European Food Safety Authority

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CONCLUSION ON PESTICIDE PEER REVIEW

Peer review of the pesticide risk assessment of the active substance malathion[1]

(Question No EFSA-Q-2009-587)

Re-Issued on 17 July 2009

SUMMARY

Malathion is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[2], as amended by Commission Regulation (EC) No 1490/2002[3]. 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 notifier Cheminova A/S. There was also another notifier (Cequisa) according to Commission Regulation (EC) No. 703/2001[4] 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 discussion of the outcome of the consultation of experts following the procedure set out in Commission Regulation (EC) 451/2000 took place with representatives from the Member States on 30 November 2005 leading to the conclusions set out in the EFSA Conclusion finalised on 13 January 2006 (EFSA Scientific Report (2006) 63)

Following the Commission Decision of 6 June 2007 (2007/389/EC)[5] concerning the non-inclusion of malathion in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant, Cheminova A/S made a resubmission application for the inclusion of malathion in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No.

[1] For citation purposes: Conclusion on pesticide peer review regarding the risk assessment of the active substance malathion. *EFSA Scientific Report* (2009) 333, 1-118

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

[3] OJ No L 224, 21.08.2002, p. 25

[4] OJ No L 98, 07.04.2001, p. 6

[5] OJ No L146, 8.6.2007, p. 19

33/2008[6]. The resubmission dossier included further data in response to the areas of concern identified in the review report (European Commission, 2007) as follows:

- the presence in the technical material of isomalathion, the genotoxicity of which cannot be excluded,
- the consumer exposure
- the long term risk to mammals

and concerns were identified with regard to:

- the exposure of operators, workers and bystanders which cannot be concluded due to the presence of isomalathion in the technical material
- the acute and chronic risk for consumers, due to the insufficient information on the effects of certain toxicologically relevant metabolites
- the high risk to aquatic organisms, honey bees and non-target arthropods.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, The United Kingdom, being the designated rapporteur Member State, submitted an evaluation of the additional data on malathion in the format of an Additional Report (The United Kingdom, 2009a). The Additional Report was received by EFSA on 11 February 2009. In accordance with Article 19, the EFSA distributed the Additional Report to the Member States and the applicant for comments on 13 February 2009. The EFSA collated and forwarded all comments received to the Commission on 17 March 2009. At the same time, the collated comments were forwarded to the rapporteur Member State for compilation in the format of a Reporting Table.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 24 April 2009, the Commission requested the EFSA to arrange a peer review of the Additional Report provided by the rapporteur Member State, and to deliver its conclusion on the risk assessment within 90 days.

The peer review commenced with EFSA's consideration of the Reporting Table containing the applicant's response to the comments and the RMS' evaluation of the comments and response. All points that were identified as unresolved at the end of the comment evaluation phase were further considered in a series of scientific meetings and a telephone conference with Member State experts in June 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in June 2009. The EFSA conclusion has therefore been re-issued to update the risk assessment in all areas.

The original conclusion from the review was reached on the basis of the evaluation of the representative uses as acaricide and insecticide as proposed by the notifier, which comprised foliar spraying to control various harmful organisms in apples, strawberries, alfalfa and ornamentals at application rate up 1.8 kg malathion per hectare. The uses on apple and alfalfa were no longer supported in the resubmission application, and therefore the conclusion has

[6] OJ No L 15, 18.01.2008, p. 5

only been updated in relation to the risk assessment of the representative uses presented in the Additional Report, i.e. only the use in strawberries and ornamentals at application rates of maximum 1.2 kg and 0.114 kg malathion per hectare respectively.

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 to monitor all compounds given in the respective residue definitions, however a data gap was identified concerning amendments to the description of the sample preparation for the method for residues in plants. In case of food of plant origin, malathion and malaoxon[7] can also be determined by a multi-residue method. No method for the determination of malathion in food of animal origin is required for the representative uses of the resubmission. In the 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 lower than 3 days.

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[8] 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 at the EPCO meeting 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.

The level of isomalathion in the current 5-batch analysis showed a mean content of 0.048-0.076%. This implied that the limit of 0.03% regarding the toxicological data package would not be feasible. Thus, the toxicological assumptions had 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 had 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 (MMCA[9]) and dicarboxylic (MDCA[10]) acids of malathion. Malathion is 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

[7] Malaoxon: diethyl (2*RS*)-2-[(dimethoxyphosphoryl)sulfanyl]butanedioate
[8] Isomalathion: diethyl (2*RS*)-2-{[methoxy(methylsulfanyl)phosphoryl]sulfanyl}butanedioate
[9] MMCA: (2*RS*)-2-[(dimethoxyphosphorothioyl)sulfanyl]-4-ethoxy-4-oxobutanoic acid
[10] MDCA: (2*RS*)-2-[(dimethoxyphosphorothioyl)sulfanyl]butanedioic acid

effect in short and long term studies is the decrease of acetylcholinesterase 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 with a 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, based on human data (isomalathion content 0.24%), is 1.5 mg/kg bw, with a safety factor of 10 added. Exposure estimates indicate levels of exposure for operators wearing PPE within the AOEL for both boom sprayer and knapsack application; the bystander and worker exposure is below the AOEL (gloves have to be worn for workers re-entering the treated fields).

The metabolism of malathion in plants was studied in different crops. Results of those studies indicate that, even though the metabolic pattern appeared comparable across the different crops, significant differences in quantity of the formed metabolites, and therewith in their relevance for consumer exposure, exist. The metabolism of malathion yields the major metabolites malathion mono- and dicarboxylic acid (MMCA and DMCA), and desmethyl-malathion[11] (DMM), and, though at lower levels, malaoxon.

In the resubmission procedure, the relevance of metabolites and degradation products of malathion for consumer safety could be addressed and a residue definition for consumer risk assessment could be established. Considering the toxicological effects of malathion and its metabolites as well as the occurrence of these compounds in crops and processed commodities, the residue definition relevant for consumer risk assessment was established as: Malathion and its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion toxic equivalents.

Pending the final confirmation of a toxic equivalency factor to consider the higher toxicity of malaoxon, a provisional factor of 30 was applied to convert malaoxon residues in malathion toxic equivalents. A factor of 7 proposed by the RMS could not be concluded on during the peer review without having considered in detail all the existing studies. A reassessment performed by the RMS after the experts' discussions indicated that malaoxon is 6-7 fold more toxic than malathion, however this assessment has not been peer reviewed.

Information is still necessary to fully address residues in processed commodities and succeeding crops. Moreover, four additional residue trials in strawberries are still required. However, the experts in the teleconference meeting PRAPeR TC 12 considered a provisional, indicative consumer risk assessment would be possible with the available data on strawberries. This assessment indicates that consumer intakes are below 10 % of the ADI and of both ARfD, respectively.

It should be noted that malathion and its metabolites consist of two enantiomers, but the dossier provides no information on whether either isomer is metabolised more quickly than the other in matrices relevant for consumer exposure. Consideration of any impact for the risk from consumer exposure to different enantiomer ratios of malathion and its relevant metabolites would be necessary to finalise the risk assessment. However, despite the

[11] DMM:diethyl (2*RS*)-2-{[hydroxy(methoxy)phosphorothioyl]sulfanyl}butanedioate

uncertainties in the provisional risk assessment presented in this document, the margin of safety between the currently estimated consumer exposure and the allocated toxicological reference values is considered sufficiently big with respect to the notified use of malathion in strawberries.

The available data demonstrate that in soil malathion degrades to the major (>10% applied radioactivity) metabolites malathion monocarboxylic acid (MMCA) and 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.

For the representative use on strawberry appropriate aquatic exposure assessment in accordance with FOCUS 2001 surface water guidance is available for malathion and its metabolites MMCA and MDCA. In addition for malathion spray drift mitigation was implemented in aquatic exposure assessments in accordance with FOCUS 2007 landscape and mitigation guidance. This assessment has been demonstrated to encompass the exposure expected from the use assessed on glasshouse ornamentals, when a Dutch procedure for estimating emissions from glasshouses to surface water is followed.

The available FOCUS groundwater modelling indicates that the potential for groundwater contamination as a consequence of the applied for representative uses (both in the original application and in the resubmission application) 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).

Data were not available to conclude on the acute and long-term risk to insectivorous birds following application in strawberries. The risk is however considered low for all mammals and frugivorous birds. Based on the data available, malathion was considered to be very toxic

to aquatic organisms. Acute toxicity to fish and toxicity to invertebrates was driving the aquatic risk assessment for use in strawberries. Based on FOCUSsw Step 4 exposure data including maximum mitigation measures the risk was considered low in three out of four scenarios. The toxicity to bees was identified as high and risk mitigation measures should be set at Member State level. No risk mitigations measures were needed to protect other non-target arthropods off field. The risk of malathion to earthworms, other soil macro- and micro-organisms, non-target flora and biological methods of sewage treatment was assessed as low. However, a data gap was defined to address the potential risk to earthworms for the enantiomer forms of the metabolite MDCA.

Key words: malathion, 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 DAR (Finland, 2004), 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 DAR. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the revised version of the DAR was distributed for consultation on 16 April 2004 to the Member States and the main notifier Cheminova A/S as identified by the rapporteur Member State.

The comments received on the DAR 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 discussion of the outcome of the consultation of experts following the procedure set out in Commission Regulation (EC) 451/2000 took place with representatives from the Member States on 30 November 2005 leading to the conclusions set out in the EFSA Conclusion finalised on 13 january 2006 (EFSA Scientific Report (2006) 63).

Following the Commission Decision of 6 June 2007 (2007/389/EC)[12] concerning the non-inclusion of malathion in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant, Cheminova A/S made a resubmission application for the inclusion of malathion in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the areas of concern identified in the review report as follows:

- the presence in the technical material of isomalathion, the genotoxicity of which cannot be excluded,
- the consumer exposure

[12] OJ No L146, 8.6.2007, p. 19

- the long term risk to mammals

and concerns were identified with regard to:

- the exposure of operators, workers and bystanders which cannot be concluded due to the presence of isomalathion in the technical material
- the acute and chronic risk for consumers, due to the insufficient information on the effects of certain toxicologically relevant metabolites
- the high risk to aquatic organisms, honey bees and non-target arthropods.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, The United Kingdom, being the designated rapporteur Member State, submitted an evaluation of the additional data on malathion in the format of an Additional Report (The United Kingdom, 2009a). The Additional Report was received by EFSA on 11 February 2009. In accordance with Article 19, the EFSA distributed the Additional Report to the Member States and the applicant for comments on 13 February 2009. The EFSA collated and forwarded all comments received to the Commission on 17 March 2009. At the same time, the collated comments were forwarded to the rapporteur Member State for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 24 April 2009, the Commission requested the EFSA to arrange a peer review of the Additional Report provided by the rapporteur Member State, and to deliver its conclusion on the risk assessment within 90 days.

The peer review commenced with EFSA's consideration of the Reporting Table containing the applicant's response to the comments and the RMS' evaluation of the comments and response. All points that were identified as unresolved at the end of the comment evaluation phase were further considered in a series of scientific meetings and a telephone conference with Member State experts in June 2009.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States in June 2009. The EFSA conclusion has therefore been re-issued to update the risk assessment in all areas.

The original conclusion from the review was reached on the basis of the evaluation of the representative uses presented in the DAR, i.e. use as acaricide and insecticide 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. The uses on apples and alfalfa were not supported in the resubmission application, and therefore the conclusion has only been updated in relation to the risk assessment of the representative uses presented in the Additional Report. The risk assessment presented for apples and alfalfa has not been updated

A list of the relevant end points for the active substance as well as the formulation is provided in appendix A.

The documentation developed during the resubmission peer review was compiled as a **peer review report** (EFSA, 2009) comprising of the documents summarising and addressing the

comments received on the initial evaluation provided in the rapporteur Member State's Additional Report:

- the comments received
- the resulting reporting table (rev. 1-1 of 30 April 2009)
- as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:
- the reports of the scientific expert consultation
- the evaluation table (rev. 2-1 of 15 July 2009)

Given the importance of the Additional Report including its addendum (compiled version of June 2009) and the peer review report with respect to the examination of the active substance, these documents are considered respectively as background documents A and B to this conclusion. The documents of the peer review report and the final addendum developed and prepared during the course of the initial review process are made publicly available as part of the background documentation to the original conclusion, EFSA Scientific Report (2006) 63, finalised on 13 January 2006.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Malathion is the ISO common name for diethyl (dimethoxyphosphinothioylthio)succinate or *S*-1,2-bis(ethoxycarbonyl)ethyl *O,O*-dimethyl phosphorodithioate (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 review 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 notifier, which comprised foliar spraying to control various harmful organisms in apples, strawberries, alfalfa and ornamentals at application rate up to 1.8 kg malathion per hectare.

The representative uses evaluated during the resubmission comprise applications by foliar spraying to control various harmful organisms

-in strawberries at the ripening of the fruit, in Southern EU countries, at maximum four applications, at maximum application rate per treatment of 1.2 kg a.s./ha, with interval between applications of 10 days, and

-in ornamentals, in all EU countries, at maximum application rate per treatment of 0.114 kg a.s./ha, with interval between applications of 7-10 days.

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 racemic mixture. The technical material contains four impurities that have to be regarded as relevant. The proposed maximum levels are 1 g/kg for malaoxon[13], 15 g/kg for the MeOOSPS-triester[14], 5 g/kg for the MeOOOPS-triester[15] and 2 g/kg for isomalathion[16]. The value for isomalathion 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 value than 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

[13] Malaoxon: diethyl (2*RS*)-2-[(dimethoxyphosphoryl)sulfanyl]butanedioate
[14] MeOOSPS-triester: *O*,*O*,*S*-trimethyl phosphorodithioate
[15] MeOOOPS-triester: *O*,*O*,*O*-trimethyl phosphorothioate
[16] isomalathion: diethyl (2*RS*)-2-{[methoxy(methylsulfanyl)phosphoryl]sulfanyl}butanedioate

the MeOOOPS-triester. However, as 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, the maximum content of isomalathion in the representative formulation ('CHA 3110', 'Fyfanon 440') should not be higher than 0.88 g/L. According to the results of the shelf-life studies, all amounts were in compliance with these limits.

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 A.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Adequate analytical methods are available for the determination of malathion in the technical material and in the representative formulation (GC-FID, CIPAC 12/TCM/-) There are also methods available for the determination of the significant and relevant impurities in the technical material as well as for the determination of the relevant impurities in the formulation (HPLC-UV and GC-FID)

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

Residues of malathion and malaoxon in food of plant origin can be monitored by GC/FPD with LOQs of 0.001 mg/kg (strawberry and apple) for each compound. None of them is enantio-selective. Residues of malathion and malaoxon can also 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) with LOQs of 0.25 mg/kg (strawberry and apple) for each analyte. 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 experts at PRAPeR Meeting TC 12 (4 June 2009) concluded that cryogenic milling of whole fruit samples has to be part of the analytical method for monitoring in order to avoid any degradation of malathion, as the Additional Report showed that the nature of the metabolites detected might change, depending if the analysis is performed on the whole fruit or on the homogenised sample. As a consequence, EFSA identified a data gap for cryogenic milling of the samples to be included in the description of the monitoring methods and method amendments should be made available.

An analytical method for the determination of residues in food of animal origin is not needed for the proposed representative uses on strawberries and ornamentals.

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 lower 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 and MDCA[17] in soil and water are available.

Adequate LC-MS/MS methods are available to monitor residues of malathion and MDCA in soil with LOQs of 0.01 mg/kg for each compound. Residues of malathion in ground and surface water can be monitored by LC-MS/MS with a LOQ of 0.1 µg/kg. It should also be

[17] MDCA: (2*RS*)-2-[(dimethoxyphosphorothioyl)sulfanyl]butanedioic acid

noted that a LC-MS/MS method also exists for monitoring MDCA and MMCA[18] in surface water with LOQs of 0.5 mg/kg for each analyte.
Residues of malathion in air can be determined by LC-MS/MS with a LOQ of 5 µg/m^3.

Analytical methods for the determination of residues in body fluids and tissues are not required as malathion is not classified as toxic or highly toxic.

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 and in the PRAPeR telephone conference TC11 held in June 2009.

The purity of the technical malathion used in the studies submitted in the DAR ranged from 92.1 % to 98 % active substance (minimum purity > 95%). Four impurities were regarded as relevant of which isomalathion is of toxicological concern. One of the major problems was 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 at the EPCO meeting 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 was 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 implied that the limit of 0.03% regarding the toxicological data package would not be feasible and that the toxicological assumptions had 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 had to be based on the 0.2% level.

During the teleconference held for the resubmission, the experts re-considered the overall validity of the database considering the low amount of isomalathion tested in the relevant studies. The experts acknowledged the weaknesses of the database, however the increased SF for ADI and AOEL was considered to cover the uncertainties rising from low levels of isomalathion in the concerned batches.

[18] MMCA: (2*RS*)-2-[(dimethoxyphosphorothioyl)sulfanyl]-4-ethoxy-4-oxobutanoic acid

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 (MMCA) and dicarboxylic (MDCA) 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 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%. (Both R22 and R43 risk phrases are confirmed by the Annex I to Directive 67/548/EEC reporting the 31st ATP outcomes).

2.3 Short term toxicity

The target effect in short term studies is the decrease of acetylcholinesterase activities. The information on the isomalathion content in the dog studies available 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 EPCO experts´ meeting 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 acetylcholinesterase 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 acetylcholinesterase 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 acetylcholinesterase 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 (Unscheduled DNA Synthesis) 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 that was performed at lower concentrations. The *in vivo* tests with assays of somatic cells were both 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 was provided in the DAR. For an isomalathion content of 0.03%, the experts agreed 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.

In the Additional Report a new valid Ames test was provided which shows that malathion containing up to 0.25% isomalathion was not genotoxic; further data were not required.

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 acetylcholinesterase activity.

The occurrence of nasal tumours in the rat was discussed in the addendum to the DAR and during the EPCO 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 by 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 acetylcholinesterase 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 developmental NOAEL of 25 mg/kg bw/day. The isomalathion content in the batch used was 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 acetylcholinesterase 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 acetylcholinesterase 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 acetylcholinesterase 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.

During the PRAPeR TC11 a question was raised with regard to the different potency of malaoxon and malathion. It was noted that considering the NOAELs from the two long term toxicity studies (29 mg/kg bw/day for malathion and 1 mg/kg bw/day for malaoxon) a conservative factor of about 30 would be derived. The RMS proposed a factor of 7 according to the ratio of the two LOAELs from the two long term toxicity studies. However, it was not possible to conclude on that without considering in detail all the existing studies. Therefore a new open point was defined for the RMS. In the addendum to the Additional Report (June 2009) the RMS performed an extensive comparison of short term and long term data: according to the levels of RBC and brain cholinesterase inhibition (similar between short and long term studies) it was confirmed that malaoxon is 6-7 fold more toxic than malathion.

EFSA notes that this value is not peer-reviewed.

Isomalathion

No studies have been provided by the notifier.

According to the review by Litchfield (2003 and 2004) presented in the addendum to the DAR 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 is linked to increased acute toxicity.

Malathion dicarboxylic acid (MDCA)

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).

During the resubmission some Member States commented on the need of additional studies for the major metabolites (mainly MMCA), based on their residue amounts and the low amount in mammalian metabolism. Available metabolism data demonstrate that malathion is metabolised in rat and human mainly to malathion mono- and di-carboxylic acids (MMCA and MDCA) which are rapidly excreted in the urine (60 - 80% of dose). The experts agreed that based on that there was no need to perform further toxicological studies.

Desmethyl-malathion (DMM)

No studies have been provided by the notifier on desmethyl-malathion[19] (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. In the Additional Report (The United Kingdom, 2009a) the RMS established that malathion has the highest potential for RBC ChE inhibition compared to the metabolite DMM. Taking all available studies into account, the overall picture of the relative toxicity shows that malathion has the highest potential of cholinesterase inhibition compared to the metabolite. The experts in the PRAPeR TC 11 agreed that the metabolite should be considered as less toxic than malathion, but should be considered toxicologically relevant because of its acetylcholinesterase inhibition activity.

The same applied to monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA): available studies seemed to indicate a lower toxicity than malathion, however based on their toxicological properties (same end points as malathion), it was agreed to consider them as toxicologically relevant.

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 to 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 EPCO 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 case of an isomalathion content in this study of 0.2% or above a safety factor of 10 would be appropriate. In the case the

[19] DMM: diethyl (2*RS*)-2-{[hydroxy(methoxy)phosphorothioyl]sulfanyl}butanedioate

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 ~~i~~was 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 and long term studies the range of the content of the impurity isomalathion is 0.03% - 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 were agreed to be 0.3 mg/kg bw/day (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 acetylcholinesterase were 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 at the EPCO in the case the specification would be 0.2% of isomalathion and a new Ames test with malathion containing 0.2% isomalathion was required. In the Additional Report a new valid Ames test has been provided which shows that malathion containing up to 0.25% isomalathion was not genotoxic; further data were not required.

The resulting ADI as well as AOEL was 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 was 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 and not acetyl cholinesterase inhibition. The ARfD is ~~it is~~ supported by the data from the rat studies where 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 therefore 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**.

In the PRAPeR TC11 the experts reconsidered and confirmed the use of the additional SF of 10 for ADI and AOEL to cover uncertainties from the isomalathion amount in the batches tested. It was confirmed as well that in case of ARfDs an extra safety factor of 10 was not used because the two studies concerned for setting the ARfD had a high amount of isomalathion considered to cover the uncertainties for the impurity.

2.11. 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 Member States 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 to the DAR and discussed during the EPCO 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 *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.

2.12. 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.

Malathion is used for controlling harmful pest organisms in apples, strawberries, alfalfa and glasshouse ornamentals (with the resubmission only uses in strawberries and ornamentals are supported). 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 application rates for strawberries and ornamentals (as supported in the GAP table for resubmission) are 1.2 and 0.114 kg a.s./ha, respectively.

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 EPCO 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 to the DAR and these are summarised in the table below.

Scenario	Model	No PPE	With PPE*
High crops (apples)**	German	4791	262
	UK POEM	2871	1185
Low crops (alfalfa,)**	German	1525	71
	UK POEM	2240	163
Low crops (strawberries)	German	915	43
	UK POEM	1527	127
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

** Not any longer representative uses under the resubmission

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.

In the Additional Report, the operator exposure assessment for application in strawberries outdoor was calculated with the UK POEM. The RMS presented the calculations according to the currently used default of 50 ha area treated; a refinement was also presented considering a lower area of 30 ha which was considered as more realistic. In the teleconference Member States supported the use of a lower number of ha (30 ha) for strawberries compared to

standard of 50 ha as more realistic. Assuming the work rate of 30 ha, the predicted exposure would be within the AOEL (0.0268 mg/kg bw/day corresponding to 89% of AOEL, with the use of gloves during mixing and loading and during spray application).

Scenario	Model	No PPE	With PPE
Low crops (strawberries; field crop boom sprayer)	German*	489	28
	UK POEM° (50 ha)	762	103
	UK POEM° (30 ha)	-	89
Hand held strawberries (knapsack)	German*	952	79
	UK POEM§	1359	229
Ornamentals, indoor	Dutch	20	7

*PPE=gloves worn during mixing and loading operation and gloves, coveralls and sturdy footwear are worn during spray application.

°PPE=gloves worn during mixing and loading and gloves are worn during spray application.

§PPE=gloves worn during mixing and loading and gloves and impermeable coveralls are worn during spray application.

In conclusion, estimates with the German model indicate levels of exposure for operators wearing PPE (gloves when mixing, loading, gloves coverall and sturdy footwear while spraying) within the AOEL for both methods of application. Assuming 30 ha work rate, the predicted exposure with UK POEM would be within the AOEL with the use of PPE. For hand-held application, the German model shows exposure levels below the AOEL with the use of PPE; the UK POEM assessment shows predicted exposure above the AOELeven with the use of PPE.

Worker exposure

The worker exposure assessment after the EPCO meeting was calculated using dermal absorption rate of 15% (spray solution). The dermal, as well as inhalation, re-entry exposure estimations were 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 (169-660%) even when personal protective equipment is worn (coverall and gloves). For roses (glass house) the re-entry exposure is below AOEL (96% without PPE, 25% with gloves).

In the commenting phase on the Additional Report for the resubmission, some concerns were raised with regard to re-entry exposure in strawberry fields. Some Member States were concerned about the real possibility of using PPE in such scenario. It was agreed to give information on exposure with and without PPE as usually done. The experts also discussed the refinement of estimated exposure according to estimated half-life of the a.s.. Some uncertainties were highlighted in the Additional Report related to this approach. In addition, the majority of experts considered the use of only one application for the exposure estimate as acceptable.

In the addendum to the Additional Report (The United Kingdom, 2009b) the RMS presented revised calculation.

Crop inspection: it was assumed that a worker re-enters the crop soon after application to carry out crop inspection activities. The duration of this activity is 2 hours and it is assumed there is no degradation of malathion after the final application. Calculations assume a Transfer Coefficient of 3000 cm^2 (EUROPOEM value for hand harvesting strawberries), a 60 kg worker and 15% dermal absorption. Systemic exposure for a single application of malathion was estimated to be 0.054 mg/kg bw/day, i.e.180% of the AOEL.

Hand-harvesting: it was assumed that a worker re-enters the crop 3 days after the final application to carry out hand harvesting. The duration of this activity is 8 hours and it is assumed there is no degradation of malathion after the final application. Calculations assume the Transfer Coefficient of 3000 cm^2 , a 60 kg worker and 15% dermal absorption. Systemic exposure was estimated to be 0.216 mg/kg bw/day, i.e.720% of the AOEL (single application).

Based on the dissipation of malathion DFR on treated apples, exposures for workers using bare hands to pick strawberry were calculated ranging from 11% to 437% of AOEL. If protective gloves are used predicted exposures are within the AOEL (<22% with the use of gloves, considering DT_{50} values for malathion of 0.5 days to 3.3 days, as from residue trial studies, not confirmed by the experts). However, it was noted how uncertain and representative this scenario is.

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 also by amateurs in strawberry, apple and ornamental cultivations in home gardens, however this is not a representative use in the Additional Report. Amateur exposure was estimated in an addendum to the DAR. 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.

In the GAP table of the Additional Report no mention of amateur use is done. Some MS highlighted that in case of need of PPE for amateurs national authorisation would not be granted. However this is not an intended use of the applicant and it was not considered further in the assessment.

3. Residues

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

The evaluation of new information and data in the framework of the resubmission procedure for malathion was discussed by experts in the telephone conference PRAPeR TC12 held in June 2009 on the basis of the Additional Report of February 2009.

3.1. Nature and magnitude of residues in plant

It is noted that malathion consists of two optical isomers (enantiomers). It should also be noted that the methods of analysis used in all the residue studies were not stereoselective. Thus the regulatory dossier provides no information on the behaviour of each individual malathion enantiomer or enantiomers of the major metabolites in plants. Therefore, all residues reported as malathion or isomalathion, malaoxon, desmethyl-malathion (DMM), malathion monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA) in this section of the conclusion are for the sum of the two enantiomers. It is not known if either isomer is metabolised or degraded more quickly than the other in the matrices studied.

3.1.1. Primary crops

The metabolism of 14C-malathion was initially studied in four different crops: alfalfa, cotton, lettuce and wheat. Later in the peer review process of 2004 / 2005 a metabolism study on apples was submitted and evaluated in addendum 1 to the DAR. Malathion was applied to apples at the normal field rate (N rate), and to alfalfa and wheat forage at approx. 2.5 N rate in terms of the representative uses notified. Uses on other than the tested crops, such as oilseeds or leafy crops, were not part of the peer review.

The most recent evaluation of the residue behaviour and the consumer risk assessment of malathion in the resubmission procedure is only based on a use in strawberries (fruit crop group). The representative use on ornamentals in glasshouses was not considered in this section, as significant consumer exposure through the diet is not expected from this use.

In the available metabolism studies the majority of the radioactive residue was identified or characterised. Unchanged malathion was detected 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 the amount (percentage TRR) of desmethyl-malathion was much lower in the other crops (0.1-0.5% TRR); however, the expert meeting on residues EPCO 19 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 necessary.

Previously, the experts' meeting for toxicology (EPCO 18) advised that without experimental data it was not possible to conclude that desmethyl-malathion is less toxic than malathion.

Comparison of all data during the resubmission procedure lead to the conclusion that desmethyl-malathion is less toxic compared to malathion but yet relevant as for its acetylcholinesterase inhibiting properties (refer to 2.8).

Another outcome of the previous EPCO 18 meeting was that malathion dicarboxylic acid should be considered as of equivalent toxicity as malathion. This might also apply to malathion monocarboxylic acid. However, this information was made available after the residues experts' meeting EPCO 19, and thus, at that time could not be considered in the residue assessment.

In the resubmission procedure, the experts in toxicology in PRAPeR TC 11 confirmed MDCA and MMCA should be considered as toxicologically relevant.

Malaoxon, already initially proven as a toxicologically significant metabolite (refer to 2.8), was found in all tested crops. Determined levels of malaoxon 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 in the EPCO 19 meeting 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 the LOQ (0.01 mg/kg). The meeting in cotton seed and up to 7.7 % TRR (0.20 mg/kg) in apples (PHI 7). The experts in the EPCO agreed that this discrepancy needed further elaboration and explanation by the applicant, before a conclusion could be drawn whether or not consumer exposure to malaoxon residues in apples might be significant.

In order to address this point a new report on apple metabolites was provided in the resubmission dossier. Samples from the apple metabolism study were re-analysed almost 2 years after the first analysis. A significant decline of the total residue was observed in all samples when compared to the initial analysis. The identification rate was low, and the proportions of the individual compounds were different from the first analysis, indicating that apart from the residue levels also the composition of the residue has changed during the storage period. Hence, the experts in PRAPeR TC 12 agreed that this re-analysis data would only confirm the nature of the compounds already identified in previous metabolism studies. The new results are not reliable from a quantitative point of view, and thus cannot be used to conclude whether metabolites are present at significant levels or to derive any conversion factor to conduct a risk assessment.

However, the re-analysis data indicated that the nature of the metabolites might change, depending if the analysis is performed on the intact or on the homogenised fruit. A significant decrease of levels of malathion and metabolite MDCA was observed in the homogenised sample when compared to the intact fruit. The experts recommended this information to be taken into account for the analytical method to be used to determine residues of malathion (see section 1).

Previously, low amounts of isomalathion, a relevant impurity of malathion, were found in alfalfa hay (0.2 % of TRR, 0.43 mg/kg). In the metabolic study on apples non-radioactive isomalathion was detected 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 succinic acid. The succinate was apparently incorporated into small organic acids and sugars via the citric acid cycle. In fruit, a main route of metabolism seems to be the transformation of malathion to desmethyl-malathion. However, the presence of malathion dicarboxylic acid indicates that, via 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 differences in terms of their relevance for 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 more labile and degrades rapidly to desmethyl-malathion.

Taking into account the observations in terms of desmethyl-malathion in the apple metabolism study and in the simulated processing study, EPCO 19 concluded in 2005 that the residue of concern for risk assessment in plants should be the sum of malathion, malaoxon and also desmethyl-malathion, expressed as malathion. At that time the residue experts were not aware of the considerations by the toxicologists in EPCO 18 with regard to the toxicological properties of MDCA and MMCA.

As for the peer review of the resubmitted dossier, the experts in PRAPeR TC12 considered the metabolites malaoxon, desmethyl-malathion, malathion dicarboxylic acid and malathion monocarboxylic acid as relevant compounds for consumer risk assessment as for their toxicological properties, and followed the proposal of the RMS to include them in addition to malathion in the residue definition for risk assessment.

The residue definition for **consumer risk assessment** was agreed as: Malathion and its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion toxicological equivalents, to be compared to the toxicological reference values of malathion.

During PRAPeR TC11 on toxicology it was concluded that the toxicological effect is the same for malathion and the mentioned metabolites, but the potency is different (refer to 2.8). In particular, the higher toxicity of malaoxon needs to be considered when residues are converted into malathion equivalents. Pending the final assessment by the toxicologists, the residue experts in PRAPeR TC12 agreed to take the higher toxicity of malaoxon into account in the consumer risk assessment with a toxic equivalency factor of 30.

After the meeting a reassessment of this factor was provided in the addendum to the Additional Report. The RMS performed an extensive comparison of short term and long term data and it was concluded that malaoxon is 6-7 fold more toxic than malathion. However, this factor has not been peer reviewed (refer to 2.8).

For **monitoring and MRL setting** purposes, the residue should be defined as malathion and malaoxon. The proposal takes into account the higher toxicity of malaoxon compared to

parent malathion, however malaoxon alone would not be a sufficiently good indicator compound for monitoring residues of malathion.

Both compounds can be analysed separately (refer to chapter 1 of this document), and hence separate results could be reported (option 1). Risk managers may possibly consider a residue defined as the sum of malathion and malaoxon expressed as malathion as proposed by the RMS (option 2). However, due to their different toxicity a consumer risk assessment, if intended on monitoring data, will result in a higher uncertainty when based on the sum of both compounds, unless monitoring laboratories would calculate and report the residues as malathion toxic equivalents (option 3) considering a respective factor for malaoxon.

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 validated analytical methods. Residues were analysed and expressed as malathion and malaoxon. However, desmethyl-malathion, MMCA and MDCA were not analysed in the initially submitted supervised field trials. Thus, the available data do not correspond to the proposed residue definition for risk assessment, but might be suitable to propose MRLs.

With the resubmission dossier four new residue trials in strawberries were submitted, that analyse for malathion, malaoxon, desmethyl-malathion, MMCA and MDCA. According to the findings in these new residue trials, the ratio of malathion / malaoxon residues to the total relevant residue including metabolites desmethyl-malathion, MMCA and MDCA is changing from day 0 to day 3, making the conversion factor from the monitoring to the risk assessment definition increase over time. As only four residue trials according to the residue definition for risk assessment were submitted for a major crop, the experts agreed to request the applicant to provide four additional residue trials. In these trials, also residue levels for longer PHIs (up to 10 days) should be determined in order to assess the possibility to establish a critical, generally usable conversion factor (monitoring to risk assessment) for strawberries.

In terms of the residue definition for monitoring as suggested by the RMS (malathion and malaoxon expressed as malathion), it was proposed that, provisionally, a suitable conversion factor for monitoring to risk assessment may be 8. This conversion factor takes also into account the different toxicity of malathion and malaoxon. However, this factor is based on only four trials in strawberries, and moreover, it is only applicable to an application scenario as defined by the notified critical GAP, in particular in terms of application rate and PHI (3 days). Further data will be necessary to verify any general validity of this preliminarily proposed factor.

The effect of processing on residue levels of malathion and malaoxon was investigated in apples and tomatoes. Other metabolites of malathion were 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 food consumed by humans. However, the conclusion on processing studies had to be reconsidered in the light of the relevance of desmethyl-malathion, MMCA and MDCA for consumer risk assessment.

The expert meeting EPCO 19 had phrased a data gap for the applicant to present data on the level of desmethyl-malathion on raw agricultural commodities (RAC) and processed products, and data demonstrating the stability of desmethyl-malathion under storage conditions.

PRAPeR TC 12 considered the following: A hydrolysis study with malathion indicated that desmethyl-malathion would be the main compound of concern in processed products, as it accounted for more than 50% of the TRR under simulated processing conditions. The processing studies with strawberries in the Additional Report of February 2009 show an increase in desmethyl-malathion levels in jam but not in canned fruit. In contrast, a significant degradation of MDCA was observed in jam and canned fruit with MDCA residues decreasing from ca 0.5 mg/kg in the raw commodity to around the LOQ in the processed fractions. A decrease was also observed for MMCA but to a lower extend, the residue in processed fraction being reduced by ca 50% compared to the residue observed in the raw commodity.

Concerning the decrease of MMCA and MDCA, the experts in TC 12 agreed the applicant should address the fate of MMCA and MDCA metabolites under processing conditions, preferably by a radiolabel hydrolysis study.

Provisionally and awaiting the requested information, the meeting agreed to define the residue of concern in the processed commodity as for the raw agricultural commodity.

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 by 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 EPCO 19 proposed a data gap in order to clarify the residue situation of desmethyl-malathion in rotational crops, which was not addressed by the information available. EFSA noted after the meeting EPCO 19 that potential uptake of MMCA and MDCA into rotational crops might have to be addressed, too.

In the resubmission dossier no further data on residues in rotational crops were submitted but a case was made that strawberries are usually not rotated and therefore further data as previously requested by EPCO 19 for the use in strawberries and alfalfa would not be necessary. However, the experts in PRAPeR TC 12 confirmed that growing other crops after strawberries is agricultural practice in some Member States, and that it is necessary to address residues in succeeding crops.

The initial evaluation in the DAR submitted during the 2004/2005 peer review focussed only on malathion and malaoxon residues. Therefore, the experts in PRAPeR TC 12 requested the RMS to re-assess the confined rotational study in the light of the currently established residue definition for risk assessment. It should be considered whether the sum of relevant residues, i.e. malathion and the metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid, may reach significant levels in succeeding crops. A re-assessment was provided by the RMS in the addendum 2 to the Additional Report (June 2009) but has not been peer reviewed, and thus no decision can be taken whether the data gap identified by EPCO 19 to address residues in succeeding crops could be waived. It is noted that in their assessment the RMS considered it unlikely that positive residues of malathion would result in rotational crops from the use on strawberries,

however the RMS concluded that for the use on other crops, further data on rotational crops ('cold studies') may be required.

3.2. Nature and magnitude of residues in livestock

With the resubmission the notified uses have changed to strawberries only. These are usually not used in livestock feeding. Therefore, in the framework of the assessment of the representative use under the resubmission procedure data on livestock and potential MRLs in food of animal origin are not relevant and were therefore not considered any further.

The conclusion of the peer review on malathion in 2004/ 2005 presented here below is related to the previously notified uses in apples and alfalfa and is kept for the sake of transparency. Issues identified as open or inconclusive at that time have not been addressed.

It should be noted that the regulatory dossier provides no information on the behaviour of each individual malathion enantiomer or enantiomers of the major metabolites in livestock, and therefore, all residues in this section of the conclusion are for the sum of the two enantiomers of the respective compounds.

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 not only malathion (and malaoxon) but also 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, the 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 the 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, the 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. < 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 the 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 was not possible to conclude whether or not MRLs for food of animal origin would have to be proposed with respect to uses relevant for livestock exposure.

3.3. Consumer risk assessment

At the end of the previous peer review procedure in 2004/2005 no sound conclusion on the consumer risk assessment was possible due to significant data gaps.

During the peer review of the resubmitted dossier the relevance of metabolites and degradation products of malathion for consumer safety could be addressed and a residue definition for consumer risk assessment could be established. Considering the toxicological effects of malathion and its metabolites as well as the occurrence of these compounds in crops and processed commodities, the **residue definition for consumer risk assessment** was agreed as: Malathion and its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion toxic equivalents, to be compared to the toxicological reference values of malathion.

Pending the final confirmation of a toxic equivalency factor by the toxicologists, the residue experts agreed to consider in the risk assessment the higher toxicity of malaoxon with a factor of 30 in order to adequately convert malaoxon residues into malathion toxicological equivalents. After the experts' discussions in PRAPeR TC11 (Mammalian toxicology) and TC12 (Residues) the RMS submitted a reassessment of the toxic equivalency factor. It was concluded by the RMS that malaoxon is 6-7 fold more toxic than malathion, but this factor has not been peer reviewed (refer to 2.8).

Further information is still necessary to fully address residues in processed commodities and in succeeding crops. Moreover, four additional residue trials in strawberries are still required.

However, the experts in PRAPeR TC12 considered an indicative consumer risk assessment would be possible with the available data on strawberries.

This indicative consumer risk assessment is based on the four available residue trials in strawberries wich provided analysis for the full residue definition for risk assessment.

Provisionally, the total residue level expressed as malathion toxic equivalents, using a factor of 30 for malaoxon and of 1 for desmethyl-malathion, MDCA, MMCA, respectively,

indicates consumer intakes according to the EFSA PRIMo are less than 3% of the ADI of 0.03 mg/kg bw/day and less than 8% of the ARfD of 0.3 mg/kg bw/ day, respectively. If the ARfD of 1.5 mg/kg bw/day based on a human study is considered, acute consumer exposure is estimated to be less than 2% of the ARfD.

If the lower toxic equivalency factor for malaoxon proposed by the RMS is used, the outcome will be only marginally different since the major contribution to the total amount of residues in strawberries relevant for consumer exposure is due to the metabolites MMCA and MDCA.

It should be noted that malathion and its relevant metabolites consist of two enantiomers, but the dossier provides no information on whether either isomer is metabolised or degraded more quickly than the other in strawberries or in any other matrix relevant for consumer exposure. Consideration of any impact for the risk from consumer exposure to different enantiomer ratios of malathion and its relevant metabolites would be justified in order to finalise the consumer risk assessment.

However, despite the uncertainties in the provisional risk assessment as presented above, the margin of safety between the currently estimated exposure of consumers to malathion residues in strawberries and the established toxicological reference values for malathion is considered big.

3.4. Proposed MRLs

Eight residue trials in strawberries are available that analyse for the compounds proposed as the relevant residue for monitoring and MRL setting. A final decision on how the determined residues will have to be reported and expressed, will be up to risk managers.

Based on these eight trials in **strawberries,** the following parameters were estimated (not peer reviewed), considering

1) the residue definition for monitoring proposed by the experts in PRAPeR TC 12, **malathion and malaoxon**, separately reported: Malathion Rmax 0.24, Rber 0.26; Malaoxon Rmax 0.01, Rber 0.02
2) the residue definition for monitoring proposed by the RMS as **sum of malathion and malaoxon, expressed as malathion** (without taking into account their different toxicological potencies): Rmax 0.32, Rber 0.42; the RMS has proposed the MRL to be set at 0.3 mg/kg.
3) the **Sum of malathion and malaoxon, expressed as malathion toxic equivalents** on the basis of a provisional toxic equivalency factor

of 30 for malaoxon (considered by PRAPeR TC12): Rmax 0.54, Rber 0.86 and

of 6-7 (proposed by the RMS, not peer reviewed): Rmax 0.31, Rber 0.40

4. Environmental fate and behaviour

In January-February 2005 malathion was discussed in the EPCO expert meeting on Environmental fate and behaviour (EPCO 16). It should be noted that the methods of analysis used in all the fate and behaviour studies were not stereoselective. Therefore the regulatory dossier provides no information on the behaviour of each individual malathion enantiomer or

enantiomers of the major (>10%AR) breakdown products in the environment. Therefore all residues reported as malathion or major breakdown products in this section of the conclusion are for the sum of the 2 enantiomers. It is not known if either isomer is degraded more quickly than the other in the environmental matrices studied. However as the degradation of malathion and malathion monocarboxylic acid (MMCA) for their sums of isomers is rapid, this is not expected to impact on the risk assessments for these two isomer pairs in this case . A consideration of any impact for the risk from exposure to different malathion dicarboxylic acid (MDCA) enantiomer ratios is justified. However there are large margins between effects concentrations to tested aquatic species and potential exposure levels, such that conclusions on the aquatic risk assessment for MDCA would not change if there was preferential degradation of just one of it's enantiomers. The earthworm risk assessment is not completely finalised (see section 5).

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 MMCA (max. 25% of applied radioactivity (AR)) and subsequently to 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). In three of the available soil incubations unidentified polar radioactivity at the origin of normal phase TLC plates accounted for >5%AR in samples taken at 2-4 days in two of the soils and 4 to 29 days in the third soil. 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 (DT_{90} 0.38-2.4 d) and 1.2-5.3 days (DT_{90} 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.s/ha in 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:

$\log K_{oc}$ = -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

columns 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 substance 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 were not necessary to address this issue. The EFSA agrees with this conclusion for this active substance.

In the Additional Report of February 2009 and its addendum of May 2009 an appropriate aquatic exposure assessment in accordance with FOCUS (2001, surface water and 2007, landscape and mitigation) guidance was provided for malathion (up to step 4) and its metabolites MMCA and MDCA (up to step 2) for the use on strawberries. The resulting predicted environmental concentrations estimated are presented in appendix A. For parent malathion at step 4 only spray drift mitigation was implemented. This assessment in the Additional Report also demonstrated, that when a Dutch procedure for estimating emissions from glass houses to surface water is followed, the concentrations estimated for strawberry will be higher than the exposure expected from the use applied on glasshouse ornamentals.

The assessments that are available with the exception of those for strawberry and glasshouse ornamentals 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 DT_{90} 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 unless uses are requested on strawberry or glasshouse ornamentals and their national situation would be covered by the available assessments for these crops.

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).

- 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 Kfoc value of 26 mL/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 (0.36 kg/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).

- In section B.8.6.1 of the final 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 Kfoc values would be lower than the 26 mL/g value used in the simulation described at 1 above. The Kfoc values used as modelling input were 4.2, 10.9, 25.7, 19.3, 7.4 and 6.1 mL/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).
- 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 (0.9 kg/ha first application 0.54 kg/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 Kfoc of 10.9 mL/g and at the Piacenza scenario using the Kfoc of 19.3 mL/g to account for pH dependent adsorption. Predicted concentrations were less than the parametric drinking water limit of 0.1µg/L. (See final addendum to the DAR (Finland, 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 Chateaudun, 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 final addendum to the DAR 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 was provided in the Additional Report of February 2009 and its addendum of May 2009. This assessment confirms that for this use, the potential for groundwater exposure by malathion or its soil metabolites MMCA and MDCA above the parametric drinking water limit of 0.1µg/L, will be low, provided that not more than 45 applications at 114g malathion /ha are made per calendar year.

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 2005and in the PRAPeR TC13 held in June 2009.

The degradation pattern of the enantiomers of malathion and major breakdown products thereof (malathion monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA)) are unknown (see section 4). However, as the degradation of malathion and MMCA for their sums of isomers is rapid, this is not expected to impact on the risk assessments for these two isomer pairs in this case. Furthermore, there are large margins between effects concentrations to tested aquatic species and potential exposure levels, such that conclusions on the environmental risk assessment for MDCA would not change if there was preferential degradation of just one of its enantiomers. For the earthworm risk assessment EFSA notes that the TER calculation for MDCA was based on surrogate toxicity data (i.e. 10 times more toxic that the parent substance). As the TER value was quite close to the Annex VI trigger and the metabolite degradation rates are in the range of days, EFSA recommend a data gap for the applicant to address the potential risk to earthworms for the enantiomer forms of MDCA. Please note that this issue was not discussed during PRAPeR TC13.

The risk assessment was conducted according to the following guidance documents: European Commission (2002a), European Commission (2002b), European Commission (2002c) and SETAC (2001)

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 end point 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 the two other 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 end point). 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 (Estimated Theoretical Exposure) 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 (residue data) 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 were above the relevant Annex VI trigger indicating a low risk. The residue

data and calculations were provided in the DAR, supplemented with addendum 1 and 3. The final assessment was however not peer reviewed. The acute TER value for herbivorous birds in alfalfa is 8.8. The RMS supports the notifier's 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 was not peer reviewed by Member States.

In view of the fact that the final assessment of the review evaluation was not peer reviewed, the risk was assessed for insectivorous and frugivorous birds in the Additional Report of February 2009 . At tier I the short-term risk to insectivorous and frugivorous birds was assessed as low, whereas further refinements were required to address the acute and long-term risk. Refined risk assessment based on initial 90th percentile and mean residue in strawberries presented in Section B.7 of the original DAR and the default DT_{50} of 10 days indicated a low acute and long-term risk to frugivorous birds. Use of the residue studies by Knäbe (Finland, 2004, Vol.3 B.9.1) to address the risk to insectivorous birds was considered of limited value by RMS, as the study was carried out in an apple orchard and not in strawberries, only one site used, site located in North Europe (intended use in South Europe) and 90th percentile initial residues values could not be calculated. The RMS considered the residue data inappropriate for refining the acute risk assessment and was extreme cautious about their use in the long-term risk assessment, including estimates of the dissipation time. Member State experts at PRAPeR TC13 agreed to the assessment of the RMS and suggest a data gap for the applicant to address the acute and long-term risk to insectivorous birds.

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 to the DAR), proportion of different food types (PD) in the diet of bank voles[20] and portion of diet obtained in the treated are[21] (PT) from the notifier is presented in addendum 3 to the DAR. 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 to the DAR 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.

[20] 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.
[21] DEFRA Project PN0915 Improving estimates of wildlife exposure to pesticides in arable crops.

In the Additional Report of February 2009 the risk was assessed for insectivorous and frugivorous mammals. At tier I the acute and long-term risk to insectivorous mammals was assessed as low. TER values from the acute risk assessment for frugivorous mammals indicated a low risk, whereas further refinements were required to address the long-term risk to frugivorous mammals. Refined risk assessment based on mean residue in strawberries presented in Section B.7 of the original DAR indicated a low long-term risk to frugivorous mammals (see Appendix A). Member State experts at PRAPeR TC13 agreed on the revised risk assessment.

The exposure to birds and mammals was considered to be minimal from the use of malathion on protected ornamentals.

The risk to birds and mammals from exposure to contaminated drinking water is based on the PECsw 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.

The metabolites malathion mono- (MMCA) and dicarboxylic (MDCA) 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 Pow 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 EPCO 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 proposed to revisit the assessment when the opinion of the panel has been adopted.

The acute risk to fish was reassessed in the Additional Report of February 2009 based on the toxicity ranking approach (Method 2) presented in the EFSA Journal (2005). A refined acute toxicity end point of 40 µg a.s./L for fish based on 'Method 2' was supported by Member

State experts at PRAPeR TC13 since it maintains the same level of protection. TER calculations in two out of four relevant FOCUSsw Step 4 scenarios meet the Annex VI trigger, based on the refined acute fish toxicity end point. The exposure was however updated in the addendum to the Additional Report of May 2009 (see section 4.2.1) and providing TER values above the Annex VI trigger in three of four scenarios (see Appendix A).

One Member State did consider the use of Species Sensitivity Distribution a more appropriate option to derive an end point from the acute fish toxicity data and they suggested a novel approach. According to this approach the HC_5 should always be based on LC_{10}/NOEC values for fish, because they are vertebrates and they have a relatively long life cycle. A mean HC_5 NOEC's of 1.821 µg a.s./L was calculated from the six acute fish toxicity. An assessment factor of 5, based on the acute to chronic fish toxicity ratio, was applied to derive a regulatory end point of 0.36 mg a.s./L (i.e. 1.821/5). Member state experts agreed to include the NOEC values from the fish acute toxicity studies in Appendix A in order to provide the opportunity for Member States to recalculate the regulatory end point based on this proposal.

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 EPCO 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 10-20 m buffer zones are required.

The risk to invertebrates was reassessed in the Additional Report of February 2009 and updated in the addendum to the DAR of May 2009 based on revised exposure estimates (see section 4.2.1). TER calculations based on buffer zones of 30 to 40 meters indicated a low risk to invertebrates in three out of four relevant $FOCUS_{sw}$ scenarios regardless of which assessment factor was used (see section above).

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 %).

The risk to aquatic organisms from use on protected ornamentals was assessed as low based on the Dutch glasshouse exposure model (see section 4.2.1).

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 EPCO 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.

Member State experts at PRAPeR TC13 agreed to propose risk mitigation at Member State level. Labelling: Dangerous to bees. To protect bees and pollinating insects do not apply to crop plants when in flower. Do not use where bees are actively foraging. Do not apply when flowering weeds are present.

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 notifier.

In the Additional Report of February 2009 supplementary information from the applicant was assessed. The formulations tested contained between 0.014 and 0.017% isomalathion. According to the Section B.2 of the DAR malathion will contain on average 0.027% of isomalathion, therefore the effect studies were conducted at a lower rate of isomalathion (approximately 1.5 times) than will be present in the proposed formulation. There were no data on the toxicity of isomalathion to non-target arthropods and therefore, it was not possible to determine whether the difference in the content in the effect studies was significant or not.

It is considered that the field use on strawberries at 1.2 kg a.s./ha applied 4 times is covered by the above, and that the in and off-field risk is considered as low based on the standard assumptions.

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 malathion monocarboxylic (MMCA) and malathion dicarboxylic acid (MDCA) 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 was considered low. Please note that concern was raised by EFSA after PRAPeR TC13 regarding the enantiomer form of MDCA (see section 5). As the TER value was quite close to the Annex VI trigger and the metabolite degradation rates are in the range of days, EFSA recommends a data gap for the applicant to address the potential risk to earthworms for the enantiomer forms of MDCA.

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 was presented in Addendum 3 to the DAR dated September 2005, but was 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.

The limit test on vegetative vigour was assessed in the Additional Report of February 2009, without changing the study conclusion. TER values based on 1 meter non-spray buffer zones indicated a low risk to non-target plants for the intended use in strawberries.

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

6.1. Soil

Definitions for risk assessment: malathion; malathion monocarboxylic acid[22] (MMCA) and malathion dicarboxylic acid[23] (MDCA)

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

6.2. Water

6.2.1. Ground water

Definitions for risk assessment: malathion; malathion monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA)

Definitions for monitoring: malathion

6.2.2. Surface water

Definitions for risk assessment: surface water: malathion; malathion monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA)

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).

6.3. Air

Definitions for risk assessment: malathion

Definitions for monitoring: malathion

6.4. Food of plant origin

Definitions for risk assessment: Malathion and its metabolites malaoxon[24], desmethyl-malathion[25] (DMM), malathion monocarboxylic acid (MMCA) and malathion dicarboxcylic acid (MDCA) expressed as malathion toxicological equivalents.

Definitions for monitoring: Malathion and malaoxon should be monitored, reporting to be decided by risk managers (see section 3.1.1)

6.5. Food of animal origin

Definitions for risk assessment: Not required for the representative use assessed

Definitions for monitoring: Not required for the representative use assessed

[22] MMCA: (2*RS*)- 2-[(dimethoxyphosphorothioyl)sulfanyl]-4-ethoxy-4-oxobutanoic acid
[23] MDCA: (2*RS*)- 2-[(dimethoxyphosphorothioyl)sulfanyl]butanedioic acid
[24] Malaoxon: diethyl (2*RS*)-2-[(dimethoxyphosphoryl)sulfanyl]butanedioate
[25] DMM: diethyl (2*RS*)-2-{[hydroxy(methoxy)phosphorothioyl]sulfanyl}butanedioate

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

6.6.1. 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)	Risk to earthworms and micro-organisms assessed as low.
malathion monocarboxylic acid (MMCA)	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 (MDCA)	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. EFSA suggests a data gap to address the potential riks to earthworms for the enantiomer forms of MDCA

6.6.2. Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
malathion	medium mobility (Koc = 151-308 mL/g)	FOCUS modelling: No	Yes	Yes	Yes
malathion monocarboxylic acid (MMCA)	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 (MDCA)	Very high to high mobility (Koc = 6-64 mL/g) pH dependent	FOCUS modelling: No pH dependent adsorption taken account 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

6.6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
malathion	Very toxic to aquatic organisms. Risk to fish and invertebrates was assessed as low in 3 of 4 $FOCUS_{sw}$ scenarious.
malathion monocarboxylic acid (MMCA)	>2 orders of magnitude less toxic than malathion
malathion dicarboxylic acid (MDCA)	>2 orders of magnitude less toxic than malathion

6.6.4. 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

- Amendments to the method descriptions for monitoring residues in food of plant origin, to include cryogenic milling of the samples, in order to avoid any degradation of malathion (relevant for all representative uses evaluated, data gap identified by EFSA after PRAPeR TC 12 meeting (June 2009), date of submission unknown; refer to chapter 1 and 3)
- 4 additional trials are requested where samples are analysed for the residue definition for risk assessment and at longer PHIs up to 10 days. The applicant should also pay attention to how the samples are homogenised (cryogenic milling). Moreover, considering the storage stability data provided, samples have to be analysed within 2 months after harvest. (relevant for the representative use on strawberries evaluated, data gap identified in PRAPeR TC 12 meeting (June 2009), date of submission unknown, however applicant indicated in the evaluation table planning further residue trials in 2009; refer to chapter 3.1.1)
- The applicant should address the fate of plant metabolites MMCA and MDCA under processing conditions, preferably by a radiolabel hydrolysis study (relevant for all representative uses evaluated, data gap identified in PRAPeR TC 12 meeting (June 2009), date of submission unknown; refer to chapter 3.1.1)
- The residue situation in rotational crops needs to be clarified. (relevant for all representative uses evaluated; date of submission unknown, data gap identified in the experts' meeting for residues EPCO 19 and still pending, refer to chapter 3.1.2)
- Any impact for the risk from consumer exposure to different enantiomer ratios of malathion and its relevant metabolites has to be addressed (relevant for all representative uses evaluated, data gap identified by EFSA after the PRAPeR TC 12 meeting (June 2009), date of submission unknown; refer to chapter 3.3)
- The acute and long-term risk to insectivorous birds needs to be further addressed (relevant for field use in strawberries; date of submission unknown; agreed by Member State experts at PRAPeR TC 13 June 2009; refer to section 5.1)
- The potential risk to earthworms for the enantiomer forms of MDCA needs to be addressed (relevant for field use in strawberries; identified by EFSA after the peer review of the resubmission June 2009; date of submission unknown; refer to section 4 and section 5)

CONCLUSIONS AND RECOMMENDATIONS

OVERALL CONCLUSIONS

The original conclusion from the review was reached on the basis of the evaluation of the representative uses as acaricide and insecticide as proposed by the notifier, which comprised foliar spraying to control various harmful organisms in apples, strawberries, alfalfa and ornamentals at application rate up 1.8 kg malathion per hectare. The conclusion of the peer review of the resubmission 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 strawberries at the ripening of the fruit, in Southern EU countries, at maximum four applications, at maximum application rate per treatment of 1.2 kg a.s./ha
- in ornamentals, in all EU countries, at maximum application rate per treatment of 0.114 kg a.s./ha.

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 to monitor all compounds given in the respective residue definitions, however a data gap was identified concerning amendments in the description of the sample preparation for the method for residues in plants. In case of food of plant origin, malathion and malaoxon can also be determined by a multi-residue method. No method for the determination of malathion in food of animal origin is required for the representative uses of the resubmission. 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 lower than 3 days.

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 at the EPCO meeting 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.

The level of isomalathion in the current 5-batch analysis showed a mean content of 0.048-0.076%. This implied that the limit of 0.03% regarding the toxicological data package would not be feasible. Thus, the toxicological assumptions had 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 had 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 (MMCA) and dicarboxylic (MDCA) acids of malathion. Malathion is 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 acetylcholinesterase 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 with a 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, based on human data (isomalathion content 0.24%), is 1.5 mg/kg bw, with a safety factor of 10 added. Exposure estimates indicate levels of exposure for operators wearing PPE within the AOEL for both boom sprayer and knapsack application; the bystander and worker exposure is below the AOEL (gloves have to be worn for workers re-entering the treated fields).

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 across the different crops, significant differences in quantity of the formed metabolites, and therewith in their relevance for consumer exposure, exist. The metabolism of malathion yields the major metabolites malathion mono- and dicarboxylic acid (MMCA and DMCA), and desmethyl-malathion[26] (DMM), and, though at lower levels, malaoxon[27].

In the resubmission procedure, the relevance of metabolites and degradation products of malathion for consumer safety could be addressed and a residue definition for consumer risk assessment could be established. Considering the toxicological effects of malathion and its metabolites as well as the occurrence of these compounds in crops and processed commodities, the residue definition relevant for consumer risk assessment was established as: Malathion and its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion toxic equivalents.

Pending the final confirmation of a toxic equivalency factor to consider the higher toxicity of malaoxon, a provisional factor of 30 was applied to convert malaoxon residues in malathion toxic equivalents. A factor of 7 proposed by the RMS could not be concluded on during the peer review without having considered in detail all the existing studies. A reassessment performed by the RMS after the experts' discussions indicated that malaoxon is 6-7 fold more toxic than malathion, however this assessment has not been peer reviewed.

Information is still necessary to fully address residues in processed commodities and succeeding crops. Moreover, four additional residue trials in strawberries are still required. However, the experts in the teleconference meeting PRAPeR TC 12 considered a provisional, indicative consumer risk assessment would be possible with the available data on strawberries. This assessment indicates consumer intakes are below 10 % of the ADI and of both ARfD, respectively.

It should be noted that malathion and its metabolites consists of two enantiomers, but the dossier provides no information on whether either isomer is metabolised more quickly than the other in matrices relevant for consumer exposure. Consideration of any impact for the risk

[26] DMM:diethyl (2*RS*)-2-{[hydroxy(methoxy)phosphorothioyl]sulfanyl}butanedioate
[27] Malaoxon: diethyl (2*RS*)-2-[(dimethoxyphosphoryl)sulfanyl]butanedioate

from consumer exposure to different enantiomer ratios of malathion and its relevant metabolites would be necessary to finalise the risk assessment. However, despite the uncertainties in the provisional risk assessment presented in this document, the margin of safety between the currently estimated consumer exposure and the allocated toxicological reference values is considered sufficiently big with respect to the notified use of malathion in strawberries.

The information available on the fate and behaviour in the environment is sufficient to carry out appropriate environmental exposure assessments at the EU level. The one exception is that for the uses assessed on apple and alfalfa 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 any national assessments made by the member states unless it has been demonstrated that their situation is covered by the EU level assessments available on strawberries and glasshouse ornamentals. For the notified intended 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 were not available to conclude on the acute and long-term risk to insectivorous birds following application in strawberries. The risk is however considered low for all mammals and frugivorous birds. Based on the data available, malathion was considered to be very toxic to aquatic organisms. Acute toxicity to fish and toxicity to invertebrates was driving the aquatic risk assessment for use in strawberries. Based on FOCUSsw Step 4 exposure data including maximum mitigation measures the risk was considered low in three out of four scenarios. The toxicity to bees was identified as high and risk mitigation measures should be set at Member State level. No risk mitigations measures were needed to protect other non-target arthropods off field. The risk of malathion to earthworms, other soil macro- and micro-organisms, non-target flora and biological methods of sewage treatment was assessed as low. However, a data gap was defined to address the potential risk to earthworms for the enantiomer forms of the metabolite MDCA.

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED (for the supported uses in the resubmission)

- The maximum content of isomalathion in the representative formulation (‘CHA 3110’, ‘Fyfanon 440’) should not be higher than 0.88 g/L.
- PPE have to be worn in order to have an operator and worker exposure below the AOEL.
- Risk mitigation measures comparable to 30-40 m buffer zones are required for the use in strawberries to protect the aquatic environment.
- Risk to bees should be addressed by mitigation at Member State level. Labelling: Dangerous to bees. To protect bees and pollinating insects do not apply to crop plants when in flower. Do not use where bees are actively foraging. Do not apply when flowering weeds are present (refer to point 5.2).

ISSUES THAT COULD NOT BE FINALIZED

- Quantification of the different potency of malaoxon and malathion is not peer reviewed.
- The consumer risk assessment is provisional.

CRITICAL AREAS OF CONCERN (for the supported uses in the resubmission)

- Based on the available data, it was not possible to address the acute and long-term risk to insectivorous birds from the intended field use in strawberries.

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APPENDICES

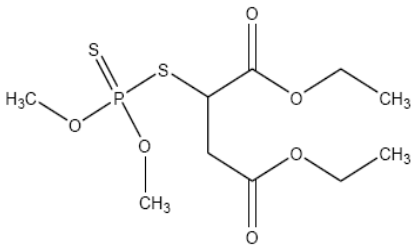
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

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	United Kingdom
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	diethyl (dimethoxyphosphinothioylthio)succinate or *S*-1,2-bis(ethoxycarbonyl)ethyl *O*,*O*-dimethyl phosphorodithioate racemate
Chemical name (CA) ‡	butanedioic acid, [(dimethoxyphosphinothioyl)thio]-, diethyl ester racemate
CIPAC No ‡	12
CAS No ‡	121-75-5
EC 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 ‡	950 g/kg (racemic mixture)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	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 g/mol

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 (state purity)	174 °C, purity 99.1%
Appearance (state purity) ‡	Clear liquid, purity 98.9%
Vapour pressure (state temperature, state purity) ‡	4.5×10^{-4} Pa at 25 °C 3.1×10^{-3} Pa at 35 °C 1.9×10^{-2} Pa at 45 °Cpurity 98.9%
Henry's law constant ‡	1.0×10^{-3} Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	148 mg/l at 25 °C (unbuffered solution)
Solubility in organic solvents ‡ (state temperature, state purity)	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
Surface tension ‡ (state concentration and temperature, state purity)	58 mN/m at 20 °C, purity 96.0%
Partition co-efficient ‡ (state temperature, pH and purity)	log P_{ow} = 2.75 at 25 °C (unbuffered solution) log P_{ow} = 2.40 (CLOGP Med Chem program)
Dissociation constant (state purity) ‡	Does not dissociate in water
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	No absorbance above 290 nm.
Flammability ‡ (state purity)	Not applicable. Flash point 173 °C
Explosive properties ‡ (state purity)	Non explosive
Oxidising properties ‡ (state purity)	Non oxidising

List of representative uses evaluated*(malathion)

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	0.12	1000	1.2	3	[1]
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	There is no maximum number of applications

[1] The acute and long-term risk to insectivorous birds has not been addressed

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

Appendix 1.2: Methods of Analysis

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

Technical as (analytical technique)	a) GC-FID b) CIPAC method GC-FID
Impurities in technical as (analytical technique)	HPLC-UV and GC-FID
Plant protection product (analytical technique)	GC/FID

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Malathion plus its metabolite malaoxon
Food of animal origin		Not required for the representative use assessed
Soil		Malathion or MDCA depending on soil type
Water	surface	Malathion or MDCA
	drinking/ground	Malathion
Air		Malathion

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique 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 cryogenic milling of the samples must be included in the description of the monitoring methods	
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Method not required as the proposed uses are on strawberries and ornamentals	
Soil (analytical technique and LOQ)	LC/MS/MS;	LOQ: 0.01 mg/kg malathion LOQ: 0.01 mg/kg MDCA
Water (analytical technique 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 (analytical technique and LOQ)	LC/MS/MS;	LOQ: 5 µg/m^3 malathion

Body fluids and tissues (analytical technique and LOQ) – Human urine	GC-FPD LOQ: 0.1 mg/l malathion LOQ: 0.1 mg/l malaoxon LOQ: 0.03 mg/l MDCA LOQ: 0.03 mg/l MDCA LOQ: 0.03 mg/l dimethyl phosphate LOQ: 0.03 mg/l dimethyl thiophosphate LOQ: 0.03 mg/l dimethyl dithiophosphate

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

	RMS/peer review proposal
Active substance	None

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 malaoxon Impurities (isomalathion significantly increases the toxicity of malathion). Desmethyl malathion, Malathion mono- and dicarboxylic acids which are all cholinesterase inhibitors.

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)

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). An additional Ames test (0.25% isomalathion) which was also negative 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)

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 mono and dicarboxylic acid	Both metabolites were identified in rat metabolism studies. Malathion monocarboxylic acid LD50 >2000 mg/kg bw Ames test negative cholinesterase inhibitors. Malathion dicarboxylic acid LD50 >2000 mg/kg bw Ames test negative cholinesterase inhibitors.

Desmethyl-malathion	This was identified in rat metabolism studies. LD50 >2000 mg/kg bw Ames test negative cholinesterase inhibitors.
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.

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]

[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.
[2] The safety factor was reduced to 10 due to low inter species variability.

Dermal absorption (Annex IIIA, point 7.3)

.....	5 % for a concentrate 15 % for a spray solution based on human *in vivo* data

Acceptable exposure scenarios (including method of calculation)

Operator	The estimated exposure (% of the AOEL) is:: Indoor (ornamentals) Dutch model: 20 (without PPE); 7 (with PPE) Field crop (boom) sprayer German 28 (with PPE) UK-POEM 103 (with PPE) Hand held (knapsack) German 79 (with PPE) UK-POEM 229 (with PPE)
Workers	The estimated exposure is below the AOEL for ornamentals in glasshouse applications (EUROPOEM II). For use on outdoor strawberry it is uncertain whether levels of exposure for re-entry workers would be within or above the AOEL. Estimates of exposure have been presented which do show both outcomes. If protective gloves were used by workers all predicted exposures are within the AOEL.
Bystanders	The estimated exposure is below the AOEL (1%)

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.

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)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Apple, tomato, strawberry
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes, however further information is required on the fate of MMCA and MDCA upon processing
Plant residue definition for monitoring	Malathion and malaoxon
Plant residue definition for risk assessment	Malathion, malaoxon, desmethyl-malathion, monocarboxcylic acid-malathion and dicarboxylic acid-malathion expressed as malathion toxicological equivalents [28]
Conversion factor (monitoring to risk assessment)	Pending, further consideration necessary

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
Time needed to reach a plateau concentration in milk and eggs	Milk - 2 days Eggs - no plateau reached after 4 days
Animal residue definition for monitoring	Not required for the representative use assessed (strawberries, ornamentals)
Animal residue definition for risk assessment	Not required for the representative use assessed ((strawberries, ornamentals)
Conversion factor (monitoring to risk assessment)	-
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	No

[28] Quantification of the different toxicological potency of malaoxon and malathion is not peer reviewed. Based on the NOAELs in the two long term toxicity studies a conservative factor of 30 has provisionally been used, RMS proposed a factor of 7 according to the ratio of the two LOAELs.

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

Based on the DT_{50} and DT_{90} in soil positive residues would not be expected, however 1.5 N confined rotational crop study indicates significant total residues may occur in succeeding crops (roots 0.11 mg/kg; lettuce 0.07 mg/kg; wheat grain 0.27 mg/kg). Re-assessment of the study in terms of identity and amount of relevant residues in crops not peer reviewed. Further information is necessary.

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 Malathion, malaoxon and demethyl-malathion stable in frozen samples of strawberries for at least 3 months Monocarboxcylic acid-malathion and dicarboxylic acid-malathion stable in frozen samples of strawberries for at least 2 months

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	No	No	No
Potential for accumulation (yes/no):			
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)			
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle			
Liver			
Kidney			
Fat			
Milk			
Eggs			

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

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Strawberry	SMS (outdoor)	Risk assessment: Malathion, desmethyl-malathion, MMCA and MDCA expressed as malathion: 2 x 0.76, 0.82, 1.14 Malaoxon: 3 x <0.01, 0.01 Total malathion toxic equivalents (with factor 30 for malaoxon[29]): 1.07, 1.08, 1.14, 1.46 Monitoring 2007 trials : Malathion: 0.04, 2 x 0.05, 0.07 Malaoxon: 4 x <0.01	Total malathion (for risk assessment) Four trials carried out in 2008 support the proposed critical GAP with residues of total malathion (malathion plus its metabolites malaoxon, desmethyl-malathion, MMCA and MDCA expressed as malathion toxic equivalents) in strawberries Further season trials data requested Malathion and malaoxon (for monitoring) Four further trails carried out in 2007 are available which support the proposed GAP, the fruit samples were analysed for malathion, malaoxon and desmethyl-malathion, and can thus be used for MRL setting purposes.	Malathion 0.3 (provisional)	1.46 (provisional)	1.11 (provisional)

[29] Quantification of the different toxicological potency of malaoxon and malathion is not peer reviewed. Based on the NOAELs in the two long term toxicity studies a conservative factor of 30 has provisionally been used, RMS proposed a factor of 7 according to the ratio of the two LOAELs.

		2008 trials: Malathion: 0.11, 2 x 0.13, 0.16 Malaoxon: 3 x <0.01, 0.01	Risk managers to decide on expression of the residue for MRL setting (refer to 3.4 in the EFSA conclusion)			

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

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

ADI	0.03 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	Less than 1%
TMDI (% ADI) according to national (to be specified) diets	Less than 3% (FR toddler, EFSA PRIMo)
IEDI (WHO European Diet) (% ADI)	Less than 1%
NEDI (specify diet) (% ADI)	Less than 7% (UK toddler)
Factors included in IEDI and NEDI	-
ARfD	0.3 mg/kg bw/day Based on a human study (for 0.2% isomalathion): 1.5 mg/kg bw / day
IESTI (% ARfD)	Less than 8% (German child, EFSA PRIMo); less than 2% of the ARfD based on human data
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Less than 3% (UK child)
Factors included in IESTI and NESTI	-

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

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%)
		Transfer factor	Yield factor	
Strawberry Jam	4	0.3*	Not calculated	Not calculated
Strawberry Canned	4	0.3*	Not calculated	Not calculated

*Total malathion = Parent malathion plus its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid (MMCA) and malathion dicarboxcylic acid (MDCA), without taking into account higher potency of malaoxon. With the provisional toxic equivalency factor of 30, processing factors would become marginally higher (0.35); however no significant change with the equivalency factor of 7 proposed by the RMS.

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

Strawberry	A final decision on how the determined residues in monitoring should be reported (whether the higher toxicological potency of malathion should be particularly considered) will be up to risk managers Refer to 3.4 in the EFSA conclusion.

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
Soil accumulation and plateau concentration ‡	No data submitted and not required

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

Laboratory studies ‡

Parent	Aerobic conditions						
Soil type	X[30]	pH in $CaCl_2$	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa [31]	St. (r^2)	Method of calculation
Loam	-	6.1	22 ± 2°C/ 75% of 0.33 bar	0.1/0.3	0.17	NR	Single First Order
Sand	-	5.7	20 ± 2°C/ 45% MWHC	0.18/0.62	0.18	0.8788	Single First Order
Silty Clay	-	7.3	20 ± 2°C/ 45% MWHC	0.17/0.55	0.107	0.8420	Single First Order
Silty Loam	-	5.1	20 ± 2°C/ 45% MWHC	0.25/0.84	0.21	0.9804	Single First Order
Silty Loam	-	5.8	20 ± 2°C/ 45% MWHC	0.25/0.83	0.193	0.9489	Single First Order
Geometric mean/arithmetic mean					0.17/0.17		

Malathion monocarboxylic acid	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa[2]	St. (r^2)	Method of calculation
Sand	-	5.7	20 ± 2°C/ 45%	0.18/0.59	[a]	0.18	0.7995	Single First Order[d]
Silty Clay	-	7.3	20 ± 2°C/ 45%	0.12/0.38	[a]	0.08	0.9815	Single First Order[d]
Silty Loam	-	5.1	20 ± 2°C/ 45%	0.65/2.2	[a]	0.54	0.9106	Single First Order[d]
Silty Loam	-	5.8	20 ± 2°C/ 45%	0.72/2.4	[a]	0.56	0.7447	Single First Order[d]
Arithmetic mean/geometric mean						0.34/0.26 [c]		

[30] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.
[31] Normalisation calculated assuming a Q10 of 2.2 and Walker equation coefficient of 0.7

[a] = Value not available, not calculated. In the groundwater modelling a 100% conversion from malathion to malathion monocarboxylic acid was assumed.
[c] = In the groundwater modelling the longer arithmetic mean DT50 was used.
[d] = estimated in studies where malathion was dosed using data points after the peak measured metabolite amounts, i.e. the DT50 represents the observed decline.

Malathion dicarboxylic acid	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20 °C pF2/10kPa[2]	St. (r^2)	Method of calculation
Sand	-	5.7	20 ± 2°C/ 45%	1.2/4.1	[b]	1.2	0.9938	Single First Order[d]
Silty Clay	-	7.3	20 ± 2°C/ 45%	5.3/17.8	[b]	3.3	0.9414	Single First Order[d]
Silty Loam	-	5.1	20 ± 2°C/ 45%	4.7/15.7	[b]	3.9	0.7945	Single First Order[d]
Silty Loam	-	5.8	20 ± 2°C/ 45%	4.5/15.1	[b]	3.5	0.4290	Single First Order[d]
Arithmetic mean/geometric mean						3.0/2.7[c]		

[b] = Value not available, not calculated. For the groundwater modelling a 100% conversion from malathion monocarboxylic acid to malathion dicarboxylic acid was assumed.
[c] = In the groundwater modelling the longer arithmetic mean DT50 was used.
[d] = estimated in studies where malathion was dosed using data points after the peak measured metabolite amounts, i.e. the DT50 represents the observed decline.

Field studies ‡

Parent	Aerobic conditions								
Soil type.	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) Norm.	Method of calculation
Loamy sand (bare and cropped)	Georgia, USA	-	6.6	120 (cropped) 30 (bare)	NR[d]	NR[d]	NR[d]	NR[d]	NR[d]
Sandy loam (bare and cropped)	California, USA	-	6.1	120 (cropped) 30 (bare)	NR[d]	NR[d]	NR[d]	NR[d a]	NR[d]
Geometric mean/median					-	-	-	-	

[d] = Malathion degraded rapidly and a DT50/ DT90 could not be calculated.

Malathion dicarboxylic acid	Aerobic conditions								
Soil type	Location	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90} (d) actual	St. (r2)	DT_{50} (d) Norm.	Method of calculation
Sandy loam (bare and cropped)	California, USA	-	6.1	120 (cropped) 30 (bare)	1.7 to 2.7	NR[d]	-	-	Estimation
Geometric mean/median					-				

[d] = dissipation too rapid to be determined

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	0.55	6.9	-	-	0.83	151	0.904
Sand	0.4	6.2	-	-	1.23	308	0.912
Loam	1.0	6.1	-	-	1.76	176	0.978
Silt loam	1.35	7.4	-	-	2.47	183	0.973
Sandy loam	0.6	4.5	-	-	1.60	267	0.924
Arithmetic mean						217	0.94
pH dependence, Yes or No			No				

Koc for Malathion monocarboxylic acid could not be determined as it degraded before reaching equilibrium.

Malathion dicarboxylic acid ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand	0.50	5.5 – 5.6	-	-	0.0773	15	0.72
Silty Clay	2.07	7.3 – 7.5	-	-	0.1198	6	1.07
Silty loam	1.29	5.0 – 5.3	-	-	0.8319	64	1.06
Silty loam	1.44	5.6 – 5.7	-	-	0.2662	18	1.06
Arithmetic mean						25.8	0.98
pH dependence (yes or no)			Yes. 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

PEC (soil) (Annex IIIA, point 9.1.3)

Parent

Method of calculation	DT_{50} : 0.25 days Kinetics: 1st order Laboratory: worst case data from the laboratory
Application rate	Crop: strawberries Depth of soil layer: 5cm Soil bulk density: 1.5g/cm^3 Crop interception: 60 % Number of applications: 4 Interval (d): 10 Application rate(s): 1200 g as/ha

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.640	0.640	0.640	0.640
Short term 1d	0.040	0.216	0.040	0.216
2d	0.003	0.115	0.003	0.115
4d	0.000	0.058	0.000	0.058
Long term 7d	0.000	0.033	0.000	0.033
28d	0.000	0.008	0.000	0.008
50d	0.000	0.005	0.000	0.005
100d	0.000	0.002	0.000	0.002

Metabolites

Malathion monocarboxylic acid (MMCA) Method of calculation	Molecular weight relative to the parent: 0.91 DT_{50} (d): 0.72 days Kinetics: SFO Field or Lab: worst case from lab studies.
Application data	Application rate assumed: 4 x 1200 g as/ha (assumed Met I is formed at a maximum of 25 % of the applied dose) and 60% interception.

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.146		0.146	

Malathion dicarboxylic acid (MDCA) Method of calculation	Molecular weight relative to the parent: 0.83 DT_{50} (d): 5.3 days Kinetics: SFO Field or Lab: worst case from lab studies.
Application data	Application rate assumed: 4 x 1200 g as/ha (assumed Met II is formed at a maximum of 61.7 % of the applied dose) and 60% interception.

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial	0.446		0.446	

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 (1st order, r^2=0.875 and 0.933, n=2) DT_{50} whole system 8 – 10 hours; DT_{90} whole system 27 – 35 hours (1st order, r^2=0.881 and 0.918, n=2) **MMCA**: DT_{50} water 3 – 4 days, DT_{90} water 9 – 12 days (1st order, r^2=0.943 and 0.915, n=2); DT_{50} whole system 3 – 4 days, DT_{90} whole system 9 – 12 days (1st order, r^2=0.952 and 0.926, n=2) **MDCA:** DT_{50} water 15 – 17 days, DT_{90} water 50 – 57 days (1st order, r^2=0.712 and 0.831, n=2); DT_{50} whole system 13 – 21 days, DT_{90} whole system 45 – 71 days (1st 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 47.7 % AR at day 2 (n=2) MDCA maximum of 34.9 % AR at day 4 (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)

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

Parent

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of FOCUS calculator: FOCUS v 1.1 Molecular weight (g/mol): 330 Water solubility (mg/L): 148 K_{OC}/K_{OM} (L/kg): 217/ 125.9 DT_{50} soil (d): 0.17 days (Lab. In accordance with FOCUS SFO) DT_{50} water (d): 0.38 DT_{50} sediment (d): 1000 Crop interception (%): 0% interception STEP 1, full canopy STEP 2. Application window: March-May
Parameters used in FOCUSsw step 3 and 4 (if performed)	Version control no.'s of FOCUS software: FOCUS SWASH 2.1, TOXSWA v 2.1.1 Vapour pressure: 4.4×10^{-4} K_{OC}/K_{OM} (L/kg): 217/ 125.9 1/n: 0.94 (Freundlich exponent general) Q_{10} =2.2, Walker equation coefficient =0.7
Application rate	Crop: Vegetables, fruiting Crop interception: Calculated by model dependent on growth stage at time of application Number of applications: 1 Interval (d): N/A Application rate(s): 1200 g a.s/ha Application timing: D6 = 7 May R2 = 7 May R3 = 18 May R4 = 4 May or 11 May

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	321.2738		673.2161	
	24 h	51.4435	186.3587	111.6324	392.4243
	2 d	8.3013	105.0051	18.0138	221.8741
	4 d	0.2162	53.6107	0.4691	113.3417
	7 d	0.0009	30.6515	0.002	64.8032
	14 d	0	15.3258	0	32.4017
	21 d	0	10.2172	0	21.6011
	28 d	0	7.6629	0	16.2009
	42 d	0	5.1086	0	10.8006

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	11.036		12.3741	
	24 h	1.5144	6.2752	4.4729	8.4235
	2 d	0.4143	3.6198	1.4676	5.6969
	4 d	0.0425	1.8999	0.1784	3.1733
	7 d	0.0016	1.0914	0.0076	1.8386
	14 d	0	0.5458	0	0.9199
	21 d	0	0.3639	0	0.6133
	28 d	0	0.2729	0	0.4599
	42 d	0	0.1819	0	0.3066
Southern EU	0 h	11.036		12.3741	
	24 h	1.5144	6.2752	4.4729	8.4235
	2 d	0.4143	3.6198	1.4676	5.6969
	4 d	0.0425	1.8999	0.1784	3.1733
	7 d	0.0016	1.0914	0.0076	1.8386
	14 d	0	0.5458	0	0.9199
	21 d	0	0.3639	0	0.6133
	28 d	0	0.2729	0	0.4599
	42 d	0	0.1819	0	0.3066

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D6	Ditch	0 h	7.505		0.893	
		24 h	0.028	2.012	0.427	0.707
		2 d	0.004	1.011	0.306	0.552
		4 d	0.001	0.506	0.219	0.411
		7 d	0.001	0.290	0.167	0.319
		14 d	0.000	0.145	0.120	0.231
		21d	0.000	0.097	0.098	0.190
		28 d	0.000	0.073	0.085	0.166
		42 d	0.000	0.484	0.069	0.136
R2	Stream	0 h	6.739		0.409	
		24 h	0.001	0.693	0.154	0.259
		2 d	0.000	0.347	0.107	0.195
		4 d	0.000	0.173	0.076	0.143
		7 d	0.000	0.111	0.094	0.118
		14 d	0.000	0.059	0.061	0.096
		21 d	0.000	0.037	0.050	0.082
		28 d	0.000	0.028	0.043	0.073
		42 d	0.000	0.019	0.036	0.062
R3	Stream	0 h	7.063		0.864	
		24 h	0.011	1.825	0.385	0.651
		2 d	0.002	0.915	0.276	0.502
		4 d	0.001	0.458	0.198	0.372
		7 d	0.000	0.269	0.161	0.293
		14 d	0.000	0.135	0.114	0.214
		21 d	0.000	0.089	0.094	0.177
		28 d	0.000	0.067	0.081	0.155
		42 d	0.000	0.044	0.066	0.128
R4	Stream	0 h	4.895		0.312	
		24 h	0.000	0.519	0.116	0.240
		2 d	0.000	0.259	0.081	0.208
		4 d	0.000	0.130	0.058	0.174

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
		7 d	0.028	0.136	0.153	0.153
		14 d	0.000	0.074	0.118	0.133
		21 d	0.000	0.050	0.094	0.122
		28 d	0.000	0.037	0.080	0.113
		42 d	0.000	0.025	0.064	0.099

FOCUSsw STEP 4
Application rate

Number of applications: 1 or 4
Interval (d): 10 days (4 applications)
Application rate(s): 1200 g a.s/ha
Application timing:
D6 = 7 May
R2 = 7 May
R3 = 18 May
R4 = 4 May or 11 May (see table below)

FOCUS STEP 4 maximum PECsw for malathion (30m or 40m buffer zone mitigation).

FOCUS STEP 4 Scenario	Water body	Buffer zone (m)	Application timing	Maximum PEC_{SW} (µg/L)
D6	Ditch	30	7 May	0.380 (1 application)
R2	Stream	40	1. 7 May 2. 20 May 3. 3 June 4. 25 June	0.393 (4 applications)
R3	Stream	40	18 May	0.365 (1 application)
R4	Stream	40	1. 4 May 2. 27 May 3. 6 June 4. 16 June	0.620 (4 applications)
			1. 11 May 2. 27 May 3. 6 June 4. 16 June	1.824 (4 applications)

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 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) 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	2.77	0.57	0.29	0.2	0.15	0.1	0.07	0.06
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

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

PEC (sediment) information in respect of uses on apples and alfalfa.

Parent

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

Metabolite malathion monocarboxylic acid (MMCA) Parameters used in FOCUSsw STEP 1 and 2	Molecular weight: 302 Water solubility (mg/L): 148 Soil or water metabolite: soil and water metabolite Koc/Kom (L/kg): 25.8/ 15.0 DT_{50} soil (d): 0.34 days (Lab. In accordance with FOCUS SFO) DT_{50} water (d): 3.5 DT_{50} sediment (d): 1000 Crop interception (%): 0% interception STEP 1, full canopy STEP 2. Maximum occurrence observed (% molar basis with respect to the parent) Soil: 25 Water/Sediment: 47.7
Parameters used in FOCUSsw step 3 (if performed)	STEP 3 not performed. Vapour pressure: N/A Kom/Koc: N/A 1/n: (Freundlich exponent general or for soil, susp. solids or sediment respectively) N/A Metabolite kinetically generated in simulation (yes/no): N/A Formation fraction in soil (k_{dp}/k_f): (If formation degradation of metabolite is kinetically simulated by PRZM) N/A
Application rate	Crop: vegetables, fruiting (surrogate for strawberries) Number of applications: 1 Interval (d): N/A Application rate(s): 1200 g as/ha Depth of water body: 30 cm Application window: March-May
Main routes of entry	All routes (spray drift, runoff/drainflow) considered at STEP 1 and 2.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	93.2892		22.8257	
	24h	76.397	84.8431	19.7104	21.2681
	2d	62.6712	77.0754	16.1692	19.5747
	4d	42.1746	64.4118	10.881	16.4629
	7d	23.2823	50.4347	6.0068	12.9234
	14d	5.8206	31.5153	1.5017	8.0866
	21d	1.4551	22.0599	0.3754	5.6619
	28d	0.3638	16.7417	0.0939	4.2972
	42d	0.0227	11.2021	0.0059	2.8754

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	4.8175		0.8005	
	24 h	3.8644	4.3409	0.6687	0.7346
	2 d	3.1844	3.9327	0.5514	0.6723
	4 d	2.1691	3.2918	0.5558	0.5885
	7 d	1.2074	2.5836	0.3135	0.5182
	14 d	0.3175	1.6259	0.0825	0.3459
	21 d	0.0835	1.1425	0.0217	0.2458
	28 d	0.022	0.8684	0.0057	0.1873
	42 d	0.0015	0.5815	0.0004	0.1256
Southern EU	0 h	4.8175		0.8005	
	24 h	3.8644	4.3409	0.6687	0.7346
	2 d	3.1844	3.9327	0.5514	0.6723
	4 d	2.1691	3.2918	0.5558	0.5885
	7 d	1.2074	2.5836	0.3135	0.5182
	14 d	0.3175	1.6259	0.0825	0.3459
	21 d	0.0835	1.1425	0.0217	0.2458
	28 d	0.022	0.8684	0.0057	0.1873
	42 d	0.0015	0.5815	0.0004	0.1256

Metabolite malathion dicarboxylic acid (MDCA) Parameters used in FOCUSsw step 1 and 2	Molecular weight: 274 Water solubility (mg/L): 148 Soil or water metabolite: Soil and water metabolite. Koc/Kom (L/kg): 25.8/15.0 DT_{50} soil (d): 3 days (Lab. In accordance with FOCUS SFO) DT_{50} water (d): 17 DT_{50} sediment (d): 1000 Crop interception (%): 0% interception STEP 1, full canopy STEP 2. Maximum occurrence observed (% molar basis with respect to the parent) Soil: 61.7 Water/Sediment: 34.9
Parameters used in FOCUSsw step 3 (if performed)	STEP 3 not performed. Vapour pressure: N/A Kom/Koc: N/A 1/n: (Freundlich exponent general or for soil ,susp. solids or sediment respectively) N/A Metabolite kinetically generated in simulation (yes/no): N/A Formation fraction in soil (k_{dp}/k_f): (If formation degradation of metabolite is kinetically simulated by PRZM) N/A
Application rate	Crop: vegetables, fruiting (surrogate for strawberries) Number of applications: 4 Interval (d): 10 Application rate(s): 1200 g as/ha Depth of water body: 30 cm Application window: March-May
Main routes of entry	All routes (spray drift, runoff/drainflow) considered at STEP 1 and 2.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	805.2079		204.4433	
	24h	772.6288	788.9183	199.3382	201.8908
	2d	741.7597	773.0038	191.374	198.6099
	4d	683.6722	742.6626	176.3874	191.1944
	7d	604.9577	700.1698	156.0791	180.4081
	14d	454.7487	613.2276	117.3252	158.0949
	21d	341.8361	540.6886	88.1937	139.4191
	28d	256.9593	479.8618	66.2955	123.7454
	42d	145.1969	385.1713	37.4608	99.3349

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	9.5933		2.4619	
	24 h	9.1675	9.3804	2.3668	2.4144
	2 d	8.8132	9.1854	2.2753	2.3677
	4 d	8.1452	8.8306	2.1029	2.278
	7 d	7.2368	8.3388	1.8683	2.1518
	14 d	5.4919	7.332	1.4179	1.8924
	21 d	4.1678	6.488	1.076	1.6747
	28 d	3.1629	5.7767	0.8166	1.4911
	42 d	1.8215	4.6615	0.4703	1.2033
Southern EU	0 h	14.8294		3.8119	
	24 h	14.1944	14.5119	3.6646	3.7383
	2 d	13.6458	14.216	3.523	3.666
	4 d	12.6114	13.6698	3.2559	3.5271
	7 d	11.205	12.9096	2.8928	3.3317
	14 d	8.5034	11.3515	2.1953	2.93
	21 d	6.4531	10.045	1.666	2.5929
	28 d	4.8972	8.9438	1.2643	2.3087
	42 d	2.8204	7.2173	0.7281	1.8631

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, and alfalfa as listed for parent above.
Main routes of entry	Spray drift to a 30cm deep static water body

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
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
Alfalfa	0	4.0	-

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 flowering	0	76.9
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 (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) Q_{10} =2.2, Walker equation coefficient =0.7 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

PEC(gw) - FOCUS modelling results

Model /Crop	Scenario	Parent (µg/l)	Metabolite (µg/l)		Site specific Kfoc (ml/g)
			MMCA	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
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, monocarboxylic acid (MMCA) 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

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

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
1.2 kg a.s./ha	Strawberries	Small insectivorous bird	Acute	**3.3**	10
1.2 kg a.s./ha	Strawberries	Small insectivorous bird	Short-term	17.3	10
1.2 kg a.s./ha	Strawberries	Small insectivorous bird	Long-term	**0.375**	5
1.2 kg a.s./ha	Strawberries	Frugivorous bird	Acute	7.9	10

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
1.2 kg a.s./ha	Strawberries	Frugivorous bird	Short-term	99	10
1.2 kg a.s./ha	Strawberries	Frugivorous bird	Long-term	**2.4**	5
1.2 kg a.s./ha	Strawberries	Frugivorous bird	Acute	46[1]	10
1.2 kg a.s./ha	Strawberries	Frugivorous bird	Short-term	99	10
1.2 kg a.s./ha	Strawberries	Frugivorous bird	Long-term	9.4[1]	5
1.2 kg a.s./ha	Strawberries	Frugivorous mammals	Acute	70.3	10
1.2 kg a.s./ha	Strawberries	Frugivorous mammals	Long-term	9.3[1]	5
1.2 kg a.s./ha	Strawberries	Small insectivorous mammal	Acute	168	10
1.2 kg a.s./ha	Strawberries	Small insectivorous mammal	Long-term	6.8	5

[1] Refined risk assessment is based on using initial 90th and mean residue in strawberries (sprayed four times at 10 days interval) presented in Section B.7 of the original DAR. These values are 1.91 mg a.s./kg and 1.1 mg a.s./kg for the 90th and mean respectively; if these are combined with an application rate of 1.2 kg a.s./kg and an FIR/bw of 2.02 (for birds) / 1.92 (for mammals) and, for the long-term risk assessment an Ftwa of 0.53, an acute ETE of 4.6 for birds is produced and a long-term ETE of 2.7 (for birds) / 3.7 (for mammals).

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
1.2	Strawberries	Frugivore	Acute	860	10
1.2	Strawberries	Frugivore	Short-term	6670	10
1.2	Strawberries	Frugivore mammal	Long-term	20	5

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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
Laboratory tests ‡				
Fish – three-spined stickleback	Malathion technical	96 hour	Mortality; LC_{50} NOEC	0.022 0.005
Fish – sheepshead minnow	Malathion technical	96 hour	Mortality; LC_{50} NOEC	0.040 0.018
Fish – bluegill sunfish	Malathion technical	96 hour	Mortality; LC_{50} NOEC	0.054 0.032
Fish – rainbow >	Malathion technical	96 hour	Mortality; LC_{50} NOEC	0.18 0.091
Fish – fathead minnow	Malathion technical	96 hour	Mortality; LC_{50} NOEC	>7.98 0.946
Fish – common carp	Malathion technical	96 hour	Mortality; LC_{50} NOEC	>10 1.0
Fish	Malathion technical	ELS	Growth NOEC	0.021
Daphnia	Malathion technical	48 hour	Mortality; EC_{50}	0.00072
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

Group	Test substance	Time-scale	Endpoint	Toxicity (mg/l)
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.

Toxicity/exposure for aquatic organisms at FOCUS Step 1 assuming application to strawberries at 1.2 kg a.s./ha (Annex IIIA, point 10.2)

Test substance	**Organism**	**Toxicity endpoint (µg/L)**	**Time scale**	**PECi (µg/L)**	**PECtwa**	**TER**	**Annex VI Trigger**
a.s.	Fish	22	Acute	321.3	n.r.	**0.07**	100
a.s.	Fish	21	Chronic	321.3	n.r.	**0.06**	10
a.s.	Aquatic invertebrates	5	Mesocosm	321.3	n.r.	**0.01**	5*
a.s.	Aquatic invertebrates	5	Mesocosm	321.3	n.r.	**0.01**	3*
a.s.	Algae	410	Chronic	321.3	n.r.	**1.28**	10
Monocarboxylic acid	Fish	79000	Acute	93.3	n.r.	847	100

Monocarboxylic acid	*Daphnia*	3500	Acute	93.3	n.r.	**37.5**	100
Dicarboxylic acid	Fish	>100000	Acute	805.2	n.r.	124.2	100
Dicarboxylic acid	*Daphnia*	71000	Acute	805.2	n.r.	**88.2**	100

* The trigger value is based on the assessment factor agreed at the expert meeting.

Toxicity/exposure for aquatic organisms at FOCUS Step 2 assuming application to strawberries at 1.2 kg a.s./ha (Annex IIIA, point 10.2)

Test substance	N/S MS	Organism	Toxicity endpoint (µg/L)	Time scale	PEC[1] (µg/L)	TER	Annex VI Trigger
a.s.	S	Fish	22	Acute	11.0	**2.0**	100
a.s.	S	Fish	21	Chronic	11.0	**1.9**	10
a.s.	S	Aquatic invertebrates	5	Meso-cosm	11.0	**0.45**	5*
a.s.	S	Aquatic invertebrates	5	Meso-cosm	11.0	**0.45**	3*
a.s.	S	Algae	410	Chronic	11.0	37.3	10
Monocarboxylic acid	S	*Daphnia*	3500	Acute	4.8	729	100
Dicarboxylic acid	S	*Daphnia*	71000	Acute	9.6	7396	100

[1] maximum values have been used.
* The trigger value is based on the assessment factor agreed at the expert meeting.

Toxicity/exposure for aquatic organisms at FOCUS Step 3 assuming application to strawberries at 1.2 kg a.s./ha (Annex IIIA, point 10.2)

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity endpoint (µg/L)	PEC (µg/L)	TER	Annex VI trigger
a.s.	D6	Ditch	Fish	Acute	22	7.5	**2.9**	100
a.s.	R2	Stream	Fish	Acute	22	6.7	**3.3**	100
a.s.	R3	Stream	Fish	Acute	22	7.1	**3.1**	100
a.s.	R4	Stream	Fish	Acute	22	4.9	**5**	100
a.s.	D6	Ditch	Fish	Chronic	21	7.5	**2.8**	10
a.s.	R2	Stream	Fish	Chronic	21	6.7	**3.1**	10
a.s.	R3	Stream	Fish	Chronic	21	7.1	**3.0**	10

a.s.	R4	Stream	Fish	Chronic	21	4.9	**4.3**	10
a.s.	D6	Ditch	Aquatic inverte-brates	Meso-cosm	5	7.5	**0.67**	5*
a.s.	R2	Stream	Aquatic inverte-brates	Meso-cosm	5	6.7	**0.75**	5*
a.s.	R3	Stream	Aquatic inverte-brates	Meso-cosm	5	7.1	**0.70**	5*
a.s.	R4	Stream	Aquatic inverte-brates	Meso-cosm	5	4.9	**1.0**	5*
a.s.	D6	Ditch	Aquatic inverte-brates	Meso-cosm	5	7.5	**0.67**	3*
a.s.	R2	Stream	Aquatic inverte-brates	Meso-cosm	5	6.7	**0.75**	3*
a.s.	R3	Stream	Aquatic inverte-brates	Meso-cosm	5	7.1	**0.70**	3*
a.s.	R4	Stream	Aquatic inverte-brates	Meso-cosm	5	4.9	**1.0**	3*
a.s.	D6	Ditch	Algae	Acute	410	7.5	**54.7**	10
a.s.	R2	Stream	Algae	Acute	410	6.7	**61.2**	10
a.s.	R3	Stream	Algae	Acute	410	7.1	**57.7**	10
a.s.	R4	Stream	Algae	Acute	410	4.9	**83.7**	10

* The trigger value is based on the assessment factor agreed at the expert meeting.

Toxicity/exposure for aquatic organisms at FOCUS Step 4 assuming application to strawberries at 1.2 kg a.s./ha (Annex IIIA, point 10.2)

Scenario	Water body	Test organism	Time scale	Toxicity endpoint (µg/L)	Buffer zone distance (m)	PEC (µg/L)	TER	Annex VI trigger
D6	Ditch	Fish	Acute	40#	30	0.380	105	100
R2	Stream	Fish	Acute	40#	40	0.393	102	100
R3	Stream	Fish	Acute	40#	40	0.365	110	100

R4	Stream	Fish	Acute	40[#]	40	0.620[a]	**65**	100
						1.824[b]	**22**	100
D6	Ditch	Fish	Chronic	21	30	0.380	55	10
R2	Stream	Fish	Chronic	21	40	0.393	53	10
R3	Stream	Fish	Chronic	21	40	0.365	58	10
R4	Stream	Fish	Chronic	21	40	0.620[a]	34	10
						1.824[b]	12	10
D6	Ditch	Aquatic invertebrates	Mesocosm	5	30	0.380	13	3*
R2	Stream	Aquatic invertebrates	Mesocosm	5	40	0.393	13	3*
R3	Stream	Aquatic invertebrates	Mesocosm	5	40	0.365	14	3*
R4	Stream	Aquatic invertebrates	Mesocosm	5	40	0.620[a]	8	3*
						1.824[b]	**2.7**	3*
D6	Ditch	Aquatic invertebrates	Mesocosm	5	30	0.380	13	5*
R2	Stream	Aquatic invertebrates	Mesocosm	5	40	0.393	13	5*
R3	Stream	Aquatic invertebrates	Mesocosm	5	40	0.365	14	5*
R4	Stream	Aquatic invertebrates	Mesocosm	5	40	0.620[a]	8	5*
						1.824[b]	**2.7**	5*

[#] Refined endpoint based on 'Method 2' og the PPR opinion (EFSA Journal (2005) 301, 1-45)
[*] The trigger value is based on the assessment factor agreed at the expert meeting.
[a =] Application window beginning 4 May
[b =] Application window beginning 11 May

[*] The toxicity endpoints quoted incorporate uncertainty; hence the trigger value has been revised to 1.

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

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				
1.2	Strawberries	Oral	3510	50
1.2	Strawberries	Contact	8775	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.

Proposed risk mitigation at Member State level. Labelling: Dangerous to bees. To protect bees and pollinating insects do not apply to crop plants when in flower. Do not use where bees are actively foraging. Do not apply when flowering weeds are present.

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

Test Substance: CHA3110 (440 g/L EW formulation)[32]

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 = 14** at 1.2 kg a.s./ha)		HQ < 2
Aphidius rhopalosiphi	Dose-response	48-hour LR_{50}	LR_{50} : 0.06125 g a.s./ha (**HQ = 19592** at 1.2 kg a.s./ha)		HQ < 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 of 27.0, 94.5, 279.0, 2160.0 and 6300 g a.s./ha.	Mortality & repro.	Corrected mortality rates was 87.5% No repro	Corrected mortality rates was 94% No repro	50% effect
	Aged residue rate-response deposit of 27.0, 94.5, 279.0, 2160.0 and 6300 g a.s./ha. Bioassays were carried out 5, 10 and 14 days after application.		Corrected mortality at 5 days was 30.6%; 10.1 eggs/female compared to 9.4 in the control. Corrected mortality at 10 days was 6.3%; 11.3 eggs/female compared to 10.2 in the control. Corrected mortality at 14 days was 2.2%; repro not determined.	Corrected mortality at 5 days was 43.9%; 10.2 eggs/female compared to 9.4 in the control. Corrected mortality at 10 days was 35.4%; 9.3 eggs/female compared to 10.2 in the control. Corrected mortality at 14 days was 22.5%; repro not determined.	

[32] The risk assessment for non-target arthropods was addressed only for formulation with a content of isomalathion <0.0017%.

Species	Dose (kg as/ha)	Endpoint	Effect		ESCORT 2
Aphidius rhopalosiphi	Fresh spray deposit	Mortality & parasitism rate	Corrected mortality rates was 100%; repro not determined.	Corrected mortality rates was 100% mortality; repro not determined.	50% effect
	Aged residue rate-response deposit of 27.0, 94.5, 279.0, 2160.0 and 6300 g a.s./ha. Bioassays were carried out 5, 10, 14, 21, 28, 35, 42, 49, 56, 63, 70 and 77 days after application.		Corrected mortality at 5 – 21 days was 100%; ; repro not determined. Corrected mortality at 28 days was 83.78%; repro not determined. Corrected mortality at 35 days 12.5%; repro was 7.17 mummies per female compared to 6.80 in the control. Corrected mortality at 42 days was -5.41%; repro was 8.80 mummies per female compared to 5.80 in the control. Corrected mortality at 49 days was 2.63%; repro was 8.53 mummies per female compared to 6.00 in the control Corrected mortality at 56 to	Corrected mortality at 5 – 49 days was 100%; repro was not determined. Corrected mortality at 56 days was 92.11% and repro was not determined. Corrected mortality at 63 days was 80.0% and repro was not determined. Correct mortality at 70 days was 2.50%; repro was 19.93 mummies per female compared to 19.07 in the control. Correct mortality at 77 days and repro was 21.07 mummies per female compared to 30.67 in the control.	

Species	Dose (kg as/ha)	Endpoint	Effect		ESCORT 2
			77 days was not determined.		
Chrysoperla carnea	Fresh spray deposit	Mortality & parasitism rate	Corrected mortality was 100% and repro was not determined	Corrected mortality was 100% and repro was not determined	50% effect
	Aged residue rate-response deposit of 27.0, 94.5, 279.0, 2160.0 and 6300 g a.s./ha. Bioassays were carried out 5, 10, 14, 21, 28, 35, 42, 49, 56, 63, 70 and 77 days after application.		Corrected mortality at 5 days was 97.6% and repro was not determined. Corrected mortality at 10 days was 64.4% and repro was not determined. Corrected mortality at 14 d Corrected mortality at 14 days was 16.8% and 29.8 and 94.1 mean no of eggs/female and mean hatching rate (%) respectively. Corrected mortality at 21 days was 9.3% and 27.9 and 57.1 mean no of eggs/female and mean hatching rate (%) respectively. Corrected mortality at 28 days was 4.2% and 31.3 and 93.9 mean no of eggs/female and	Corrected mortality at 5 days was 97.6% and repro was not determined. Corrected mortality at 10 days was 64.4% and repro was not determined. Corrected mortality at 14 d Corrected mortality at 14 days was 87.0% and 24.3 and 91.6 mean no of eggs/female and mean hatching rate (%) respectively. Corrected mortality at 21 days was 14.0% and 29.8 and 54.7 mean no of eggs/female and mean hatching rate (%) respectively. Corrected mortality at 28 days was 15.3% and 37.3 and 90.0 mean no of eggs/female and mean hatching rate (%) respectively.	

Species	Dose (kg as/ha)	Endpoint	Effect		ESCORT 2
			mean hatching rate (%) respectively.		
Orius laevigatus	Fresh spray deposit	Mortality & parasitism rate	100% mortality; repro not assessed	100% mortality; repro not assessed	50% effect
	Aged residue rate -response		Corrected mortality at 5 days was 100% and repro was not determined. Corrected mortality at 9 days was 100% and repro was not determined. Corrected mortality at 14 days was 52.38%; reduction in repro rate 29.22%. Corrected mortality at 21 days was 34.88% and reduction in repro rate 10.86%. Corrected mortality at 28 days was 22.30% and reduction in repro rate -796%. Corrected mortality at 36 days was 13.04% and reduction in repro rate 40.39%. Corrected mortality at 42 days was 7.14% and reduction in	Corrected mortality at 5, 9 and 14 days was 100% and repro was not determined. Corrected mortality at 21 days was 79.07% and reduction in repro rate 0.90%. Corrected mortality at 28 days was 40.32% and reduction in repro rate -700%. Corrected mortality at 36 days was 2.17% and reduction in repro rate 38.32%. Corrected mortality at 42 days was 7.14% and reduction in repro rate was not determined. Corrected mortality at 49 days was 10.64% and reduction in repro rate 42.54%. Corrected mortality at 61 days was 6.69% and reduction in repro rate was -63.98.	

Species	Dose (kg as/ha)	Endpoint	Effect		ESCORT 2
			repro rate was not determined. Corrected mortality at 49 days was 2.13% and reduction in repro rate 14.75%. Corrected mortality at 61 days was not determined and nor was reduction in repro rate.		

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:

MMCA and MDCA: 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				
	Strawberries	14-day acute	91	10
Metabolites				
Dicarboxylic acid	Strawberries	14-day acute	13	10
Monocarboxylic acid	Strawberries	14-day acute	40	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

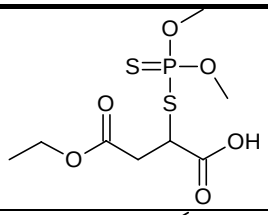
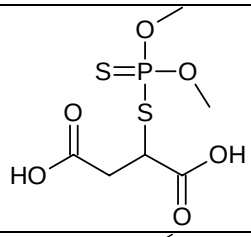
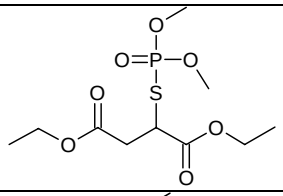
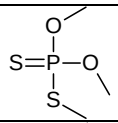
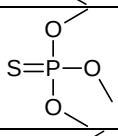
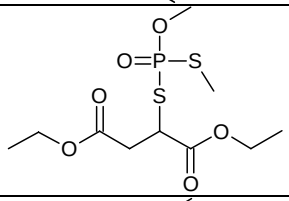
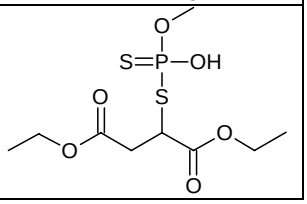
Most sensitive species	Test substance	ER50 (g/ha)[2] vegetative vigour	ER50 (g/ha)[2] emergence	Exposure[1,2] (g/ha)[3]	TER	Trigger
All six species	formulation	> 1800 g a.s./ha		33.2	>54.1	5

[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

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
MMCA malathion monocarboxylic acid	(2*RS*)- 2-[(dimethoxyphosphorothioyl)sulfanyl]-4-ethoxy-4-oxobutanoic acid	
MDCA malathion dicarboxylic acid	(2*RS*)- 2-[(dimethoxyphosphorothioyl)sulfanyl]butanedioic acid	
malaoxon	diethyl (2*RS*)-2-[(dimethoxyphosphoryl)sulfanyl]butanedioate	
MeOOSPS-triester	*O*,*O*,*S*-trimethyl phosphorodithioate	
MeOOOPS-triester	*O*,*O*,*O*-trimethyl phosphorothioate	
isomalathion	diethyl (2*RS*)-2-{[methoxy(methylsulfanyl)phosphoryl]sulfanyl}butanedioate	
DMM desmethyl-malathion	diethyl (2*RS*)-2-{[hydroxy(methoxy)phosphorothioyl]sulfanyl}butanedioate	

ABBREVIATIONS

°C	degree Celsius (centigrade)
µg	microgram
a.s.	active substance
AChE	acetylcholinesterase
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
approx	approximate
AR	applied radioactivity
ARfD	acute reference dose
BCF	bioconcentration factor
bp	boiling point
bw	body weight
c	centi- (x 10-2)
CAS	Chemical Abstract Service
ChE	cholinesterase
CIPAC	Collaborative International Pesticide Analytical Council Limited
cm	centimetre
cv	coefficient of variation
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DAR	draft assessment report
DFR	dislodgeable foliar residue
DM	dry matter
DO	dissolved oxygen
DOC	dissolved organic carbon
DT50	period required for 50 percent disappearance (define method of estimation)
DT90	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC50	effective concentration (biomass)
EC50	effective concentration
ECD	electron capture detector
ECHA	European Chemical Agency
ECU	European currency unit
ED50	median effective dose
EDI	estimated daily intake
EINECS	European Inventory of Existing Commercial Chemical Substances
ELF	early life stage
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate/effective rate, median
ERC	environmentally relevant concentration
ErC50	effective concentration (growth rate)
ESCORT	European Standard Characteristics of Beneficials Regulatory Testing

ETE	Estimated theoretical exposure
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
F	field
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIA	fluorescence immuno assay
FID	flame ionisation detector
FIR	Food intake rate
FMC	maximum field capacity
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
fp	freezing point
FPD	flame photometric detector
FPLC	fast protein liquid chromatography
FSA	fish screening assay
FSO	first single-order
g	gram
G	glasshouse
GAP	good agricultural practice
GC	gas chromatography
GC-EC	gas chromatography with electron capture detector
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GC-MSD	gas chromatography with mass-selective detection
GC-NPD	gas chromatography with nitrogen phosphorous detector
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GEP	good experimental practice
GFP	good field practice
GGT	gamma glutamyl transferase
GI	gastro-intestinal
GIT	gastro-intestinal tract
GL	guideline level
GLC	gas liquid chromatography
GLP	good laboratory practice
GM	geometric mean
GMM	genetically modified micro-organism
GMO	genetically modified organism
GPC	gel-permeation chromatography
GPPP	good plant protection practice
GPS	global positioning system
GS	growth stage
GSH	glutathion
GV	granulose virus
h	hour(s)
H	Henry's Law coefficient (calculated as a unitless value) (see also K)
ha	hectare

Hb	haemoglobin
HC_5	Hazard concentration 5%
HCG	human chorionic gonadotropin
Hct	haematocrit
HDT	highest dose tested
HEED	high energy electron diffraction
HID	helium ionisation detector
hL	hectolitre
HPAEC	high performance anion exchange chromatography
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HPPLC	high pressure planar liquid chromatography
HPTLC	high performance thin layer chromatography
HQ	hazard quotient
HR	hazard rate
HRGC	high resolution gas chromatography
Hs	Shannon-Weaver index
Ht	haematocrit
I	indoor
I50	inhibitory dose, 50 %
ID	ionisation detector
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
IGR	insect growth regulator
ILV	inter laboratory validation
im	intramuscular
inh	inhalation
ip	intraperitoneal
IPM	integrated pest management
IR	infrared
ISBN	international standard book number
ISO	International Organisation for Standardisation
ISSN	international standard serial number
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
IVF	in vitro fertilisation
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
k	kilo
K	Kelvin or Henry's Law constant (in atmospheres per cubic meter per mole) (see also H)
Kads	adsorption constant
Kdes	apparent desorption coefficient
Kdoc	organic carbon linear adsorption coefficient
Kdom	organic matter linear adsorption coefficient

kg	kilogram
KFoc	Freundlich organic carbon adsorption coefficient
KFom	Freundlich organic matter adsorption coefficient
Koc	organic carbon adsorption coefficient
L	litre
LAN	local area network
LASER	light amplification by stimulated emission
LBC	loosely bound capacity
LC	liquid chromatography
LC50	lethal concentration, median
LCA	life cycle analysis
LCLo	lethal concentration low
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD50	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LDLo	lethal dose low
LOAEC	lowest observable adverse effect concentration
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOEC	lowest observable effect concentration
LOEL	lowest observable effect level
LOQ	limit of quantification (determination)
LPLC	low pressure liquid chromatography
LR	lethal rate
LSC	liquid scintillation counting or counter
LSD	least squared denominator multiple range test
LSS	liquid scintillation spectrometry
LT	lethal threshold
m	metre
M	molar
M/L	mixing and loading
MAF	multiple application factor
MC	moisture content
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
MDL	method detection limit
MFO	mixed function oxidase
mg	milligram
MHC	moisture holding capacity
min	minute(s)
mL	millilitre
MLD	minimum lethal dose
MLT	median lethal time
mm	millimetre
mN	Milli-Newton

mo	month(s)
mol	Mol
MOS	margin of safety
mp	melting point
MRE	maximum residue expected
MRL	maximum residue limit or level
mRNA	messenger ribonucleic acid
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity
n	normal (defining isomeric configuration)
NAEL	no adverse effect level
nd	not detected
NEDI	no effect daily intake (mg/kg body wt/day)
NEL	no effect level
NERL	no effect residue level
NESTI	national estimated short-term intake
NIR	Near-Infrared-(Spectroscopy)
ng	nanogram
nm	nanometer
NMR	nuclear magnetic resonance
no	number
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOED	no observed effect dose
NOEL	no observed effect level
NPD	nitrogen-phosphorus detector or detection
NPV	nuclear polyhedrosis virus
NR	not reported
NTE	neurotoxic target esterase
OC	organic carbon content
OCR	optical character recognition
ODP	ozone-depleting potential
ODS	ozone-depleting substances
OM	organic matter content
op	organophosphorus pesticide
Pa	Pascal
PAD	pulsed amperometric detection
pc	paper chromatography
PD	proportion of different food types
PEC	predicted environmental concentration
PECair	predicted environmental concentration in air
PECgw	predicted environmental concentration in ground water
PECsed	predicted environmental concentration in sediment
PECsoil	predicted environmental concentration in soil

PECsw	predicted environmental concentration in surface water
PED	plasma-emissions-detector
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
PIXE	proton induced X-ray emission
pKa	negative logarithm (to the base 10) of the dissociation constant
PNEC	predicted no effect concentration
po	by mouth (per os)
POP	persistent organic pollutants
Pow	partition coefficient between n-octanol and water
ppb	parts per billion (10-9)
PPE	personal protective equipment
ppm	parts per million (10-6)
ppp	plant protection product
ppq	parts per quadrillion (10-24)
ppt	parts per trillion (10-12)
PRL	practical residue limit
PrT	prothrombin time
PSP	phenolsulfophthalein
PT	proportion of diet obtained in the treated area
PTDI	provisional tolerable daily intake
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r	correlation coefficient
r2	coefficient of determination
RAC	raw agricultural commodity
RBC	red blood cell
Rber	calculated maximum residue level (EU Method II)
REI	restricted entry interval
Rf	ratio of fronts
RfD	reference dose
RH	relative humidity
RL50	residual lifetime
Rmax	calculated maximum residue level (EU Method I)
RMS	rapporteur Member State
RNA	ribonucleic acid
RP	reversed phase
RPE	respiratory protective equipment
rpm	reversed phase material
rRNA	ribosomal ribonucleic acid
RRT	relative retention time
RSD	relative standard deviation
RUD	residue per unit dose
s	second
SAR	structure/activity relationship

sc	subcutaneous
SC	suspension concentrate
sce	sister chromatid exchange
SD	standard deviation
SE	standard error
SEM	standard error of the mean
SEP	standard evaluation procedure
SETAC	Society of Environmental Toxicology and Chemistry
SF	safety factor
SFC	supercritical fluid chromatography
SFE	supercritical fluid extraction
SFO	single first-order
SIMS	secondary ion mass spectroscopy
SOP	standard operating procedure
sp	species (only after a generic name)
SPE	solid phase extraction
SPF	specific pathogen free
SPI	spraying
SRU	low volume spraying
spp	subspecies
sq	square
SSD	species sensitivity distribution
STEL	short-term exposure limit
STMR	supervised trials median residue
t	tonne (metric ton)
t1/2	half-life (define method of estimation)
T3	tri-iodothyroxine
T4	thyroxine
TAR	total applied radioactivity
TBC	tightly bound capacity
TC	technical material
TCD	thermal conductivity detector
TER	toxicity exposure ratio
TERA	toxicity exposure ratio for acute exposure
TERI	toxicity exposure ratio for initial exposure
TERLT	toxicity exposure ratio following chronic exposure
TERST	toxicity exposure ratio following repeated exposure
tert	tertiary (in a chemical name)
TF	transfer factor
TID	thermionic detector, alkali flame detector
TIFF	tag image file format
TK	technical concentrate
TLC	thin layer chromatography
Tlm	median tolerance limit
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TMRC	theoretical maximum residue contribution

TMRL	temporary maximum residue limit
TOC	total organic chlorine
Tremcard	Transport emergency card
tRNA	transfer ribonucleic acid
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UF	uncertainty factor (safety factor)
ULV	ultra low volume
UV	ultraviolet
v/v	volume ratio (volume per volume)
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
wt	weight