TABLE OF CONTENTS

List of all reports from PRAPeR Expert Meetings

Date		Section
4 June 2009	PRAPeR expert meeting TC 11	Mammalian Toxicology
4 June 2009	PRAPeR expert meeting TC 12	Residues
5 June 2009	PRAPeR expert meeting TC 13	Ecotoxicology

Report of PRAPeR Expert MEETING TC 11

MALATHION

Rapporteur Member State: UK

Specific comments on the active substance in the section

2. Mammalian Toxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
none		

2. Documents submitted for meeting:

Date	Supplier	File Name
28.05.2009	UK	Malathion evaluation table rev 1-0 (2009-05-28).doc
May 2009	UK	malathion list of end points May 2009.doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** Malathion 440 g/L EW

5. **Classification and labelling:** not discussed

6. **Recommended restrictions/conditions for use:** not discussed

7. **Reference List:** not discussed

Areas of concern: XXX

Appendix 1: Discussion table: Malathion

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Malathion (In)

2. Mammalian toxicology

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 2.1 RMS to amend the list of end points. See reporting table 2(2)	Still open, to be done after the TC.	Open point open: RMS to revise the list of end points
	Open point: 2.2 MSs to discuss the outcomes of the study by Pratt 2006, and the impact it might have on the relevant end points and on the risk assessment. See reporting table 2(5)	The study is summarised on page 44 of the Additional report. According to conclusion RMS established that malathion has the highest potential for RBC ChE inhibition compared to the metabolite DMM. No information on Brain ChE inhibition is available in this study. Nevertheless, in the study by Barnett, 2008 Brain ChE inhibition was measured. Taking all studies together, the overall picture of the relative toxicity shows that malathion has the highest potential inhibition compared to the metabolite. The experts agreed that the metabolite should be considered as less toxic than malathion, but should be considered toxicologically relevant because of its acetylcholinesterase inhibition activity. Open point fulfilled.	Open point fulfilled.
	Open point: 2.3 Pending confirmation from the residue section group, MSs to discuss the relevance of metabolite MMCA See reporting table 2(7)	Available information is summarised in the additional report. The available studies for the 3 metabolites desmethyl malathion (DMM),malathion monocarboxylic acid (MMCA) and malathion dicarboxylic acid (MDCA) seem to indicate a lower toxicity than malathion, however based on their toxicological properties (same endpoints as malathion), it was agreed to consider them as toxicological relevant. Open point fulfilled.	Open point fulfilled. Metabolites DMM, MCA and MDCA are considered as toxicological relevant.
	Open point: 2.4 MSs to discuss the need of further tox studies for MMCA	Available metabolism data demonstrate that malathion is metabolised in rat and human mainly to malathion mono- and di-carboxylic acids (MMCA and MDCA). This is a common metabolic pathway catalysed by carboxylesterases, usually in the liver.	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 2(8)	The malathion carboxylic acids are rapidly excreted in the urine (60 - 80% of dose). The experts agreed that based on that there is no need to perform further toxicological studies. Open point fulfilled.	There is no need to perform futher toxicological studies.
	Open point: 2.5 MSs to agree on the need of further genotoxicity information on MMCA See reporting table 2(9)	See point 2.4 Open point fulfilled.	Open point fulfilled See point 2.4
	Open point: 2.6 MSs to revise ADI and AOEL with regard to the SF applied See reporting table 2(13)	In the assessment presented in the EFSA conclusion in 2006, an additional safety factor of 10 was added at the 100 default depending on the technically estimated amount of isomalathion up to 0.2%, taking into account its unknown genotoxic potential (now an Ames test is under assessment) and also the effects of isomalathion on the ChE inhibition (isomalathion estimated more acutely toxic than malathion by a factor 2-10). The majority of studies in the dossier have been performed with an amount of isomalathion lower than the one proposed in the specification. It was also noted that the amount of isomalathion in the batches can increase. Based on that the SF was increased (higher toxicity of batches with higher isomalathion content). The EPCO meeting held in 2005 decided that if malathion containing 0.2 % isomalathion was negative in an Ames test there would be no concern for genotoxicity Malathion containing 0.2 % isomalathion has been shown to be non-genotoxic as confirmed with an Ames test which is included in the Additional report. However, the experts confirm the use of additional SF of 10 (in total 1000) for ADI and AOEL to cover uncertainties from the isomalathion amount in the batches tested.	Open point fulfilled ADI 0.03 mg/kg bw/day AOEL 0.03 mg/kg bw/day ARfD 0.3 mg/kg bw ARfD 1.5 mg/kg bw (based on human study)

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		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. This information should be included in the list of end points. Open point fulfilled.	
	General point raised during the meeting.	The experts discussed the overall validity of the database considering the low amount of isomalathiion. The meeting acknowledged the weaknesses of the database, however the increased SF for ADI and AOEL was considered to cover the uncertainties raising from low levels of isomalathion in the concerned batches. Open point fulfilled.	The increased SF for ADI and AOEL was considered to cover the uncertainties raising from low levels of isomalathion in the concerned batches.
	Open point: 2.7 MSs to confirm worker exposure assessment after field application on strawberries See reporting table 2(14)	Available information is summarised in the Additional Report: "*The original exposure assessment assumes worker re-entry into field strawberries immediately after the final application to perform harvesting activities. This assumption is considered by the applicant to be overly conservative as the critical GAP specifies a PHI of 3 days before harvest. Therefore, the applicant has proposed worker re-entry can be considered for 2 possible scenarios.* *1. Crop inspection immediately after application* *2. Harvest activities at the PHI of 3 days* *This evaluation agrees these are the realistic re-entry scenarios to be considered.* *Assuming 60 kg body weight and 15 % dermal absorption, systemic exposure is estimated to be 0.054 mg/kg bw/day, i.e.180% of the short-term systemic AOEL. This is for a single application of malathion. As this product may be applied up to 4*	Open point fulfilled. New open point proposed, see below: RMS to present in an addendum worker exposure estimates with and without the use of PPE, also according to EUROPOEM II (as it was not presented in the additional report) and considering one application.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		times in a programme of treatments (10 day interval between treatments), if levels of DFR accumulate between treatments, levels of exposure could be higher than have been predicted. Further refinement of the exposure assessment is therefore required." *Using specific studies from field trials 2007, still to be assessed, a refinement was possible according to the applicant:"Using the information given exposure to workers re-entering crops treated with a programme of 4 treatments of 'Malathion 440 g/L EW'is predicted for crop inspection (2 hours exposure) and hand-harvesting (8 hours exposure). The calculations assume a half life of 0.5 days. Assessments have also been produced which assume a calculated half-life of 3.3 days (linear fit, first order degradation) and 1.86 days (non linear fit, first order degradation). The exposure levels resulted well below the AOEL"* There are 3 points to be discussed: 1. Use of PPE 2. Refinement according to field trials 3. Number of applications The use of PPE: some concerns were raised about the possibility of using PPE in such scenario. Some MS considered harvesting of strawberries with PPE is not realistic. It was proposed to give information of exposure with and without PPE as usually done. The experts agreed. Refinement according to estimated half life: some uncertainties were raised related to this approach summarised in the additional report. It seems that in this case a safe use might be found, however the approach is not considered fully reliable. No realistic field studies are available to measure DFR value. This can be required at MS level. Number of applications: the majority of experts considered the use of only one application. Open point fulfilled, new open point proposed for the RMS: RMS to present worker	

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		exposure estimates with and without the use of PPE, also according to EUROPOEM II (as it was not presented in the additional report) and considering one application.	
	New open point 2.10 RMS to present in an addendum worker exposure estimates with and without the use of PPE, also according to EUROPOEM II (as it was not presented in the additional report) and considering one application		Open point open
	Open point: 2.8 MSs to address the need of amateur exposure See reporting table 2(15)	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. Open point fulfilled	Open point fulfilled There is no need to address the amateur exposure.
	Open point: 2.9 MSs to agree on the number of hectares to be considered in the UK POEM for application in row crops. See reporting table 2(26)	In the additional report, the operator exposure assessment for application in strawberries outdoor was calculated with the UK POEM . Correctly, 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, considered as more realistic. MS supported the use of lower number of ha (30 ha) for strawberries compared to standard of 50 ha. Open point fulfilled	Open point fulfilled MS supported the use of lower number of ha (30 ha) compared to standard of 50 ha.
	Message from section 3 to section 2. MS to confirm a difference in the potency of malaoxon vs malathion.	RMS proposed a difference in the potency of malaoxon vs malathion of 7 times according to the ratio of the two LOAELs from the two long term toxicity studies. However, it was not possible to conclude on that with such short notice. New open point for the RMS: RMS to revise the difference in the potency of malaoxon and malathion based on the overall database. It was noted that value that	Answer from section 2 to section 3: New open point proposed see below: RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		will be proposed by the RMS will not peer-reviewed.	
	New open point 2.11 RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.		Open point open

Appendix 2: Evaluation table

2. Mammalian toxicology

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 2 Open points: ***9*** Points for clarification: ***0*** Data gaps: ***0***			Section 2 Open points: ***3*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 2.1 RMS to amend the list of end points. See reporting table 2(2)	Notifier: Agreed	RMS: Full amended end points will be provided after the expert telecon.	PRAPeR TC 11 (4 June 2009): Open point open: RMS to revise the list of end points
	Open point: 2.2 MSs to discuss the outcomes of the study by Pratt 2006, and the impact it might have on the relevant end points and on the risk assessment. See reporting table 2(5)	Notifier: We agree with the RMS that the most important information derived from the Pratt 2006 study is the cholinesterase inhibition potential of DMM. The overall conclusion from the study by Pratt 2006 together with the other relevant studies (Barnett and Fulcher) indicates that the metabolites DMM, MMCA and MDCA are potential cholinesterase inhibitors, and that they are less potent than malathion. They clearly exhibit lower toxicity and AChE inhibition in both erythrocytes and brain than malathion. The Notifer therefore understands that there is a need to include these metabolites in the residue definition for risk assessment. Since the consumer risk assessment is based on	RMS: Agreed	PRAPeR TC 11 (4 June 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		comparison of total malathion equivalent residues with toxicological endpoints for malathion, it is concluded that this would provide a conservative assessment of exposure and therefore a worst case scenario. The current consumer risk assessment shows a large margin of safety can be achieved using this scenario.		
	Open point: 2.3 Pending confirmation from the residue section group, MSs to discuss the relevance of metabolite MMCA See reporting table 2(7)	Notifier: In the rat metabolism study the major metabolites in urine and faeces are MMCA and MDCA, with >80% of the malathion dose recovered. The metabolic route of malathion to MDCA can only be via MMCA and so the toxicity of MMCA can be said to have been thoroughly investigated in the toxicological tests conducted with malathion. The toxicological properties of MMCA are therefore already accounted for in the endpoints that have been set for malathion. Any exposure to MMCA through residues in treated crops can be considered to be fully addressed when the measured residues of MMCA are converted to malathion by calculation and compared with the toxicological endpoint set for malathion.	RMS: Agreed, this is an acceptable approach.	PRAPeR TC 11 (4 June 2009): Open point fulfilled Metabolites DMM, MCA and MDCA are considered as toxicological relevant.
	Open point: 2.4 MSs to discuss the need of further tox studies for MMCA	Notifier: We agree with the RMS that long term testing is not necessary given MMCA is a major rat metabolite. Please	RMS: Agreed	PRAPeR TC 11 (4 June 2009): Open point fulfilled

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 2(8)	also reference the discussion in the reporting table 2(8) on expected level of auto-exposure to MMCA in chronic toxicity/oncogenicity study. Comparing the urinary excretion of MMCA in the rat metabolism and human volunteer study shows that MMCA is formed in both rat and human and at similar levels. Therefore already submitted data on toxicity of malathion itself adequately reflects the toxicity of this metabolite and no further data should be necessary.		
	Open point: 2.5 MSs to agree on the need of further genotoxicity information on MMCA See reporting table 2(9)	Notifier: We agree with the RMS that given MMCA is a major rat metabolite, *in vivo* genotoxicity studies conducted with malathion will adequately reflect the genotoxic potential of this metabolite. Results from *in vivo* studies show malathion is not genotoxic and therefore no further data are necessary. The additional Ames test on MMCA supports this overall conclusion.	RMS: Agreed	PRAPeR TC 11 (4 June 2009): Open point fulfilled See point 2.4
	Open point: 2.6 MSs to revise ADI and AOEL with regard to the SF applied See reporting table 2(13)	Notifier: The unknown genotoxic potential of isomalathion was a contributory factor in setting an additional safety factor of 10. Now that isomalathion has been shown not to be genotoxic, the safety factor could be revised.	RMS: It is not completely clear whether the addition safety factor was a result of the unknown genotoxic potential of isomalathion, or due to the increased toxicity of malathion as a result of it's presence (given the lower levels of isomalathion present in the batches used for toxicity testing compared to the proposed technical specification). It is the view of the RMS that the increased	PRAPeR TC 11 (4 June 2009): Open point fulfilled ADI 0.03 mg/kg bw/day AOEL 0.03 mg/kg bw/day ARfD 0.3 mg/kg bw ARfD 1.5 mg/kg bw (based on human study)

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			safety factor is due to the uncertainty over the increased toxicity of malathion as a result of isomalathion at levels higher than those tested.	
	Open point: 2.7 MSs to confirm worker exposure assessment after field application on strawberries See reporting table 2(14)	Notifier: According to the original DAR and EUROPOEM guidance, the use of PPE in worker exposure assessments is an acceptable approach. Using reasonable worst case assumptions, a safe worker exposure scenario has been demonstrated for field strawberries across the range of DT50 values proposed. It is concluded this is sufficient for Annex I listing and any differences in opinion regarding work practices in different countries can be dealt with at MS level.	RMS: The UK position is that the use of PPE by workers should only be considered where the specified PPE are worn habitually by workers when carrying out their respective work tasks. Workers generally will not know what the crop has been treated with and the precautions to be taken as a result. The realistic worse case is therefore to consider exposure for an unprotected worker. Appropriate and objective usage data would be needed to justify the use of PPE by workers for exposure assessment purposes. This is the approach the UK would apply at national level, although we understand that some Member States take a different approach.	PRAPeR TC 11 (4 June 2009): Open point fulfilled. New open point proposed, see below: RMS to present in an addendum worker exposure estimates with and without the use of PPE, also according to EUROPOEM II (as it was not presented in the additional report) and considering one application.
	New open point 2.10 RMS to present in an addendum worker exposure estimates with and without the use of PPE, also according to EUROPOEM II (as it was not presented in the additional report) and considering one application			PRAPeR TC 11 (4 June 2009): Open point open
	Open point: 2.8 MSs to address the need of	Notifier: This is not necessary because amateur use is not supported as a	RMS : Agree. Amateur use has not been considered as it is not a	PRAPeR TC 11 (4 June 2009): Open point fulfilled

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	amateur exposure See reporting table 2(15)	representative use for Annex I listing.	representative use for Annex I listing.	There is no need to address the amateur exposure
	Open point: 2.9 MSs to agree on the number of hectares to be considered in the UK POEM for application in row crops. See reporting table 2(26)	Notifier: We welcome this discussion but consider it a more general question appropriate for all active substances as there is currently no EU guidance as to what is acceptable. For malathion, an acceptable operator exposure has been shown using the German model and therefore this discussion should not affect Annex I listing. However, since many MS require the UK POEM model to be acceptable at Annex III assessment of the approach of reducing the default area for row crops to refine operator exposure would be helpful.	RMS : The UK adopts a default value of 30ha for boom sprayer treatments to row crops in recognition of the slower forward speeds involved when treating such crops. In POEM such a revision only affects the mixing/loading part of the model as the (default) assessment still assumes 6 hours of spraying plus the time taken for mixing/loading operations and travelling to and from the field(s).	PRAPeR TC 11 (4 June 2009): Open point fulfilled MS supported the use of lower number of ha (30 ha) compared to standard of 50 ha.
	Message from section 3 to section 2. MS to confirm a difference in the potency of malaoxon vs malathion.			PRAPeR TC 11 (4 June 2009): Answer from section 2 to section 3: New open point proposed see below: RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.
	New open point 2.11 RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.			PRAPeR TC 11 (4 June 2009): Open point open

REPORT OF PRAPeR EXPERT MEETING TC 12

MALATHION

Rapporteur Member State: UK

Specific comments on the active substance in the section

3. Residues

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
none		

2. Documents submitted for meeting:

Date	Supplier	File Name
28.05.2009	UK	Malathion evaluation table rev 1-0 (2009-05-28).doc
May 2009	UK	malathion list of end points May 2009.doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
04.06.2009	EFSA	Table with individual residue data created by EFSA_TC 12

The conclusions of the meeting were as follows:

4. **Data on preparations:** Malathion 440 g/L EW

5. **Classification and labelling:** not discussed

6. **Recommended restrictions/conditions for use:** none

7. **Reference List:** not discussed

Areas of concern: none

Appendix 1: Discussion table: MALATHION

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Malathion (In)

3. Residues

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 3.1 Experts to discuss whether despite the shortcoming of the re-analysis metabolism data in apple with regard to storage stability (TRR has significantly decreased, degradation occurred) the study can still be considered reliable to conclude on a residue definition and on comparability of metabolism in all crops See reporting table 3(2)	Samples from the apple metabolism study were re-analysed almost 2 years after the first analyses. This re-analysis has to be considered qualitative rather than from a quantitative point on view, since there was a decline of the TRR, the % of identified compounds was lower and the proportions of the different compounds was not similar to the first analysis. Most of the experts were of the opinion that this new results are not reliable from a quantitative point of view. These re-analyses only confirm the nature of the compounds already identified in previous metabolism studies. This new study can not be used to derive any conversion factor for the risk assessment.	Open point fulfilled The re-analysis results have to be considered as informative only. They confirm the nature of the compounds identified in the initial apple study.
	Open point: 3.2 Experts to consider the results generated in the strawberry residue trials in the light of the effect homogenisation of samples apparently has on the residue levels	In the additional report of February 2008 it was shown that the nature of the metabolites detected might change, depending if the analyse is performed on the whole fruit or on the homogenised sample (see table B.7.4 in additional report). The parent malathion account for 3.8% TRR (0.06 mg/kg) when analysis is performed on the whole sample but for only 0.4% (<0.01 mg/kg, virtually not present) in the homogenised sample. Also levels of the MDCA metabolite were decreased [3.4% TRR (0.06 mg/kg) in intact fruit vs. 0.6% TRR (0.01 mg/kg) in homogenised fruit]	Open point fulfilled Message from section 3 to section 1: It should be noted 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.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	(upon comparative analysis of homogenised and intact samples in the fruit metabolism study a significant decrease of compounds in the residue definition was observed). See reporting table 3(4)	If the residue definition for monitoring is based on the parent, residue levels may be grossly under-estimated if the sample is not frozen when homogenised. There is an agreement that nowadays most of the laboratories use cryogenic blending that limits the possible degradation of the active substance. However, to avoid such a problem occurring, it is important to send a message to the monitoring laboratories that samples have to be milled frozen. The phys-chem / methods section will be informed that cryogenic milling of whole fruit samples has to be part of the analytical method for monitoring. In the evaluation table the applicant stated that cryogenic milling was used in the residue trials. Therefore, the residue data generated in the strawberry residue trials (according to the residue definition for RA) are considered to represent the residue on the whole fruit.	
	Open point: 3.3 Experts to discuss • whether the monitoring definition proposed for all crops can be confirmed as the most appropriate one considering that reliable conversion factors (monitoring to risk assessment) are difficult to establish • the approach suggested by the RMS not to establish conversion factors but to analyse for the full residue definition for risk assessment in case the MRL is exceeded	The initial proposal for the residue definition for monitoring is: Malathion + malaoxon expressed as malathion This definition is also the current definition adopted at Codex level. The toxicology meeting concluded that DMM, MMCA and MDCA have to be considered as toxicologically relevant (as toxic as the parent). Depending the tox end-point taken into account (NOAEL, NOEL …) Malaoxon is about 10 to 30 times more toxic than the parent but from the available studies is was not possible to have a more accurate conclusion (opne point in the tox section). For the time being taking a tox equivalence factor of 30 for malaoxon into account in the risk assessment is a worst case. The results of the residue trials performed on strawberries were discussed (see attached table with individual residue data created by EFSA). The 2008 trials show that MMCA and MDCA would be better markers for residues in strawberries, both compounds accounting for at least 80% of the total residue. Based on these residue trials and the residues levels observed after 3 days in strawberries conversion factors can be derived for the risk assessment (trials analyse separately for parent, malaoxon, DMM, MMCA, MDCA).	Open point fulfilled Residue definition for risk assessment: Malathion plus its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion Residue definition for monitoring: proposed to include malathion and malaoxon Conversion factor: for the time being proposed as 8 (provisional, to be confirmed by additional residue trials), established on the basis of the sum of malathion and malaoxon

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 3(6)	The meeting was in favour to propose a simple residue definition for monitoring in order to make the analysis effective for enforcement. Considering the higher toxicity of the malaoxon the meeting was of the opinion to include this compound in the residue definition for monitoring and to define the residue as parent malathion and malaoxon (preferably to be reported separately because of their different toxicological potency, RA will be more precise). The meeting confirmed the residue definition for risk assessment (RA) initially proposed (in the additional report) as: Malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion. The toxicological effect is the same for malathion and all metabolites. The higher toxicological potency of malaoxon needs to be considered when residues are converted into malathion equivalents. Provisionally, a conversion factor monitoring / RA of 8 was proposed by the meeting, including a tox-equivalence factor of 30 to account for malaoxon toxicological potency. It is noted that the factor applies to the sum of malathion and malaoxon expressed as malathion. According to the findings in the residue trials the conversion factor increases from day 0 to day 3. Thus the meeting was of the opinion to request the applicant to provide additional residue trials considering the residue levels for longer PHI (up to 10 days) in order to conclude on a critical conversion factor in strawberries to be used in RA.	
	Open point: 3.4 It should be discussed by experts whether a sufficient number of appropriate and valid residues trials in strawberry are available that analyse for the full residue definition for risk assessment. See reporting table	Already discussed in point 3.3 4 additional trials are requested were samples are analysed for the residue definition for risk assessment and with longer PHIs up to 10 days. 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. The risk assessment based on the 4 available residue trials with analysis of the full RA definition, using the total residue level expressed as malathion toxic equivalents (i.e. factor 30 for malaoxon and 1 for the other metabolites) indicates intakes below 10% of the ADI and the ARfD, resp.	Open point fulfilled New data dap proposed see below Applicant to provide 4 additional residue trials on strawberry taking into account the residue definition for risk assessment, longer PHIs and the sample homogenisation and storage period aspects.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	3(15)		
	New data gap 3.1 identified at PRAPeR TC 12: Applicant to provide 4 additional residue trials on strawberry taking into account the residue definition for risk assessment, longer PHIs and the sample homogenisation and storage period aspects.		Data gap open
	Open point: 3.5 RMS to present information on the nature of the residue upon processing in the list of end points using the current harmonised version Information on processing should also be corrected in a corrigendum/ addendum/revised AR as appropriate See reporting table 3(18)	RMS to use the new template for the LoEP to present available information on the nature of the residue upon processing.	Open point open RMS to use the new template in the LoEP to present available information on the nature of the residue upon processing.
	Open point: 3.6 Experts to discuss whether the available data on processing	The hydrolysis study with malathion shows that MMD is the main compound of concern, accounting for more than 50% of the TRR. The strawberry processing studies in the additional report of February 2008 (tables B.7.9	Open point fulfilled New data dap proposed see below the applicant to address the fate of

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	sufficiently address the fate of all compounds that are part of the residue definition for risk assessment. It should be noted that new information cannot be considered for 2nd stage resubmissions under the accelerated procedure (Commission Regulation (EC) No. 33/2008). See reporting table 3(19)	and B.7.10) show an increase in the DMM residue levels in jam but not in canned fruit. In contrast, a significant degradation of MDCA is observed in jam and canned fruit (residues decreasing from ca 0.5 mg/kg in RAC to ca LOQ in processed fractions). A decrease is 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 RAC). Concerning the decrease of MMCA and MDCA, the experts agreed to ask the applicant to address the fate of MMCA and MDCA metabolites under processing conditions, preferably by a radiolabel hydrolysis study. Provisionally and awaiting the requested information above, the meeting agreed to define the residue in processed commodity as for the plant (see point 3.3)	MMCA and MDCA metabolites under processing conditions; preferably by a radiolabel hydrolysis study
	Open point: 3.7 Experts to discuss how to deal with malaoxon in the consumer risk assessment, considering the residue data available, the higher chronic toxicity of malaoxon and the insufficient data on acute toxicity To facilitate the discussion RMS should report the individual residue data for malaoxon in an addendum/ revised AR	Point already discussed under point 3.3 Pending the final assessment of the toxicologists, the meeting agreed to take the higher toxicity of malaoxon in the risk assessment into account with a tox equivalence factor of 30. Provisionally, this factor was also taken into account to derive a conversion factor from monitoring to risk assessment.	Open point fulfilled See point 3.3

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	as appropriate. See reporting table 3(21)		
	Open point: 3.8 RMS to assess in an addendum the issue of potential residues in rotated crops as identified necessary (data gap) also for the strawberry use in the previous peer review on malathion. The assessment may consider the case made by the applicant. See reporting table 3(22)	From the LoEP the DT50 values are very short for the parent compound. However, the rotational crop study (reported in the DAR by Finland) indicates a significant uptake of radioactivity by plants, but the initial evaluation focussed mainly on malathion and malaoxon residues only. A data requirement was identified in a previous expert meeting (EPCO 19) that was related to the potential uptake of the tox relevant DMM metabolite. At that time it was not considered that also the MMCA and MDCA are tox relevant metabolites. It was agreed by the experts that strawberry are rotated and that there is a need to address the residue in the rotational crops. Therefore, in a first place, the RMS is asked to re-assess the confined rotational study, in the light of the residue definition for the risk assessment currently established, i.e. malathion and its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid, malathion dicarboxcylic acid. It needs to be considered whether the sum of relevant residues may reach significant levels in succeeding crops.	Open point open RMS to re-assess the confined rotational study, with particular attention to the residue definition established for risk assessment.
	Open point: 3.9 RMS to present the corrected consumer risk assessment in the list of end points using the current harmonised version Risk assessment should be corrected in a corrigendum/ addendum/revised AR as appropriate		Open point open RMS to reconsider the consumer risk assessment in the light of the results of the current discussions

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	See reporting table 3(25)		
	New open point 3.10: RMS to amend the list of end points according to the discussions during the PRAPeR TC 12	LoEP to be amended in accordance with the discussions, using the current template.	Open point open

Appendix 2: Evaluation table

3. Residues

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 3 Open points: ***9*** Points for clarification: ***0*** Data gaps: ***0***			Section 3 Open points: ***4*** Points for clarification: ***0*** Data gaps: ***2***
	Open point: 3.1 Experts to discuss whether despite the shortcoming of the re-analysis metabolism data in apple with regard to storage stability (TRR has significantly decreased, degradation occurred) the study can still be considered reliable to conclude on a residue definition and on comparability of metabolism in all crops See reporting table 3(2)	Notifier: Four metabolism studies showing a similar route of metabolism on three separate crop groups are already available to evaluate a suitable residue definition for malathion. Whilst we agree that there are certain short comings to the apple metabolism study, further investigations have shown that the route of metabolism is similar in all crops and all key metabolites have been identified. Quantitative measures of these metabolites have been shown in the supervised crop residue trials. The available data are considered sufficient to confirm the residue definition as proposed.	RMS: To add to the notifiers comments, the proposed residue definition for risk assessment is very broad covering a number of metabolites – Malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion Open point addressed	PRAPeR TC 12 (4 June 2009): Open point fulfilled The re-analysis results have to be considered as informative only. They confirm the nature of the compounds identified in the initial apple study
	Open point: 3.2 Experts to consider the results generated in the strawberry residue trials in the light of the effect homogenisation of	Notifier: Cryogenic milling of whole strawberry fruit samples will have minimised degradation at this point. Storage stability of homogenised samples over the period of frozen	RMS: Agrees with the notifiers comments Open point addressed	PRAPeR TC 12 (4 June 2009): Open point fulfilled Message from section 3 to section 1: It should be noted that cryogenic milling of

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	samples apparently has on the residue levels (upon comparative analysis of homogenised and intact samples in the fruit metabolism study a significant decrease of compounds in the residue definition was observed). See reporting table 3(4)	storage has also been adequately demonstrated. Therefore, the residue data generated in the strawberry residue trials are considered to represent the residue on whole fruit. The RMS rightly points out that based on the current approach the risk assessment would not be affected as all key metabolites are measured and converted back to malathion equivalent residues.		whole fruit samples has to be part of the analytical method for monitoring in order to avoid any degradation of malathion.
	Open point: 3.3 Experts to discuss • whether the monitoring definition proposed for all crops can be confirmed as the most appropriate one considering that reliable conversion factors (monitoring to risk assessment) are difficult to establish • the approach suggested by the RMS not to establish conversion factors but to analyse for the full residue definition for risk assessment in case the MRL is exceeded See reporting table 3(6)	Notifier: We would propose not to include further metabolites in the residue definition for monitoring. Malathion and malaoxon are suitable 'marker' compounds for monitoring and addition of less toxic metabolites such as MMCA and MDCA which may or may not be present would significantly increase monitoring costs. Residues of DMM are expected to be low and therefore inclusion of this metabolite would be of little benefit. Given the difficulties in setting a conversion factor, the approach of analysing for the full residue definition for risk assessment in case the MRL is exceeded is not unreasonable. Data provided in the setting of MRLs will also	RMS: Stands by its original conclusions that the residue definition for monitoring should be: Malathion plus its metabolite malaoxon expressed as malathion (inline with provisional EU residues definition and CODEX definition) for risk assessemnt: Malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion that conversion factors are unreliable	PRAPeR TC 12 (4 June 2009): Open point fulfilled Residue definition for risk assessment: Malathion plus its metabolites malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion Residue definition for monitoring: proposed to include malathion and malaoxon Conversion factor: for the time being proposed as 8 (provisional, to be confirmed by additional residue trials), established on the basis of

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		help to ascertain whether expected levels of metabolites would be of concern before analysis is performed.	(set based on the GAP how ever does not allow for grower using a longer PHI) and the better approach is to analyse for the full residue definition for risk assessment in case the MRL is exceeded. Open point addressed	the sum of malathion and malaoxon
	Open point: 3.4 It should be discussed by experts whether a sufficient number of appropriate and valid residues trials in strawberry are available that analyse for the full residue definition for risk assessment. See reporting table 3(15)	Notifier: Eight new trials are available to set the EU MRL for malathion on strawberry. Sufficient valid trials are available to conclude that there will be no risk when all metabolites are taken into account. The consumer risk is <3% ADI and <6% ARfD indicating a very large margin of safety for consumers. Cheminova are planning further residue trials in 2009 to support the current data set.	RMS: Agrees with comment that the acceptability of only 4 of the 8 trials being analysed for the correct residue definition should be discussed and for the other 4 trials whether an extrapolation of data can be made (residue levels corrected for MMCA and MDCA based on the levels in the trials were the correct residue definition was analysed for). Note: large margin of safety has been established on the consumer risk assessment. Open point open	PRAPeR TC 12 (4 June 2009): Open point fulfilled New data dap proposed see below Applicant to provide 4 additional residue trials on strawberry taking into account the residue definition for risk assessment, longer PHIs and the sample homogenisation and storage period aspects.
	New data gap 3.1 identified at PRAPeR TC 12: Applicant to provide 4 additional residue trials on strawberry taking into account the residue definition for risk assessment, longer PHIs and			PRAPeR TC 12 (4 June 2009): Data gap open

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	the sample homogenisation and storage period aspects			
	Open point: 3.5 RMS to present information on the nature of the residue upon processing in the list of end points using the current harmonised version Information on processing should also be corrected in a corrigendum/ addendum/revised AR as appropriate See reporting table 3(18)	Notifier: Agreed, the simulated conditions at low pH (representative of strawberry processing) are helpful to show that malathion and desmethyl malathion are the major components as shown in the processing studies performed on whole fruit.	RMS: Endpoints updated and AR revised accordingly Open point addressed	PRAPeR TC 12 (4 June 2009): Open point open RMS to use the new template in the LoEP to present available information on the nature of the residue upon processing
	Open point: 3.6 Experts to discuss whether the available data on processing sufficiently address the fate of all compounds that are part of the residue definition for risk assessment. It should be noted that new information cannot be considered for 2nd stage resubmissions under the	Notifier: The residue definition for processing is considered to be complete. All key metabolites have been identified and quantitatively determined in the processing studies performed on strawberry. The response presented in the reporting table is based on information that was already available in previously submitted studies and therefore the use of this information to provide comments on this issue should be acceptable under the accelerated procedure.	RMS: The residues definition is as for plants which covers a wide range of metabolites; Malathion plus its metabolite malaoxon, desmethyl-malathion, malathion monocarboxylic acid and malathion dicarboxcylic acid expressed as malathion Processing studies on the nature of the residues indicated that malathion was partially (50%) degraded to desmethyl	PRAPeR TC 12 (4 June 2009): Open point fulfilled New data dap proposed see below the applicant to address the fate of MMCA and MDCA metabolites under processing conditions; preferably by a radiolabel hydrolysis study

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	accelerated procedure (Commission Regulation (EC) No. 33/2008). See reporting table 3(19)		malathion. For desmethyl-malathion, the amounts in the fruit and processed products are low and indicate that metabolite is reasonably stable. In the case of MMCA and MDCA, MMCA degrades to MDCA and MDCA in turn enters the citric acid cycle (based on the proposed metabolic pathway in plants). Open point addressed	
	New data gap 3.2 identified at PRAPeR TC 12: the applicant to address the fate of MMCA and MDCA metabolites under processing conditions; preferably by a radiolabel hydrolysis study			PRAPeR TC 12 (4 June 2009): Data gap open
	Open point: 3.7 Experts to discuss how to deal with malaoxon in the consumer risk assessment, considering the residue data available, the higher chronic toxicity of malaoxon and the insufficient data on acute toxicity To facilitate the discussion RMS should report the	Notifier: As already indicated by the RMS, only in one of the trials were positive residues of malaoxon detected at 0.01 mg/kg which was insignificant compared to total residues. It is therefore concluded that an additional factor for malaoxon is not necessary in the risk assessment. This approach is in agreement with the previous RMS (Finland) who also did not think residues of malaoxon warranted a separate risk assessment.	RMS: As already stated, only in one of the trials samples contains positive residues of malaoxon of 0.01 mg/kg which is 100 fold lower than the highest total malathion residue of 1.0 mg/kg. With regards to the toxicity of malathion verses malaoxon, the NOAEL in the 2 year rat study for malathion was 30 mg/kg bw and for malaoxon 1 mg/kg bw, thus potentially only 30 times more toxic.	PRAPeR TC 12 (4 June 2009): Open point fulfilled See point 3.3

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	individual residue data for malaoxon in an addendum/ revised AR as appropriate. See reporting table 3(21)	It should also be noted that where residues of malaoxon are <0.01 mg/kg a conservative value of 0.01 mg/kg is used when calculating total malathion equivalent residues. Individual residue data are presented in the resubmission dossier.	Therefore, in the above case, even when allowing for malaoxon being 30 times more toxic (intakes would increase by 23%), the resulting intake is only slightly higher and does not alter the % of the ADI or ARfD accounted for in the NEDI, TMDI, NESTI or IESTI calculations To conclude, for the above reasons the RMS does not consider a separate risk assessment is required for malaxon, however if residue trials indicated higher % residues of malaoxon compared to malathion, then a separate risk assessment may well be required. Open point addressed	
	Open point: 3.8 RMS to assess in an addendum the issue of potential residues in rotated crops as identified necessary (data gap) also for the strawberry use in the previous peer review on malathion. The assessment may consider the case made by the applicant.	Notifier: Agreed, malathion is not a systemic compound and due to the very short half lives of malathion and the major metabolites identified in soil, the risk of uptake of residues from soil by rotated crops is considered to be negligible.	RMS: Agrees with the notifiers comments and their case is presented below; The aerobic metabolism study conducted on malathion showed that malathion rapidly degraded in soil (DT50 = 0.17 – 0.25 days at 20^{o}C, 45% MWHC). Extensive data were generated to demonstrate the rate and route of degradation. Where significant	PRAPeR TC 12 (4 June 2009): Open point open RMS to re-assess the confined rotational study, with particular attention to the residue definition established for risk assessment

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	See reporting table 3(22)		metabolites were formed, these were successfully identified and their formation and decline measured. MMCA and MDCA were formed in soil at >10% AR. Both degradates were of transient character and reached maximum values equal or less than 3.2% AR by Day 29 (MMCA max. 25%, DT_{50} = 0.12 – 0.72 days at 20^{o}C, 45% MWHC, MDCA max. 65%, DT_{50} = 1.2 – 5.3 days at 20^{o}C, 45% MWHC). Total recoveries of radioactivity ranged from 94.4 to 105.3%. Other than MMCA and MDCA there were no other metabolites detected at >10% AR (equivalent to ≥0.2ppm). Desmethyl malathion was not identified as a significant metabolite in soil. According to the EU Guidance document 7524/VI/95 rev.2, 1997 relating to potential residues in rotational crops, studies are not required if, 30 days after application, less than 10% of the of the originally applied active substance remains in the soil, including any bio-available metabolites. Based on these data it is concluded that desmethyl malathion, MMCA and MDCA would not be present in soil nor at persistent levels that would warrant consideration of possible plant uptake into rotational	

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			crops. Furthermore the confined crop rotation study conducted by Wootton, M., Johnson, T. (1993) did not identify desmethyl malathion as a metabolite in soil or crops even though it was used as one of the reference standards for metabolite identification. The results therefore provide further evidence that desmethyl malathion would not be present as a significant metabolite in rotational crops. This conclusion is in line with comments presented by the RMS in the evaluation table who concluded that desmethyl malathion should not trigger further requirements for studies in rotational crops. In addition, strawberries are not normally rotated with other crops. Open point addressed	
	Open point: 3.9 RMS to present the corrected consumer risk assessment in the list of end points using the current harmonised version Risk assessment should be corrected in a corrigendum/ addendum/revised AR as	Notifier: Agreed, the corrected risk assessment figures provided by the RMS in the reporting table confirms that there is a negligible risk to consumers with results showing a large margin of safety (TMDI 2%, IESTI 5%).	RMS: Endpoints updated Open point addressed	PRAPeR TC 12 (4 June 2009): Open point open RMS to reconsider the consumer risk assessment in the light of the results of the current discussions

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	appropriate See reporting table 3(25)			
	New open point 3.10: RMS to amend the list of end points according to the discussions during the PRAPeR TC 12			PRAPeR TC 12 (4 June 2009): Open point open
	Message from section 3 to section 2. MS to confirm a difference in the potency of malaoxon vs malathion.			PRAPeR TC 11 (4 June 2009): Answer from section 2 to section 3: New open point proposed in section 2: RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.

REPORT OF PRAPeR EXPERT MEETING TC 13

MALATHION

Rapporteur Member State: UK

Specific comments on the active substance in the section

5. Ecotoxicology

are already listed in the relevant reporting table. Comments submitted for this meeting are listed below.

1. Comments submitted for this meeting:

Date	Supplier	File Name
none		

2. Documents submitted for meeting:

Date	Supplier	File Name
May 2009	UK	Malathion addendum_B8_May 2009.doc
2009-05-28	UK	Malathion evaluation table rev 1-0 (2009-05-28).doc
May 2009	UK	malathion list of end points May 2009.doc

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. Data on preparations: Malathion 440 g/L EW

5. Classification and labelling: N, R50/53

6. Recommended restrictions/conditions for use: None

7. Reference list:

Areas of concern: insectivorous birds (acute and long-term risk), substantial risk mitigation required for aquatic organisms, risk mitigation for bees, an in-field no spray buffer zone is required as a risk mitigation measure for non-target arthropods

Appendix 1: Discussion table: MALATHION

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Malathion (In)

5. Ecotoxicology

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 5.1 MSs to discuss in an expert meeting the refined acute and long-term risk assessment to insectivorous birds based on measured residues on invertebrate from a field study of Knäbe 2004. See reporting table 5(1)	Risk assessment for insectivorous birds based on a residue trial. Assessment of the RMS was agreed by the experts. The experts suggest a data gap to address the risk further since uncertainties were identified with regard to the residue trial. When multiple applications are considered for residues in insects an appropriate time weighted average residue value should be used, i.e. the averaging time should not be longer than the application interval.	Open point fulfilled New data dap proposed see below: The acute and long-term risk to insectivorous birds needs to be addressed further.
	New data gap 5.1 identified at PRAPeR TC 13: The acute and long-term risk to insectivorous birds needs to be addressed further.		Data gap open
	Open point: 5.2 MSs to discuss in an expert meeting the derivation of acute end point for fish (the acute endpoint was refined	Both options were used in the past. Whether an SSD approach was followed depended on the distribution of the endpoints and the number of endpoints available. The SSD method was preferred by one expert. SSD method was validated by mesocosm data for invertebrates but not for fish. Experts agreed that the proposed endpoint of the RMS should be used in the risk assessment. A novel approach was proposed by one MS (acute to chronic extrapolation and an assessment factor of 5 was included to derive a regulatory	Open point open: RMS to include in the LoEP all acute LC50 and NOEC values for fish.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	according to method 2 of the PPR Opinion (EFSA (2005), Bulletin 301, 1-45); however one MS suggests to use the SSD approach since it is scientifically more sound). See reporting table 5(2)	endpoint of 0.36 mg a.s./L based on an HC5 calculation of the acute NOECs). The PPR approach was followed by the RMS since it maintains the same level of protection. The experts agreed to include the acute LC50 and NOEC values in the LoEP in order to provide the opportunity for MSs to recalculate the regulatory endpoint based on the proposal from the Netherlands: *Only four real LC50-values are available (there seems to be an error in Table B.9.2.1: according to the original DAR, the LC50 for common carp is >10 mg as/L instead of 10 mg as/L. This leaves only four real values). Furthermore, for fish, the HC5 must always be based on LC10/NOEC values, because they are vertebrates and they have a relatively long life cycle.* *The six acute NOECs amount: 0.00501, 0.018, 0.032, 0.091, 0.946 and 1.0 mg as/L. The mean HC5 based on these six NOECs is 1.821 ug as/L.* *Based on the acute and chronic studies with rainbow trout, the ratio between the acute and the chronic NOEC is 0.091/0.021 ≈ 5. This factor can be used to correct for multiple application.* *Using this factor of five, the regulatory endpoint is 1.821/5=0.36 ug as/L.*	
	Open point: 5.3 MSs to agree the risk assessment to frugivorous birds provided in the colomn 3 of the evaluation table. RMS to consequently update the LoE and to provide the agreed risk assessment in an addendum or revised additional report. See reporting table 5(6)	Risk assessment as presented by the RMS was accepted by the experts. The default DT50 of 10 days for residue decline was used in the risk assessment. 90th percentile value in addendum 3 should be used in the acute risk assessment.	Open point open: RMS to recalculate the acute TER for frugivorous birds based on 90th percentile residue values.
	Open point: 5.4		Open point closed

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	RMS to update the LoE with the refined risk assessment to frugivorous birds. This should be considered also in an addendum or revised additional report. See reporting table 5(7)		See open point 5.3.
	Open point: 5.5 MSs to agree the risk assessment to frugivorous mammals. RMS to consequently update the LoE and to provide the agreed risk assessment in an addendum or revised additional report. See reporting table 5(9)	Risk assessment of the RMS was agreed.	Open point fulfilled.
	Open point: 5.6 RMS to update the LoE including all endpoints for fish and mention also the tested species. See reporting table 5(15)		Open point closed See open point 5.2
	Open point: 5.7	Done in the additional report. LoEP needs to be updated accordingly	Open point open:

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	RMS to update the LoE with the actual endpoint from the mesocosm study (5 ug/L) and compare the resulting TER to the chosen trigger (in this case 3-5). This should be also considered in a revised additional report. See reporting table 5(16)		RMS to update the LoEP with regard to the assessment factors/endpoints used in the risk assessment based on the mesocosm.
	Open point: 5.8 RMS to update the aquatic risk assessment in light of revised PECs that only mitigate spray drift by a mximum of 95% in addendum to the additional report and consequently update the list of endpoints ensuring that the TER for a buffer zone of 40 m are deleted. See reporting table 5(17)	This needs to be done.	Open point open: PECsw values (and TERs) need to be updated with maximum 95% mitigation of entry of the a.s. in surface water.
	Open point: 5.9 RMS to amend the LoE including the study duration and the		Open point open: RMS to amend the LoE including the study duration and the sampling dates of the

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	sampling dates of the aged-residue studies for non-target arthropods. See reporting table 5(19)		aged-residue studies for non-target arthropods.
	Open point: 5.10 MSs to discuss in an expert meeting the risk to bees and the appropriate mitigation measures. See reporting table 5(21)	Risk mitigation is proposed at MSs level. Labelling: not to be applied when crop is in flower and/or flowering weeds are present.	Open point fulfilled Risk mitigation is proposed at MSs level. Labelling: not to be applied when crop is in flower and/or flowering weeds are present.
	Open point: 5.11 RMS to amend the LoE with a footnote indicating that the risk assessment for non-target arthropods was addressed only for formulation with a content of isomalathion <0.0017%. See reporting table 5(22)	Needs to be done.	Open point open: RMS to amend the LoE with a footnote indicating that the risk assessment for non-target arthropods was addressed only for formulation with a content of isomalathion <0.0017%.

Appendix 2: Evaluation table

5. Ecotoxicology

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Section 5 Open points: ***11*** Points for clarification: ***0*** Data gaps: ***0***			Section 5 Open points: ***6*** Points for clarification: ***0*** Data gaps: ***1***
	Open point: 5.1 MSs to discuss in an expert meeting the refined acute and long-term risk assessment to insectivorous birds based on measured residues on invertebrate from a field study of Knäbe 2004. See reporting table 5(1)	Notifier: The highest initial measured malathion residue on crop dwelling insects is 9.4 mg/kg (Knäbe, 2004), based on an application rate of 1.8 kg as./ha on apples. Cheminova considers that, taking account of rate reduction, and given a similar level of crop interception, between 0.6 and 0.7 (FOCUS 2001), the residues on insects may be expected to be similar over the two crops. This argument is supported by residue data on crops. The mean initial residue of malathion on strawberries determined in eight residue trials conducted in 2007- 2008 (Brice 2008) at an application rate of 1.5 kg as./ha was 0.78 mg/kg with a 90th percentile value of 1.25 mg/kg. Thus, for strawberries the RUD value is 0.83 (1.25 mg/kg normalised for 1.0 kg	RMS: The Notifier has proposed that the study can be used and in proposing this have compared the residues on strawberries with residues on insects. The RMS is unclear as to the exact relevance of this comparison due to such issues as size of fruits compared to insects, time of application compared to time of collection. Therefore, it unclear how this helps in interpreting and hence using the study by Knäbe. The RMS has however investigated this issue further and examined data in Appendix 14 of EFSA 2008[1]. In this Appendix data are presented on the mean and 90th percentile RUD. Of the three categories for invertebrates one is considered relevant for the foliar dwelling invertebrate orchard situation,	PRAPeR TC 13 (5 June 2009): Open point fulfilled New data dap proposed see below: The acute and long-term risk to insectivorous birds needs to be addressed further.

[1] Scientific Opinion of the Panel on Plant protection products and their residues on a request from the EFSA PRAPeR Unit on risk assessment for birds and mammals. *The EFSA Journal (2008) 734, 1-181*

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
		as./ha). Given the 90th percentile measured concentration in strawberries is 1.25 mg/kg, the use of 9.4 mg/kg for risk assessment in insectivorous birds is considered conservative as it is extremely unlikely that residues in insects would be more than 8 times greater than those in strawberries. Based on the above, refinement of the risk assessment for acute risk to birds results in a TER value of 18, well in excess of the Annex VI trigger. In the reporting table 5(8) the DT50 of 10 is proposed as being potentially too conservative. We would agree with this view with all data suggesting a much shorter DT50 value which would result in an acceptable long term risk to insectivorous birds. Overall we conclude that the risk to insectivorous birds would be acceptable based on the information available.	i.e. insects (foliar dwelling invertebrates). According to the Opinion the mean RUD is 21 mg/kg, this compares to 5.2 from the Knäbe study. In comparing these two figures it is assumed that the output from the Knäbe study is equivalent to the mean value. It should be also be noted that the Opinion does not make any distinction between orchard and arable or ground crops for foliar dwelling invertebrates, thereby implying that the residue levels are likely to be the same regardless of how or where the pesticide is applied, i.e. the RUD of 21 is relevant for assessing the risk to insectivorous birds present in orchards or strawberries. The default mean RUD is greater than the RUD from the Knäbe study. The key question is whether the Knäbe study can be used to refine the residue component for malathion. It is considered that use of the Knabe study to refine the acute risk assessment is still not appropriate for the reasons stated in the Additional Report. As regards its use in the long-term/reproductive risk assessment, it is felt that caution is still required. The key reason for the caution is the point	

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			made in Appendix 14, namely: It should be noted that it has to be fully justified why new measured residue data will override the existing residue values presented in Table 1, as several studies were used to generate these generic RUDs. Therefore, it is unlikely that one study will be appropriate to replace the generic RUD value. In addition, it is not known whether the study by Knäbe has been included in the ECPA dataset and hence used to derive the mean RUD presented in Appendix 14. The Notifier highlights concerns regarding the choice of the DT50 of 10 days; it is appreciated that this is probably worst case for malathion, however the DT50 from orchard study is not considered to be appropriate for the reasons highlighted in the additional report. It is felt that the 'true' DT50 will lie somewhere between the two; however as it is key in refining the risk assessment it is felt that robust justification is required to select an appropriate value. It is proposed that the issue of appropriate RUD and associated DT50	

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			should be discussed in the Expert Meeting.	
	New data gap 5.1 identified at PRAPeR TC 13: The acute and long-term risk to insectivorous birds needs to be addressed further.			PRAPeR TC 13 (5 June 2009): Data gap open
	Open point: 5.2 MSs to discuss in an expert meeting the derivation of acute end point for fish (the acute endpoint was refined according to method 2 of the PPR Opinion (EFSA (2005), Bulletin 301, 1-45); however one MS suggests to use the SSD approach since it is scientifically more sound). See reporting table 5(2)	Notifier: Agreed, although as the RMS indicates, it will not affect the outcome significantly in this case as the two derived values are very similar.	RMS: It is proposed that this should be discussed in the Expert Meeting.	PRAPeR TC 13 (5 June 2009): Open point open: RMS to include in the LoEP all acute LC50 and NOEC values for fish.
	Open point: 5.3 MSs to agree the risk assessment to frugivorous birds provided in the column 3 of the evaluation table. RMS to consequently update the LoE and to provide the agreed risk assessment in an addendum or revised additional report. See reporting table 5(6)	Notifier: Agreed, no further comment necessary	RMS: It is proposed that this point is addressed by the response in the Reporting Table.	PRAPeR TC 13 (5 June 2009): Open point open: RMS to recalculate the acute TER for frugivorous birds based on 90th percentile residue values

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	Open point: 5.4 RMS to update the LoE with the refined risk assessment to frugivorous birds. This should be considered also in an addendum or revised additional report. See reporting table 5(7)	Notifier: Agreed, the refined risk assessment to frugivorous birds shows an acceptable acute and long term risk can be achieved with TERa 39 and TERlt 6.1 (based on default, DT50 10d) or 15 (based on more realistic residue data, DT50 3.3d).	RMS: LoE will be updated after the Expert Meeting.	PRAPeR TC 13 (5 June 2009): Open point closed See open point 5.3.
	Open point: 5.5 MSs to agree the risk assessment to frugivorous mammals. RMS to consequently update the LoE and to provide the agreed risk assessment in an addendum or revised additional report. See reporting table 5(9)	Notifier: The acute and long term risk assessment to frugivorous mammals is considered to be acceptable.	RMS: The risk to frugivorous mammals is provided in the Additional Report. It used a non-standard scenario, i.e. one that was not in SANCO 4145, however it assumed that a 25 g mouse consumed nothing but strawberries; it also assumed standard residue deposition as outlined in EPPO 2002 and the risk was considered to be acceptable. The Notifier has referenced EFSA (2008); the RMS has examined this and there does not appear to be a scenario for a frugivorous mammal in strawberries, there is however a generic focal frugivorous species for bush and cane fruit (see Appendix 3b EFSA (2008)). Using the 90th percentile and mean shortcut values of 19.4 and 9.7, the ETE are 34.9 and 17.5 respectively. If these are compared to the agreed LD50 of 1778 mg/kg bw and the long-term endpoint of 25 mg/kg bw/day, TER of 51 and 1.4 are produced. From this	PRAPeR TC 13 (5 June 2009): Open point fulfilled.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			the acute risk is acceptable (i.e. TER>10), however there is concern regarding the long-term risk (i.e. TER<5). It is proposed that the risk to frugivorous mammals is discussed in the Expert Meeting.	
	Open point: 5.6 RMS to update the LoE including all endpoints for fish and mention also the tested species. See reporting table 5(15)	Notifier: Agreed, no further comment necessary	RMS: LoE will be updated after the Expert Meeting.	PRAPeR TC 13 (5 June 2009): Open point closed See open point 5.2
	Open point: 5.7 RMS to update the LoE with the actual endpoint from the mesocosm study (5 ug/L) and compare the resulting TER to the chosen trigger (in this case 3-5). This should be also considered in a revised additional report. See reporting table 5(16)	Notifier: Agreed, as this is a presentation issue, no further comment is necessary	RMS: LoE will be updated after the Expert Meeting.	PRAPeR TC 13 (5 June 2009): Open point open: RMS to update the LoEP with regard to the assessment factors/endpoints used in the risk assessment based on the mesocosm
	Open point: 5.8 RMS to update the aquatic risk assessment in light of revised PECs that only mitigate spray drift by a maximum of 95% in	Notifier: Agreed, using PECsw values from Step 4 with 95% mitigation shows that acceptable scenarios for aquatic risk assessment can be achieved. Our opinion remains that it is the responsibility of MS to decide which	RMS has produced an Addendum to address this point and the outcome of the revised exposure estimates is that depending upon the number of applications either a 30 or 40 m buffer zone is required.	PRAPeR TC 13 (5 June 2009): Open point open: PECsw values (and TERs) need to be updated with maximum 95% mitigation of entry of the a.s. in surface water.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
	addendum to the additional report and consequently update the list of endpoints ensuring that the TER for a buffer zone of 40 m are deleted. See reporting table 5(17)	mitigation measures are appropriate and practical to achieve the needed reduction in exposure for their particular circumstances.	The assessment indicates that a 30 or 40 m buffer zone is required for a safe use in scenarios D6, R2 and R3 without the need for >95% mitigation. As regards R4 TER are still less than the appropriate trigger value with approximately 95% mitigation. It is proposed that this is discussed in the Expert Meeting.	
	Open point: 5.9 RMS to amend the LoE including the study duration and the sampling dates of the aged-residue studies for non-target arthropods. See reporting table 5(19)	Notifier: Agreed, no further comment necessary	RMS: LoE will be updated after the Expert Meeting.	PRAPeR TC 13 (5 June 2009): Open point open: RMS to amend the LoE including the study duration and the sampling dates of the aged-residue studies for non-target arthropods
	Open point: 5.10 MSs to discuss in an expert meeting the risk to bees and the appropriate mitigation measures. See reporting table 5(21)	Notifier: Agreed, appropriate risk mitigation measures to reduce risk can be set at MS level.	RMS: The risk to honeybees from the proposed use on strawberries is considered to be acceptable providing that risk mitigation is implemented at MS level.	PRAPeR TC 13 (5 June 2009): Open point fulfilled Risk mitigation is proposed at MSs level. Labelling: not to be applied when crop is in flower and/or flowering weeds are present.
	Open point: 5.11 RMS to amend the LoE with a footnote indicating that the risk assessment for non-target arthropods was addressed only for formulation with a	Notifier: Agreed, no further comment necessary	RMS: LoE will be updated after the Expert Meeting.	PRAPeR TC 13 (5 June 2009): Open point open: RMS to amend the LoE with a footnote indicating that the risk assessment for non-target arthropods was addressed only for formulation with a content of isomalathion

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	content of isomalathion <0.0017%. See reporting table 5(22)			<0.0017%.