assessed with the German model (refer to point 2.11).
- The estimated exposure during re-entry is above the AOEL following single as well as after consecutive applications for both high crop (apples) and low crop (strawberries), even when PPE (coverall and gloves) is worn (refer to point 2.11).
- The estimated bystander exposure is above the AOEL for high crop (orchards) and is 13-80% of the AOEL for low crop (alfalfa and strawberries) (refer to point 2.11).
- The estimated exposure during amateur use (not assumed to wear PPE) is above the AOEL, thus only professional use should be considered (refer to point 2.11).
- Two ARfD values are allocated. One is based on a NOAEL from animal studies with the safety factor of 100. The second one is based on the NOEL from scientifically valid human study with the safety factor of 10 applied (refer to point 2.9).
- The acute and chronic dietary risk assessment for consumers cannot be concluded. A sound risk assessment is only possible upon receipt of data addressing the identified data gaps for desmethyl-malathion and malaoxon. Furthermore the relevance of the metabolites MMCA and MDCA for consumer exposure and thus for consumer risk is currently unclear (refer to point 3.3.).
- A high risk for aquatic organisms. Risk mitigation measures comparable to 50-75 m buffer zones are required for the use in apple orchards (late application) to protect the aquatic environment, for early application >50-75 m is required. For the use in strawberry and alfalfa 10-20 m buffer zones are required (refer to point 5.2).

- A high risk for bees. Risk mitigation measures to protect bees should be set by Member States (refer to point 5.3).
- A high risk for non-target arthropods. Risk mitigation measures comparable to 20 m (early application) and 10 m (late application) buffer zones are required for the use in apple orchards to protect off-field non-target arthropods (refer to point 5.4).

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

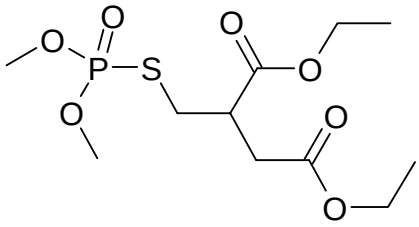
Active substance (ISO Common Name) ‡	Malathion
Function (e.g. fungicide)	Insecticide and acaricide

Rapporteur Member State	Finland
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	diethyl(dimethoxythiophosphorylthio)succinate or *S*-1,2-bis(ethoxycarbonyl)ethyl *O*,*O*-dimethyl phosphorodithioate
Chemical name (CA) ‡	Butanedioic acid, [(dimethoxyphosphinothioyl)thio]-, diethyl ester
CIPAC No ‡	12
CAS No ‡	121-75-5
EEC No (EINECS or ELINCS) ‡	204-497-7 (EINECS)
FAO Specification ‡ (including year of publication)	12/TC (December 2004) min. 950 g/kg malathion impurities: max. 1 g/kg malaoxon max. 4 g/kg isomalathion max. 15 g/kg MeOOSPS-triester max. 5 g/kg MeOOOPS-triester
Minimum purity of the active substance as manufactured ‡ (g/kg)	950 g/kg (ratio of *R*- and *S*-enantiomers 50/50)
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	max. 1 g/kg malaoxon max. 2 g/kg isomalathion max. 15 g/kg MeOOSPS-triester max. 5 g/kg MeOOOPS-triester
Molecular formula ‡	$C_{10}H_{19}O_6PS_2$
Molecular mass ‡	330.36

‡ 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) ‡	<-20 °C, purity 99.1%
Boiling point (state purity) ‡	No value determined due to decomposition, purity 99.1%
Temperature of decomposition	174 °C, purity 99.1%
Appearance (state purity) ‡	Clear liquid, purity 98.9%
Relative density (state purity) ‡	1.23 at 20 °C, purity 99.1%
Surface tension	58 mN/m at 20 °C, purity 96.0%
Vapour pressure (in Pa, state temperature) ‡	4.5×10^{-4} Pa at 25 °C 3.1×10^{-3} Pa at 35 °C 1.9×10^{-2} Pa at 45 °C purity 98.9%
Henry's law constant (Pa m^3 mol^{-1}) ‡	1.0×10^{-3} Pa m^3 mol^{-1}
Solubility in water ‡ (g/l or mg/l, state temperature)	148 mg/l at 25 °C (unbuffered solution)
Solubility in organic solvents ‡ (in g/l or mg/l, state temperature)	Xylene >250 g/l 1,2-dichloroethane >250 g/l heptane 57 – 67 g/l ethyl acetate >250 g/l methanol >250 g/l acetone >250 g/l at 20 °C
Partition co-efficient (log POW) ‡ (state pH and temperature)	log P_{ow} = 2.75 at 25 °C (unbuffered solution) log P_{ow} = 2.40 (CLOGP Med Chem program)
Hydrolytic stability (DT50) ‡ (state pH and temperature)	pH 5, 25 °C: DT_{50} = 107 days, rate constant 0.0065/day
	pH 7, 25 °C: DT_{50} = 6.21 days, rate constant 0.111/day
	pH 9, 25 °C: DT_{50} = 0.49 days, rate constant 1.41/day
Dissociation constant ‡	Does not dissociate in water
UV/VIS absorption (max.) ‡ (if absorption > 290 nm state ε at wavelength)	No absorbance above 290 nm.

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

Photostability (DT50) ‡ (aqueous, sunlight, state pH)	pH 4 to minimise hydrolysis Sensitised - DT_{50} = 93.5 days, rate constant 0.0074/day Non sensitised - DT_{50} = 156 days, rate constant 0.0045/day
Quantum yield of direct phototransformation in water at Σ > 290 nm ‡	No absorbance above 290 nm
Flammability ‡	Not applicable. Flash point 173 °C
Explosive properties ‡	Non explosive

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

List of representative uses evaluated*

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max	(days) (l)	(m)
Apples	EU North	malathion	F	*Panonychus ulmi* *Cydia pomonella* Scales Thrips Aphids *Yponomeuta sp* *Ceratitis capitata*	EW	440 g/l	foliar spray	ripening fruit (BBCH8)	1 - 3	14 days	0.18	1000	1.8	7	[1 – 4]
Apples	EU North	malathion	F	*Panonychus ulmi* *Cydia pomonella* Scales Thrips Aphids *Yponomeuta sp* *Ceratitis capitata*	EW	440 g/l	foliar spray	1. Before flowering (before BBCH 5) 2. Fruitlet stage (BBCH 7). 3.Ripening fruit (BBCH 8).	1 - 3	14 days	0.18	1000	1.8	7	[1 – 4]

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

Crop and/or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hl min max	water l/ha min max	kg as/ha min max	(days) (l)	(m)
Straw-berries	EU South	malathion	F	Lepidoptera Thrips Coleoptera Aphids	EW	440 g/l	foliar spray	ripening fruit	1 - 4	10 days	0.15	1000	1.5	3	[2 - 4]
Alfalfa	EU South	malathion	F	Aphids *Colaspidema atrum* Lepidoptera	EW	440 g/l	foliar spray	7 days before cutting	1 per crop	n/a	0.15	1000	1.5	7	[2 - 4] There may be up to four crops per season
Orna-mentals	EU North & South	malathion	G	Aphids, thrips, mealy bugs, whitefly, leaf hoppers	EW	440 g/l	hand held or gantry sprayers	when pests first seen	n/a	7-10 days	0.114	100	0.114	n/a	[2] There is no maximum number of applications

[1] The risk assessment has revealed data gap(s) in section 5
[2] The risk assessment has revealed data gap(s) in section 2
[3] The risk assessment has revealed a risk (estimated exposures exceed the AOEL) in section 2
[4] The risk assessment has revealed data gap(s) in section 3

‡ 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)	Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench	(l)	PHI - minimum pre-harvest interval
	(g)	All abbreviations used must be explained	(m)	Remarks may include: Extent of use/economic importance/restrictions

‡ 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)	a) GC-FID b) CIPAC method GC-FID
Impurities in technical as (principle of method)	HPLC-UV and GC-FID
Plant protection product (principle of method)	GC/FID

Analytical methods for residues (Annex IIA, point 4.2)

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	a) GC/FPD; LOQ: 0.001 mg/kg malathion, 0.001 mg/kg malaoxon for strawberry and apple, GC/FPD; LOQ: 0.01 mg/kg malathion, 0.01 mg/kg malaoxon for alfalfa b) DFG S8 method: GC/AFID; LOQ: 0.25 mg/kg malathion, 0.25 mg/kg malaoxon for strawberry and apple *Method for desmethyl malathion could be necessary*	
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	*Method for malathion required*	
Soil (principle of method and LOQ)	LC/MS/MS;	LOQ: 0.01 mg/kg malathion
Water (principle of method and LOQ)	LC/MS/MS;	LOQ: 0.1 µg/kg malathion (ground and surface water). LOQ: 0.5 mg/kg MDCA, LOQ: 0.5 mg/kg MMCA, (surface water)
Air (principle of method and LOQ)	LC/MS/MS;	LOQ: 5 µg/m^3 malathion
Body fluids and tissues (principle of method and LOQ)	No analytical method is required for body fluids and tissues since malathion is not classified as toxic or very toxic.	

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 ‡	Up to about 90 % absorbed within 72 h, based on urinary excretion data.
Distribution ‡	Less than 1.5 % of administered dose detected in tissues and carcass at 72 h after dosing, mainly in liver followed by skin, fat, bone and GI tract.
Potential for accumulation ‡	No evidence of accumulation.
Rate and extent of excretion ‡	>90 % of total dose excreted within 72 h. 76-88 % of total dose excreted in urine and 6-14% of total dose excreted in feces.
Metabolism in animals ‡	Malathion is mainly metabolised through hydrolysis. Major metabolites are malathion dicarboxylic acid and malathion monocarboxylic acid.
Toxicologically significant compounds ‡ (animals, plants and environment)	Malathion and malaoxonImpurities (especially isomalathion) may increase genotoxicity of malathion. Isomalathion is an acetyl cholinesterase inhibitor, which enhances the toxicity of malathion

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	1778 mg/kg bw (0.44% isomalathion) **R22**
Rat LD_{50} dermal ‡	> 2000 mg/kg bw (0.43 % isomalathion)
Rat LC_{50} inhalation ‡	> 5 mg/l air /4 h (0.43% isomalathion)
Skin irritation ‡	Non-irritant (0.43% isomalathion)
Eye irritation ‡	Non-irritant (0.43% isomalathion)
Skin sensitization ‡ (test method used and result)	Sensitising (Magnusson and Kligman test) (0.43% isomalathion) **R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Acetylcholinesterase inhibition (enzyme activity in brain)
Lowest relevant oral NOAEL / NOEL ‡	34.4 mg/kg bw/d, 90d rat (0.03% isomalathion),
Lowest relevant dermal NOAEL / NOEL ‡	300 mg/kg bw/d, 21d rabbit (0.2% isomalathion),
Lowest relevant inhalation NOAEL / NOEL ‡	90d rat: 0.45 mg/L (0.03% isomalathion)

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

Genotoxicity ‡ (Annex IIA, point 5.4)

.....	*In vivo* chromosome aberration study in rat bone marrow negative (0.2% isomalathion). *In vivo* UDS test negative (0.14% isomalathion). *In vitro* mouse lymphoma cell gene mutation test and *in vitro* chromosome aberration test with human lymphocytes positive (0.14% isomalathion). *In vitro* UDS test negative (0.2% isomalathion). Ames test negative (isomalathion content not reported). Although, *in vitro* results are inconclusive, the available data suggest that there is no genotoxic potential *in vivo.* No classification proposed.

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

Target/critical effect ‡	Nervous system (acetylcholinesterase inhibition in brain), kidney, liver. Increased nasal tumors in the rat. Liver tumors evident at high dose levels.
Lowest relevant NOAEL / NOEL ‡	29 mg/kg bw/day; 2 year rat (0.03% and 0.018% isomalathion content)
Carcinogenicity ‡	The nasal tumors were probably secondary to a local irritation. No classification proposed

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction target / critical effect ‡	Decreased pup weights at a non maternally toxic dose level, in the rat.
Lowest relevant reproductive NOAEL / NOEL ‡	Parental NOAEL: 595 mg/kg bw/day Reproductive NOAEL: 132 mg/kg bw/day (0.2% isomalathion)
Developmental target / critical effect ‡	Increased incidence of resorptions in rabbit at 50 mg/kg bw/day not related to the maternal toxic effects.
Lowest relevant developmental NOAEL / NOEL ‡	Maternal and developmental NOAEL 25 mg/kg bw/day (isomalathion content not available)

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

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

Delayed neurotoxicity	No indications of delayed neurotoxicity observed
Acute neurotoxicity	No NOAEL. (Clinical signs in acute neurotoxicity study in rat); (0.03 % isomalathion content)
Subchronic neurotoxicity	NOAEL 4 mg/kg bw/day. (Brain acetyl cholinesterase inhibition in a 13-week neurotoxicity study in rat) (0.03% isomalathion)
Developmental neurotoxicity	NOAEL 50 mg/kg bw/day (Clinical signs and results in behavioural assessment in a rat developmental toxicity study and brain acetylcholinesterase inhibition in supplementary cholinesterase determinations) (0.14% isomalathion)

Other toxicological studies ‡ (Annex IIA, point 5.8)

Single oral dose study in humans	NOEL >15 mg/kg bw for cholinesterase inhibition (0.24% isomalathion)
Metabolites: Malaoxon 2-week range-finding study in rat	NOAEL 12.1 mg/kg bw/day based on brain acetyl cholinesterase inhibition
24-month toxicity/oncogenicity study in rat	NOAEL 1 mg/kg bw/day for brain acetyl cholinesterase inhibition; evidence of leukaemia at 114 and 141 mg/kg bw/day in males and females, respectively a dose level were marked toxicity was observed.
Malathion dicarboxylic acid	It is identified in rat metabolism studies. No studies with malathion dicarboxylic acid have been performed. The toxicological assessment could be done on the basis of the data for malathion. Malathion dicarboxylic acid should be considered as of equivalent toxicity as malathion. This should also apply to malathion monocarboxylic acid.
Impurity: Isomalathion, the major impurity of malathion	No studies with isomalathion have been performed. Isomalathion is an acetyl cholinesterase inhibitor, which enhances the toxicity of malathion compounds. Positive results in genotoxicity studies may be due to isomalathion and other impurities; this has been reported also in literature.

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

Medical data ‡ (Annex IIA, point 5.9)

Medicinal surveillance on manufacturing plant personnel	No poisoning or neurological signs, no reduction in blood cholinesterase levels. No reliable evidence for increased incidences of rare types of cancer.
Exposure of pesticide workers	Severe and life-threatening poisoning incidents; the extent and severity of intoxication related to increased concentrations of isomalathion and other degradation products of malathion.
Exposure of general population	Cases of intentional and unintentional poisoning incidents. Severe poisoning reported occurring at oral doses between 15 and 25 g/person.

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡ (for 0.2% isomalathion)	0.03 mg/kg bw/day	rat, 2y study	1000[1]
AOEL ‡ (for 0.2% isomalathion)	0.03 mg/kg bw/day	rat, 90d study	1000[1]
ARfD ‡ (for 0.2% isomalathion)	0.3 mg/kg bw	rabbit teratology study	100
ARfD ‡ based on a human study (for 0.2% isomalathion)	1.5 mg/kg bw	human study	10[2]

Dermal absorption (Annex IIIA, point 7.3)

.....	5 % for a concentrate 5 % for a spray solution based on human *in vivo* data

[1] Additional factor of 10 was added to the safety factor due to the uncertainties of the toxicological impact of the impurity isomalathion in the relevant studies. Furthermore, confirmation is needed that isomalathion has no genotoxic potential.
[2] The safety factor was reduced to 10 due to low inter species variability.

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

Acceptable exposure scenarios (including method of calculation)

Until isomalathion is proven non genotoxic, the operator and worker risk assessment cannot be regarded as conclusive.

Operator	Fyfanon (EW) is applied both with tractor mounted equipment (field crop and orchard sprayers) and with hand-held application methods directed downwards or upwards as well as in door, at rates of 0.114-1.8 kg/ha. The estimated exposure (% of the AOEL) is: High crop (apples) No PPE With PPE German 4791 262 UK-POEM 2871 1185 Low crop (alfalfa, strawberries) German 1525 71 UK-POEM 2240 163 Hand held (apples, strawberries) German 569 24 UK-POEM 1804 245 Indoor (ornamentals) Dutch model 20 7
Workers	The estimated exposure is below the AOEL for ornamentals in glasshouse applications (EUROPOEM II). The estimated exposure is below the AOEL for strawberry cultivations after a 24-hour re-entry interval when PPE is used (EUROPOEM II). The estimated exposure is below the AOEL for apple cultivations after a 48-hour re-entry interval when PPE is used (EUROPOEM II).
Bystanders	The estimated exposure is below the AOEL for alfalfa in ground boom applications and strawberry in ground boom applications and hand-held methods (EUROPOEM II).
Amateurs	No acceptable uses.

‡ 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 toxicological data

Xn	Harmful
Xi	Irritating
R 22	Harmful if swallowed
R 43	May cause sensitisation by skin contact
S 2	Keep out of the reach of children
S 24	Avoid contact with skin
S 37	Wear suitable clothes.
S 46	If swallowed, seek medical advise immediately and show this container or label.

‡ 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	Alfalfa and cotton (P/O), lettuce (L), wheat (C) and apples (F)
Rotational crops	Confined study from California (USA) in turnips (R/T), lettuce (L), wheat (C)
Plant residue definition for monitoring	Malathion and malaoxon expressed as malathion *(1)* (provided desmethyl-malathion not more toxic than malathion) *or otherwise* Malathion, malaoxon and desmethyl-malathion expressed as malathion *(2)*
Plant residue definition for risk assessment	Malathion, malaoxon and desmethyl-malathion expressed as malathion *
Conversion factor (monitoring to risk assessment)	*(1)* no sufficient data available to propose a conversion factor accounting for desmethyl-malathion residues *(2)* none required

* malathion mono- and dicarboxylic acid not considered yet

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

Animals covered	Lactating goats and laying hens
Animal residue definition for monitoring	Malathion and desmethyl-malathion, expressed as malathion (RMS proposal, not peer reviewed)
Animal residue definition for risk assessment	Malathion, and desmethyl-malathion, expressed as malathion (RMS proposal, not peer reviewed)
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

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

.....	Based on the available confined rotational crop study and DT_{50} and DT_{90} in soil it is very unlikely that positive residues of malathion and malaoxon would be found in rotational crops. No information for desmethyl-malathion available

‡ 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)

.....	Malathion and malaoxon stable in frozen samples of cereals, fruits and vegetables for at least 12 months No data on storage stability of desmethyl-malathion available

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

Intakes by livestock ≥ 0.1 mg/kg diet/day:	Ruminant: yes	Poultry: yes	Pig: yes
Muscle	≤0.02 mg/kg	≤0.02 mg/kg	≤0.02 mg/kg
Liver	≤0.02 mg/kg	≤0.02 mg/kg	≤0.02 mg/kg
Kidney	≤0.02 mg/kg	≤0.02 mg/kg	≤0.02 mg/kg
Fat	≤0.02 mg/kg	≤0.02 mg/kg	≤0.02 mg/kg
Milk	≤0.02 mg/kg	n/a	n/a
Eggs	n/a	≤0.02 mg/kg	n/a

[+] No feeding studies available, derived from livestock metabolism studies with malathion only; RMS proposal, not peer reviewed

‡ 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	MRL*	STMR* [+] (b)
Apple	Northern	1 x 0.03, 2 x 0.06, 1 x 0.10, 1 x 0.14, 1 x 0.20, 1 x 0.25, 1 x 0.26		0.5	0.14
Strawberry	Mediterranean	1 x 0.02, 1 x 0.03, 2 x 0.08, 1 x 0.09, 1 x 0.10, 1 x 0.23, 1 x 0.25		0.5	0.09
Alfalfa (green matter)	Mediterranean	1 x 0.43, 1 x 0.68, 1 x 1.24, 1 x 3.53	Residues corrected for moisture content.	n/a	0.96

* Sum of malathion and malaoxon expressed as malathion
[+] Results on residues of desmethyl-malathion not available from supervised trials
n/a = Not applicable

(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	0.03 mg/kg bw/day
TMDI (European Diet) (% ADI)	consumer risk assessment cannot be concluded due to data gap
NEDI (% ADI)	consumer risk assessment cannot be concluded due to data gap
Factors included in NEDI	Not applicable
ARfD	0.3 mg/kg bw Based on a human study (for 0.2% isomalathion): 1.5 mg/kg bw
Acute exposure (% ARfD)	consumer risk assessment cannot be concluded due to data gap

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

Crop/processed crop		Number of studies	Transfer factor malathion/ (malaoxon)**	% Transference *
Apple	juice wet pomace	1	0.13 3.8 (1.1)	Not calculated
Tomato	wet pomace juice puree dry pomace catsup	1	1.7 (1.4) 13.3 (14.7) 0.03 (< 0.06) 0.58 (0.59) 0.75 (0.82)	Not calculated

*Calculated on the basis of distribution in the different portions, parts or products as determined through balance studies
** No data for desmethyl-malathion available

Proposed MRLs [+] (Annex IIA, point 6.7, Annex IIIA, point 8.6)

[+] Based on sum of malathion and malaoxon expressed as malathion; **provisional**, pending confirmation of residue definition for monitoring

Apple	0.5 mg/kg
Strawberry	0.5 mg/kg

Note: Data gap to conclude on necessity for MRL proposals for food of animal origin

‡ 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 ‡	50.3 % of AR after 92 days (dual labelled in the α carbon of each ester moiety) (n=1) 57.0-67.1 % of AR after 134 days (dual labelled in the α carbon of each ester moiety) (n=4) 58.4 % of AR after 162 days (n=1)
Non-extractable residues after 100 days ‡	<40 % of AR after 92 days (dual labelled in the α carbon of each ester moiety) (n=1) 27.7-41.2 % of AR after 120 days (dual labelled in the α carbon of each ester moiety) (n=4) 25.7 % of AR after 94 days (n=1)
Relevant metabolites - name and/or code, % of applied ‡ (range and maximum)	Malathion monocarboxylic acid (MMCA) maximum ranged from 2.8 % at 6 hours to 25.0 % of AR at 8 hours (n=5) Malathion dicarboxylic acid (MDCA) maximum ranged from 19.3 % of AR at 2 days to 61.7 % at 1 day (n=5)

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

Anaerobic degradation ‡	Mineralisation 2.3 % of AR at 62 days (n=1) Non-extractable residues 14.7 % of AR at 62 days (n=1) Metabolites: Malathion dicarboxylic acid (MDCA) maximum 27.0 % at 30 day (n=1)
Soil photolysis ‡	85.4 % of AR as malathion after 30 days; mineralisation 5.4 % of AR after 30 days (n=1) non-extractable residues 8.0 % of AR after 30 days (n=1) Metabolites: not identified

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

Method of calculation	Laboratory: First order
Laboratory studies ‡ (range or median, with n value, with r^2 value)	Malathion DT_{50lab} (20°C, aerobic): single first order DT_{50} of 0.1 days at 22°C (n=1) DT_{50} of 0.17-0.25 days (n=4, r^2 = 0.842-0.980) at 20°C Malathion monocarboxylic acid (MMCA) DT_{50lab} (20°C, aerobic) 0.12-0.72 days (n=4, r^2 = 0.744-0.981) Malathion dicarboxylic acid (MDCA) DT_{50lab} (20°C, aerobic) 1.2-5.3 days (n=4, r^2 = 0.429-0.994)

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

	For FOCUS groundwater modelling, malathion: mean DT_{50}lab 0.17 d (normalisation to pF2, 20°C, aerobic, first order kinetics); MMCA mean DT_{50}lab 0.34 days (normalisation to pF2, 20°C, aerobic, first order kinetics) MDCA mean DT50lab 3.0 days (normalisation to pF2, 20°C, aerobic, first order kinetics)
	Malathion DT_{90lab} (20°C, aerobic): DT_{90} 0.55 – 0.84 days) (n=4, r^2 0.842-0.980) Malathion mocarboxylic acid (MMCA) DT_{90lab} (20°C, aerobic): DT_{90} 0.38 – 2.4 days) (n=4, r^2= 0.744-0.981) Malathion dicarboxylic acid (MDCA) DT_{90lab} (20°C, aerobic): DT_{90} 4.1 – 17.8 days) (n=4, r^2 =0.429-0.994)
	DT_{50lab} (10°C, aerobic): No data submitted. Using a Q10 value of 2.2 (FOCUS, 1996) DT_{50} and DT_{90} values were 0.37-0.55 days and 1.2-1.8 days
	DT_{50lab} (20°C, anaerobic): < 30 days (n=1)
	Degradation in the saturated zone ‡: No data submitted and not required
Field studies ‡ (state location, range or median with n value)	United States (two studies, cotton and bare ground): malathion dissipated rapidly (< 1 day) and DT_{50f}: could not be determined Malathion dicarboxylic acid (MDCA) : DT_{50f} 1.7 to 2.7 days (n=2) DT_{90f}: too rapid to be determined with the study design used
Soil accumulation and plateau concentration ‡	No data submitted and not required

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

Soil adsorption/desorption (Annex IIA, point 7.1.2)

K_f /K_{oc} ‡ K_d ‡ pH dependence ‡ (yes / no) (if yes type of dependence)	K_{foc}: malathion 151 – 308 mL/g 1/n 0.9-0.98 (mean 217 mL/g, mean 1/n = 0.94, n=5) MMCA: unstable and degraded before the equilibrium was reached MDCA: 6 - 64 mL/g 1/n 0.72-1.07 (mean 25.8 mL/g, mean 1/n = 0.98, n=4) Malathion: No pH dependence was found MDCA: adsorption increases as pH decreases For FOCUS groundwater modelling: Koc: malathion 217 (1/n 0.94) Koc:MMCA could not be determined (extrapolated values the same as noted for MDCA at different pH were considered appropriate); Koc:MDCA correlation Log Koc=0.4158soilpH+3.7382 Chateaudun 4.2mL/g (1/n 0.98) Hamburg 41.5mL/g (1/n 0.98) Jokioinen 45.6mL/g (1/n 0.98) Kremsmunster 10.9mL/g (1/n 0.98) Okehampton 25.7mL/g (1/n 0.98) Piacenza 19.3mL/g (1/n 0.98) Porto 108mL/g (1/n 0.98) Sevilla 7.4mL/g (1/n 0.98) Thiva 6.1mL/g (1/n 0.98)

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

Column leaching ‡	No data submitted, not required
Aged residues leaching ‡	Guideline. US-EPA (FIFRA) N 163-1 Aging: ranged 0.5 hours to 14 hours depending on the soil type Precipitation: 50.8 cm rainfall, time not given Leachate: 5.0 % (silty clay) – 74.4 % (sandy loam) recovered in column leachate, 1.9 % as malathion, 17.5 – 69.1 % MDCA, 5.1 – 14.2 % MMCA
Lysimeter/ field leaching studie ‡	No data submitted, not required

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

PEC (soil) (Annex IIIA, point 9.1.3)

Only initial values used in risk assessment; other values found in DAR.

Parent

Method of calculation	DT_{50} : 0.25 days Kinetics: 1st order Laboratory: worst case data from the laboratory
Application rate	Strawberries, Alfalfa Crop interception 60 % 4x 1.5 kg a.s./ha in strawberry (10 days interval between applications; no carry over of malathion assumed between applications) 1 x 1.5 kg a.s./ha in alfalfa

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	Malathion 0.80	Malathion 0.80	Malathion 0.80	Malathion 0.80
Short term 4h 2d 4d				
Long term 7d 28d 50d 100d				

Metabolite

Method of calculation	MMCA: DT_{50} 0.72 days, 23% mass formation MDCA: DT_{50} 5.3 days, 51.5% mass formation Kinetics: single exponential 1st order Laboratory: worst case data from the laboratory
Application rate	Strawberries, Alfalfa Crop interception 60 % 4 x 1.5 kg a.s./ha, 10 days interval between applications; no carry over assumed between applications for MMCA DT_{50} : 0.72days 1 x 1.5 kg a.s/ha in alfalfa

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

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	MMCA 0.18 MDCA 0.44	MMCA 0.18 MDCA 0.44	MMCA 0.18 MDCA 0.56	MMCA 0.18 MDCA 0.56
Short term 24h 2d 4d				
Long term 7d 28d 50d 100d				

Parent

Method of calculation	DT_{50} : 0.25 days Kinetics: 1st order Laboratory: worst case data from the laboratory
Application rate	Apples Late season applications (BBCH 8 and later) Crop interception 80 % 3 x 1.8 kg a.s./ha (14 days interval between applications; no carry over of malathion assumed between applications)

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			Malathion 0.48	Malathion 0.48
Short term 24h 2d 4d				
Long term 7d 28d 50d 100d				

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

Metabolites

Method of calculation	MMCA: DT_{50} 0.72 days, 23% mass formation MDCA: DT_{50} 5.3 days, 51.5% mass formation Kinetics: single exponential 1st order Laboratory: worst case data from the laboratory
Application rate	Apples Crop interception 80 % 3 x 1.8 kg a.s./ha (14 days interval between applications; no carry over assumed between applications for MMCA)

$PEC_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			MMCA 0.11 MDCA 0.29	MMCA 0.11 MDCA 0.29
Short term 24h 2d 4d				
Long term 7d 28d 50d 100d				

Parent

Method of calculation	DT_{50} : 0.25 days Kinetics: 1st order Laboratory: worst case data from the laboratory
Application rate	Apples earlier season applications (BBCH 5) Crop interception 50% 3 x 1.8 kg a.s./ha (14 days interval between applications; no carry over of malathion assumed between applications)

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

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			Malathion 1.2	Malathion 1.2
Short term 24h 2d 4d				
Long term 7d 28d 50d 100d				

Metabolites

Method of calculation	MMCA: DT_{50} 0.72 days, 23% mass formation MDCA: DT_{50} 5.3 days, 51.5% mass formation Kinetics: single exponential 1st order Laboratory: worst case data from the laboratory
Application rate	Apples earlier season applications (BBCH 5, 7 and 8) Crop interception 50, 65 and 80 % 3 x 1.8 kg a.s./ha (14 days interval between applications; no carry over assumed between applications for MMCA, for MDCA the highest (initial) value follows the first application)

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial			MMCA 0.28 MDCA 0.62	MMCA 0.28 MDCA 0.62
Short term 24h 2d 4d				
Long term 7d 28d 50d 100d				

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

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)	Malathion: pH 5 (25 °C) DT_{50} 107 days: Malathion: pH 7 (25 °C) DT_{50} 6.2 days Malathion pH 9 (25 °C) DT_{50} 0.49 days
Photolytic degradation of active substance and relevant metabolites ‡	Malathion DT_{50} 156 test system days (laboratory study, not equated to natural light conditions)
Readily biodegradable (yes/no)	Malathion is not readily biodegradable.
Degradation in water/sediment - DT_{50} water ‡	**Malathion:** DT_{50} water 8 – 10 hours, DT_{90} water 27 - 35 hours (1^{st} order, r^2=0.875 and 0.933, n=2) DT_{50} whole system 8 – 10 hours; DT_{90} whole system 27 – 35 hours (1^{st} order, r^2=0.881 and 0.918, n=2) **MMCA**: DT_{50} water 3 – 4 days, DT_{90} water 9 – 12 days (1^{st} order, r^2=0.943 and 0.915, n=2); DT_{50} whole system 3 – 4 days, DT_{90} whole system 9 – 12 days (1^{st} order, r^2=0.952 and 0.926, n=2) **MDCA:** DT_{50} water 15 – 17 days, DT_{90} water 50 – 57 days (1^{st} order, r^2=0.712 and 0.831, n=2); DT_{50} whole system 13 – 21 days, DT_{90} whole system 45 – 71 days (1^{st} order, r^2=0..797 and 0.727, n=2)
Mineralization	57.7 – 68.6 % of AR (at 120 days, n=2)
Non-extractable residues	25.5 – 36.4 % of AR (at 120 days, n=2)
Distribution in water / sediment systems (active substance) ‡	Maximum of 1.0 – 3.5 % AR in sediment after 0.3 – 1 d (n=2). DT_{50} not calculated.
Distribution in water / sediment systems (metabolites) ‡	Water: MMCA maximum of 37.3 – 46.5 % AR after 1 - 2 d (n=2) MDCA maximum of 20.7 - 33.4 % AR after 4 - 14 d (n=2) Sediment: MMCA maximum of 2.0 – 3.3 % AR after 1 d (n=2) MDCA maximum of 4.6 – 7.5 % AR after 2 – 7 d (n=2)

‡ 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	Initial concentration used for both acute and chronic risk assessment since the effects of malathion is acute in nature. Therefore no other actual PECsw or twa PECsw are presented here, since they are not used in risk assessment. These values are however found in the DAR. No carry over of malathion residues is expected from multiple applications (DT_{50} 0.42 days).
Application rate	3x1.8kg a.s./ha (apple), 4x1.5kg a.s./ha (strawberry) 1x1.5kg a.s./ha (alfalfa)
Main routes of entry	Spray drift only

Instantaneous PECsw values (µg/l) for malathion at selected buffer distances and application rates in a static 30cm deep water body

	Buffer distance (m)							
	1	5	10	15	20	30	40	50
'late' after flowering %drift 90th/77th percentile		8.41/ 6.04	3.6/ 2.67	1.81/ 1.39	1.09/ 0.8	0.54/ 0.36	0.32/ 0.21	0.22/ 0.13
Crop and GAP								
Apples 3 x 1.8 kg a.s./ha (interval 14 days)								
90th percentile spray drift PEC		50.46	21.60	10.86	6.54	3.24	1.92	1.32
77th percentile spray drift PEC		36.24	16.02	8.34	4.80	2.16	1.26	0.78

	Buffer distance (m)							
	1	5	10	15	20	30	40	50
% drift 90th/ 77th percentile	2.77/ 2.01	0.57/ 0.41	0.29/ 0.2	0.2/ 0.14	0.15/ 0.1	0.1/ 0.07	0.07/ 0.05	0.06/ 0.04
Crop and GAP								
Strawberries 4 x 1.5 kg a.s./ha (interval 10 days)								
90th percentile spray drift PEC	13.85	2.85	1.45	1.0	0.75	0.5	0.35	0.3
77th percentile spray drift PEC	10.05	2.05	1.0	0.7	0.5	0.35	0.25	0.2
Alfalfa 1.5 kg a.s./ha								
90th percentile spray drift PEC	13.85	2.85	1.45	1.00	0.75	0.50	0.35	0.3

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

Metabolites

Method of calculation	**MMCA:** DT_{50} 4 days 43.9% mass formation Representative worst case from the water-sediment study **MDCA:** DT_{50} 17 days 28.97% mass formation Representative worst case from the water-sediment study
Application rate	Same use patterns on apples, strawberry and alfalfa as listed for parent above.
Main routes of entry	Spray drift

Instantaneous PECsw values (µg/l) for malathion monocarboxylic acid in a static water body

Crop	Time after application (days)	90th percentile spray drift (single application) 1 m	77th percentile spray drift (multiple applications) 1 – 3 m
		PECsw (µg/l)	PECsw(µg/l)
Apples after flowering	0	-	31.61
Strawberries	0	-	5.32
Alfalfa	0	6.0	-

Instantaneous PECsw values (µg/l) for malathion dicarboxylic acid in a static water body

Crop	Time after application (days)	90th percentile spray drift (single application) 1 m	77th percentile spray drift (multiple applications) 1-3 m
		PECsw (µg/l)	PECsw (µg/l)
Apples after flowering	0	-	36.07
Strawberries	0	-	6.99
Alfalfa	0	4.0	-

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

Parent

Method of calculation	Initial concentration used for both acute and chronic risk assessment since the effects of malathion is acute in nature. Therefore no other actual PECsw or twa PECsw are presented here, since they are not used in risk assessment. These values are however found in the addendum to the DAR dated February 2005. No carry over of malathion residues is expected from multiple applications (DT_{50} 0.42 days).

Instantaneous PECsw values (µg/l) for malathion at selected buffer distances and application rates in a static 30cm deep water body								
	Buffer distance (m)							
	3	5	10	15	20	30	40	50
'Early' before flowering %drift 90th percentile	29.2	19.89	11.81	5.55	2.77	1.04	0.52	0.3
Crop and GAP								
Apples 3 x 1.8 kg a.s./ha (interval 14 days)								
PECsw	175.2	119.3	70.9	33.3	16.2	6.2	3.1	1.8

Metabolites

Method of calculation MMCA: First application 'Early' before flowering 29.2% drift MDCA: First application 'Early' before flowering 23.96% drift 2nd and 3rd applications 'late' after flowering 11.01%	**MMCA:** DT_{50} 4 days 43.9% mass formation Representative worst case from the water-sediment study **MDCA:** DT_{50} 17 days 28.97% mass formation Representative worst case from the water-sediment study

Instantaneous PECsw values (µg/l) for malathion monocarboxylic acid in a static water body		
Crop	Time after application (days)	90th percentile spray drift single 1st before flowering application (highest value) 3 m
		PECsw(µg/l)
Apples before and after flowering	0	76.9

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

Instantaneous PECsw values (µg/l) for malathion dicarboxylic acid in a static water body		
Crop	Time after application (days)	77th percentile spray drift (multiple applications gives highest value) 3 m
		PECsw (µg/l)
Apples before and after flowering	0	43.2

PEC (sediment)

Parent

Method of calculation	Not relevant
Application rate	Not relevant
Remark	Malathion not found in sediment; metabolites of low toxicity to daphnia

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

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	1. FOCUS model: PRZM (2.4.1) Scenarios: Kremsmünster, Sevilla Crop: strawberries 2. FOCUS model: PRZM (2.4.1) Scenarios: all nine FOCUS scenarios Crop: apples DT50: malathion 0.17 days MMCA 0.34 days, MDCA 3 days (mean value from the laboratory study) Koc: 217, 1/n 0.94 pH dependent sorption of MMCA and DMCA taken into account (Koc values are given in result table 1/n 0.98)
Application rate	- Strawberries: 6 applications of 2.16 kg a.s./ha, 60 % interception at senescence /ripening was used in accordance with FOCUS guidance - Apples: 3 x 1.8 a.s./ha, 80 % interception Worst case late summer / early autumn applications

$PEC_{(gw)}$

Maximum concentration	No data available
Average annual concentration (Results quoted for modelling with FOCUS gw scenarios, according to FOCUS guidance)	Malathion < 0.1 µg/l MMCA < 0.1 µg/l MDCA < 0.1µg/l in all scenarios

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

PEC(gw) - FOCUS modelling results

Model /Crop	Scenario	Parent (µg/l)	Metabolite (µg/l)		
			MMCA	MDCA	MMCA and MDCA
	Strawberry: Hamburg	<0.001	<0.001	0.003	26
	Strawberry, Kremsmünster	<0.001	<0.001	0.004	10.9
	Strawberry, Jokioinen	<0.001	<0.001	0.001	26
	Strawberry, Sevilla	<0.001	<0.001	<0.001	7.4
	Apples: Châteaudun	<0.001	<0.001	0.018	4.2
	Apples: Hamburg	<0.001	<0.001	0.047	26
	Apples: Jokioinen	<0.001	<0.001	0.0014	26
	Apples: Kremsmünster	<0.001	<0.001	0.034	10.9
	Apples: Okehampton	<0.001	<0.001	0.006	25.7
	Apples: Piacenza	<0.001	<0.001	0.046	19.3
	Apples: Porto	<0.001	<0.001	<0.001	26
	Apples: Sevilla	<0.001	<0.001	0.004	7.4
	Apples: Thiva	<0.001	<0.001	0.042	6.1

Note groundwater simulations that include the pertinent lower crop interception values for 'early' before flowering applications to apples are also provided In the addendum to the DAR dated February 2005 and the EFSA addendum dated September 2005, however the annual average leachate concentrations predicted for these applications earlier in the season were lower than those presented above.

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

Direct photolysis in air ‡	No data available
Quantum yield of direct phototransformation	No data available
Photochemical oxidative degradation in air ‡	SMILES : CCOC(=O)CC(SP(=S)(OC)OC)C(=O)OCC CHEM : Malathion SUMMARY (AOP v1.91): OVERALL OH Rate Constant = 77.4198 E-12 cm3/molecule-sec HALF-LIFE = 0.414 Days (12-hr day; 0.5E6 OH/cm3) HALF-LIFE = 4.974 Hrs NO OZONE REACTION ESTIMATION

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

Volatilization ‡	from plant surfaces: no data available
	from soil: < 6 % in 16 days

PEC (air)

Method of calculation	Henry's law constant 1.0 x 10^{-3} Pa m^3mol^{-1} Vapour pressure 4.5 x 10^{-4} Pa

$PEC_{(a)}$

Maximum concentration	Not applicable

Definition of the Residue (Annex IIA, point 7.3)

Relevant (major metabolites) to the environment	Definition for risk assessment Soil: Malathion, malathion monocarboxylic acid (MMCA) (max. 25 %), malathion dicarboxylic acid (MDCA) (max. 62 %) Surface water: malathion, malathion monocarboxylic acid (MMCA) (48 %) and malathion dicarboxylic acid (MDCA) (35 %) Sediment: none Ground water: malathion and malathion dicarboxylic acid (MDCA) Air: malathion Definition for monitoring All compartments malathion. However as in surface water and soil malathion degrades very rapidly, malathion dicarboxylic acid would be a marker that was more likely to be present.

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

Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

‡ 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 fate and behaviour data	R53	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 – Malathion (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals ‡	LD_{50} 1778 mg a.s./kg bw (Rat, females)
Chronic toxicity to mammals ‡	NOAEL 25 mg a.s./kg bw/day (Rabbit; teratology study)
Acute toxicity to birds ‡	Malathion technical: LD_{50} 359 mg a.s./kg bw (Bobwhite quail) Malaoxon: LD_{50} 43 mg a.s./kg bw (Bobwhite quail) CHA3110 Formulation: LD_{50} 214 mg a.s./kg bw (Bobwhite quail)
Dietary toxicity to birds ‡	Malathion technical: LD_{50} 554 mg a.s./kg bw/day (Bobwhite quail) Malaoxon: LD_{50} 333.5 mg a.s./kg bw (Bobwhite quail)
Reproductive toxicity to birds ‡	NOEC 13.5 mg a.s./kg bw/day (Bobwhite quail)

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

Acute toxicity to birds ‡	LD_{50} 43 mg/kg bw (Bobwhite quail)
Dietary toxicity to birds ‡	LD_{50} 333.5 mg a.s./kg bw/day (Bobwhite quail)
Chronic toxicity to mammals ‡	NOAEL 1 mg a.s./kg bw/day (Rat; 24-month toxicity study)

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

TER values calculated based on the final revision of Guidance document of birds and mammals (Sanco/4145/2000, 25.9.2002). All values are based on measured residues from field trials.

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
1.5	Alfalfa	Insectivorous bird	acute	26.3 [1]	10
1.5	Alfalfa	Herbivorous bird	acute	**8.8** [2]	10
1.5	Strawberry	Insectivorous bird	acute	26.3 [1]	10
1.5	Strawberry	Frugivorous bird	acute	98.1 [2]	10
1.8	Apple orchard	Insectivorous bird	acute	21.9 [1]	10

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

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
1.5	Alfalfa	Medium herbivore mammal	acute	48.7	10
1.5	Strawberry	Medium frugivorous mammal	acute	30.4	10
1.8	Apple orchard	Small herbivore mammal	acute	13	10
1.5	Alfalfa	Insectivorous bird	short-term	68.1 [1]	10
1.5	Alfalfa	Herbivorous bird	short term	29.2 [3]	10
1.5	Strawberry	Insectivorous bird	short term	68.1 [1]	10
1.5	Strawberry	Frugivorous bird	short term	466 [3]	10
1.8	Apple orchard	Insectivorous bird	short term	56.7 [1]	10
1.5	Alfalfa	Insectivorous bird	long-term	23.7 [1]	5
1.5	Alfalfa	Herbivorous bird	long-term	6.2 [3]	5
1.5	Strawberry	Insectivorous bird	long-term	23.7 [1]	5
1.5	Strawberry	Frugivorous bird	long-term	90 [3]	5
1.8	Apple orchard	Insectivorous bird	long-term	19.8[1]	5
1.5	Strawberry	Medium frugivorous mammal	long-term	438.5 [3]	5
1.5	Alfalfa	Medium herbivore mammal	long-term	32.4 [3]	5
1.8	Apple orchard	Small herbivore mammal	long-term	**3.6** [4]	5

[1] Refined by using the worst case initial residues measured from a field residue trial of arthropods with application post-flowering. Hence pre-flowering application is not covered.
[2] Refined by using 90th percentile measured residues from field residue trials.
[3] Refined by using mean measured residues from field residue trials.
[4] Refined by using measured residues from field trial.

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

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

TER values calculated based on the final revision of Guidance document of birds and mammals (Sanco/4145/2000, 25.9.2002). All values are based on measured residues from field trials.

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
1.5	Alfalfa	Herbivorous bird	acute	143	10
1.5	Alfalfa	Insectivorous bird	acute	551	10
1.5	Strawberry	Frugivorous bird	acute	860	10
1.5	Strawberry	Insectivorous bird	acute	551	10
1.8	Apple	Insectivorous bird	acute	457	10
1.5	Alfalfa	Herbivorous bird	short-term	1113	10
1.5	Alfalfa	Insectivorous bird	short-term	4282	10
1.5	Strawberry	Frugivorous bird	short-term	6680	
1.5	Strawberry	Insectivorous bird	short-term	4282	
1.8	Apple	Insectivorous bird	short-term	3553	
1.5	Alfalfa	Herbivorous mammal	long-term	17	5
1.5	Strawberry	Frugivorous mammal	long-term	42	5
1.8	Apple	Herbivorous mammal	long-term	5.3 [1]	5

[1] Calculation has been based on the information obtained from the alfalfa residue study. The estimated RUD of 23 in short grass has been multiplied with 0.02, since around 2 % of malaoxon was found in alfalfa after treatment (see Table B.9.4.4-2).

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/l)
Laboratory tests ‡				
Fish	Malathion technical	96 hour	Mortality; LC_{50}	0.022
Fish	Malathion technical	ELS	Growth NOEC	0.021
Daphnia	Malathion technical	48 hour	Mortality; EC_{50}	0.00072

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Daphnia	Malathion technical	21 days	Reproduction NOEC	0.00006
Algae	Malathion technical	72 hours	Biomass EC_{50}	4.1
Fish	CHA3110 Formulation	96 hour	Mortality; LC_{50}	0.053
Daphnia	CHA3110 Formulation	48 hour	Mortality; EC_{50}	0.0018
Fish	Monocarboxylic acid	96 hour	Mortality; LC_{50}	79.0
Daphnia	Monocarboxylic acid	48 hour	Mortality; EC_{50}	3.5
Fish	Dicarboxylic acid	96 hour	Mortality; LC_{50}	>100
Daphnia	Dicarboxylic acid	48 hour	Mortality; EC_{50}	71
Fish	Dimethyl thiophosphate	96 hour	Mortality; LC_{50}	>1000
Daphnia	Dimethyl thiophosphate	48 hour	Mortality; EC_{50}	70.5
Fish	Dimethyl phosphate	96 hour	Mortality; LC_{50}	>1000
Daphnia	Dimethyl phosphate	48 hour	Mortality; EC_{50}	>1000

Microcosm or mesocosm tests

Mesocosm study:

Based on a single application of malathion the NOEC, LOEC and NOAEC (No Observed Adverse Effect Concentration) was considered to be as follows:

NOEC 5.0 µg a.s./l (no treatment related effects on biota were evident).

LOEC 10 µg a.s./l (based solely on the transient impact on Daphniidae and Chydoridae populations).

NOEAEC 30 µg a.s./l (long term effects were not observed).

The EAC (Ecologically Acceptable Concentration)or NOAEC was considered to be 30 µg/l. Effects at this concentration were considered to have no adverse long term ecological effect on the ecosystem with single application.

Since applied uses include multiple applications the NOEC value is used for risk assessment.

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

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Malathion*						
1.8	Apples (early application)	Fish	Acute	50	12.2	10**
		Daphnia	Acute	30	0.23	100
		Algae	Acute	5	34	10
1.8	Apples (late application)	Fish	Acute	40	11.3	10**
		Daphnia	Acute	30	0.22	100
		Algae	Acute	5	80	10
1.5	Strawberry	Fish	Acute	10	15	10**
		Daphnia	Acute	30	1.44	100
		Algae	Acute	5	1425	10
Dicarboxylic acid						
1.8	Apples (late application)	Fish	Acute	3	>2772	100
		Daphnia	Acute	3	1968	100
1.5	Strawberry	Fish	Acute	1	>14306	100
		Daphnia	Acute	1	10157	100
1.5	Alfalfa	Fish	Acute	1	>25 000	100
		Daphnia	Acute	1	17750	100
Monocarboxylic acid						
1.8	Apples (late application)	Fish	Acute	3	2499	100
		Daphnia	Acute	3	111	100
1.5	Strawberry	Fish	Acute	1	14850	100
		Daphnia	Acute	1	658	100
1.5	Alfalfa	Fish	Acute	1	13167	100
		Daphnia	Acute	1	583	100
Dimethyl thiophosphate						
1.8	Apples (late application)	Fish	Acute	3	>12019	100
1.8		Daphnia	Acute	3	919	100
Dimethyl phosphate						
1.8	Apples	Fish	Acute	3	>13280	100
		Daphnia	Acute	3	14 513	100

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

Application rate (kg as/ha)	Crop	Organism	Time-scale	Distance (m)	TER	Annex VI Trigger
Malathion*						
1.8	Apples (early application)	Fish	Chronic	50	11.6	10
		Daphnia	Chronic	40	0.02	10
		Daphnia	Refined	40	1.6	3-5
		Daphnia	Refined	50	2.8***	3-5
1.8	Apples (late application)	Fish	Chronic	40	10.9	10
		Daphnia	Chronic	30	0.019	10
		Daphnia	Refined	40	**2.6*** **	3-5
		Daphnia	Refined	50	3.8***	3-5
		Daphnia	Refined	75	7.6***	3-5
1.5	Strawberry	Fish	Chronic	10	14.5	10
		Daphnia	Chronic	30	0.12	10
		Daphnia	Refined	10	3.4***	3-5
		Daphnia	Refined	20	6.6***	3-5
0.114	Ornamentals (glasshouse)	Fish	Chronic	0	571	10
		Daphnia	Refined	0	132***	3-5

* TER values for use in alfalfa are not provided (single application 1.5 kg a.s/ha), since the use amount in strawberries is the same (4 x 1.5 kg a.s./ha). Due to rapid degradation of malathion, no carry over of residues is expected.
** Trigger-value has been lowered from 100 to 10 since 6 fish species had been tested.
*** Based on the NOEC of 5 µg/l obtained from mesocosm study

Bioconcentration

Bioconcentration factor (BCF) ‡	103
Annex VI Trigger:for the bioconcentration factor	100
Clearance time (CT_{50}) (CT_{90})	0.69 days 2.29 days
Level of residues (%) in organisms after the 14 day depuration phase	5.4 % ^{14}C-residues; no malathion

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

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

Acute oral toxicity ‡	0.40 µg a.s. per bee (formulation FYF 440 EW)
Acute contact toxicity ‡	0.16 µg a.s. per bee (formulation FYF 440 EW)

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

Application rate (kg as/ha)	Crop	Route	Hazard quotient	Annex VI Trigger
Laboratory tests				
1.8	Apple orchard	Oral	4500	50
1.8	Apple orchard	Contact	11250	50

Field or semi-field tests

- Residue studies with sprayed alfalfa showed no significant effect on mortality after 24 hours.
- Semifield and field studies have shown repellency to foraging after malathion treatment for around 1 day.
- Crop specific factors:

Apples: Application not during the flowering period

Alfalfa: Application one week before cutting when alfalfa will not be flowering

Strawberries: Application occurs during the flowering period. However the semi-field study in green house with application rate of 2.16 kg a.s./ha showed repellency during the application day, but thereafter the foraging activity was comparable to control. No significant effects were seen on mortality or effects on the brood were observed in the study. The study also showed that strawberries are unattractive as pollen source for honey bees.

Risk considered acceptable.

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

Test Substance: CHA3110 (440 g/L EW formulation)

Species	Dose (kg as/ha)	Endpoint	Effect	ESCORT 2
Laboratory species				
Typhlodromus pyri	Dose-response	7-day LR_{50}	LR_{50}: 85.4 g a.s./ha (**HQ = 21** at 1.8 kg a.s./ha)	HQ < 2
Aphidius rhopalosiphi	Dose-response	48-hour LR_{50}	LR_{50} : 0.06125 g a.s./ha (**HQ = 29388** at 1.8 kg a.s./ha)	HQ < 2

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

Species	Dose (kg as/ha)	Endpoint	Effect		ESCORT 2
Extended Laboratory tests Application rates 2.16 kg a.s/ha and 6.3 kg a.s/ha					
Species	Exposure	Endpoint	2.16 kg a.s./ha	6.3 kg a.s./ha	
Typhlodromus pyri	Fresh spray deposit	Mortality & repro.	88% mortality	94% mortality	50% effect
	Aged residue rate-response		The 50% threshold (mortality and reproduction) was not exceeded on 5-day aged residues.	The 50% threshold (mortality and reproduction) was not exceeded on 5-day aged residues.	
Aphidius rhopalosiphi	Fresh spray deposit	Mortality & parasitism rate	100% mortality	100% mortality	50% effect
	Aged residue rate -response		The 50% threshold (mortality and parasitisation rate) was exceeded up to and on 28-day aged residues.	The 50% threshold (mortality and parasitisation rate) was exceeded up to and on 63-day aged residues.	
Chrysoperla carnea	Fresh spray deposit	Mortality & parasitism rate	100% mortality	100% mortality	50% effect
	Aged residue rate -response		The 50% threshold (mortality and parasitisation rate) was exceeded up to and on 10-day aged residues.	The 50% threshold (mortality and parasitisation rate) was exceeded up to and on 14-day aged residues.	
Orius laevigatus	Fresh spray deposit	Mortality & parasitism rate	100% mortality	100% mortality	50% effect
	Aged residue rate -response		The 50% threshold (mortality and parasitisation rate) was exceeded up to and on 14-day aged residues.	The 50% threshold (mortality and parasitisation rate) was exceeded up to and on 36-day aged residues.	

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

Field or semi-field tests Field applications of malathion had little or no effect on predatory mite populations following applications to a strawberry crop. This was thought to result from incomplete spray coverage of the leaves (even at high volumes), thus allowing mites to survive in unsprayed niches. Since predatory mite populations was shown in the laboratory to be the least susceptible of the groups tested, two additional field trials was performed to address the off-field risk of malathion to non-target arthropods: one in northern France in apples with drift rates from 10 and 20 m (3 x 1.8 kg a.s/ha) and one in Italy in alfalfa with drift rate from 1 m (1 x 1.5 kg a.s/ha and 6 x 2.16 kg a.s./ha to cover use pattern in strawberry). The results showed no longer-term harmful effects of CHA 3110 formulation treatment on any of the non-target arthropods sampled in the study.

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

Acute toxicity ‡	Malathion: 14 day LC_{50} (technical): 306 mg a.s./kg soil* 14 day LC_{50} (formulation): 123 mg product/kg soil* (≈ 58 mg a.s./kg soil) Metabolites: MCA and DCA: not studied, since the rapid degradation of malathion → presumed to be present in parent study Dimethyl thiophosphate: 14 day LC_{50} > 1000 mg/kg soil Dimethyl phosphate: 14 day LC_{50} > 1000 mg/kg soil
Reproductive toxicity ‡	Malathion degrades extremely rapidly, with a DT50 in soil of 1 day (DT50 values in the laboratory were 0.2 – 2.5 days and were too fast to measure in the field). Thus, a sublethal effects study on earthworms is considered unnecessary.

* Values divided by factor 2 since malathion's logKow is 2.75

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
Malathion				
1.5	Strawberries	14-day acute	72.5	10
Metabolites				
Dicarboxylic acid	Strawberries	14-day acute	65*	10
Monocarboxylic acid	Strawberries	14-day acute	21*	10

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

Application rate (kg as/ha)	Crop	Time-scale	TER	Annex VI Trigger
Dimethyl thiophosphate	Apples (1.8 kg as/ha)	14-day acute	>617	10
Dimethyl phosphate	Apples (1.8 kg as/ha)	14-day acute	>658	10

* TER values theoretical and are calculated based on the assumption of 10-fold increase in the toxicity compared to malathion.

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

Nitrogen mineralization ‡	<25% inhibition at rates equivalent to 0.5x and 1x the maximum field application rate (based on an annual application rate of 6.3 kg a.s./ha).
Carbon mineralization ‡	<25% inhibition at rates equivalent to 0.5x and 1x the maximum field application rate (based on an annual application rate of 6.3 kg a.s./ha).

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Preliminary screening data

Limit test was provided with highest application rate of 1.8 kg a.s./ha for six species.

Laboratory limit dose test

Most sensitive species	Test substance	ER50 (g/ha)[2] vegetative vigour	ER50 (g/ha)[2] emergence	Exposure[1,2] (g/ha)[3]	TER	Trigger
All six species	formulation	> 1800 g a.s./ha		64.8[1]	> 27.8	5
All six species	formulation	> 1800 g a.s./ha		283.1[2]	> 6.4	5

[1] based on Ganzelmeier drift data with 10 m buffer zone needed to protect the off-crop arthropods
[2] based on Ganzelmeier drift data with 3 meter default buffer zone in fruit crops
[3]dose is expressed in units of a.s.

Classification and proposed labelling (Annex IIA, point 10)

with regard to ecotoxicological data	R50 Very toxic to aquatic organisms

‡ 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