PEER REVIEW REPORT ON **MALATHION** 15 07 2009

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0. General

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 0 Open points: ***1*** Points for clarification: ***0*** Data gaps: ***0***			Section 0 Open points: ***0*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 0.1 RMS to amend the end points using the current harmonised version (include UK as RMS, amend residue definitions) See reporting table 0(1)	Notifier: Agreed, the LOE should be updated based on the conclusions of the additional report.	RMS: Full amended end points will be provided after the expert telecon. RMS 17.06.09: end points have been updated	Written procedure: List of endpoints has been updated Open point fulfilled

1. Identity, Physical and chemical properties, Details of uses and further information, Methods of analysis

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 1 Open points: ***3*** Points for clarification: ***0*** Data gaps: ***0***			Section 1 Open points: ***0*** Points for clarification: ***0*** Data gaps: ***1***
	Open point: 1.1 RMS to update the List of end points with the correct structural formula for malathion. See reporting table 1(1)	Notifier: Agreed. The correct structure has been provided	RMS: List of endpoints has been updated Open point fulfilled	Written procedure: List of endpoints has been updated Open point fulfilled
	Open point: 1.2 RMS to delete the sentence “Method for desmethyl malathion could be necessary” from the LoEP See reporting table 1(1)	Notifier: Agreed, the residue definition for monitoring does not need to include desmethyl malathion since it is less toxic than malathion.	RMS: List of endpoints has been updated Open point fulfilled	Written procedure: List of endpoints has been updated Open point fulfilled
	Open point: 1.3 RMS to amend end points to that methods are not required for the uses evaluated during the re-submission (strawberries and ornamentals) See reporting table 1(2)	Notifier: Agreed, residue methods for food of animal origin are not required for the representative uses; strawberries and ornamentals.	RMS: List of endpoints has been updated Open point fulfilled	Written procedure: List of endpoints has been updated Open point fulfilled
	Message from section 3 to			Written procedure:

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 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			New data gap: 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

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: ***1*** 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. RMS 17.06.09 End points have been updated	PRAPeR TC 11 (4 June 2009): Open point open: RMS to revise the list of end points Written procedure: Open point fulfilled
	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 comparison of total	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
		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 also reference the discussion in	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)	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	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
			is the view of the RMS that the increased 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		RMS 17.06.09: Information presented in Addendum 2 to the Additional Report	PRAPeR TC 11 (4 June 2009): Open point open Written procedure: 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 additional report) and considering one application			
	Open point: 2.8 MSs to address the need of amateur exposure See reporting table 2(15)	Notifier: This is not necessary because amateur use is not supported as a representative use for Annex I listing.	RMS : Agree. Amateur use has not been considered as it is not a representative use for Annex I listing.	PRAPeR TC 11 (4 June 2009): 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)	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		RMS 17.06.09 an assessment is provided in the Addendum 2 to the Additional Report	PRAPeR TC 11 (4 June 2009): Open point open

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	and malathion based on the overall database.			Written procedure: The RMS revised the different potency of malathion and malaoxon according to the avaialbel studies. The assessment was not peer reviewed. Open point still open

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: ***0*** Points for clarification: ***0*** Data gaps: ***4***
	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 samples apparently has on the residue levels (upon comparative analysis of homogenised and	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 storage has also been adequately demonstrated. Therefore, the residue data generated in the strawberry residue trials are considered to	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 whole fruit samples has to be part of the analytical method for monitoring in order to avoid any degradation of malathion.

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
	intact samples in the fruit metabolism study a significant decrease of compounds in the residue definition was observed). See reporting table 3(4)	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.		
	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 help to ascertain whether expected levels of metabolites would be of concern before analysis is performed.	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 (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.	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 the sum of malathion and malaoxon

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 addressed	
	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 the sample homogenisation and storage period aspects			PRAPeR TC 12 (4 June 2009): Data gap open Written procedure: Data gap open
	Open point: 3.5 RMS to present information on the nature of the residue upon processing in the list of	Notifier: Agreed, the simulated conditions at low pH (representative of strawberry processing) are helpful to show that malathion and desmethyl	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

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
	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)	malathion are the major components as shown in the processing studies performed on whole fruit.	RMS 17.06.09 end points revised	to present available information on the nature of the residue upon processing Written procedure: Open point fulfilled
	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 accelerated procedure (Commission Regulation (EC) No. 33/2008). See reporting table 3(19)	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 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	PRAPeR TC 12 (4 June 2009): Open point fulfilled New data gap 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
			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 Written procedure 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 individual residue data for malaoxon in an addendum/ revised AR as appropriate. See reporting table 3(21)	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. 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.	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. 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	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
			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. See reporting table 3(22)	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 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	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 Written procedure: Re-assessment in addendum 2 not peer reviewed. Thus, EFSA propose to maintain the data gap identified during the first peer review for the applicant to further address residues in succeeding crops. 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
			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 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	

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
			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 RMS 17.06.09 See Addendum 2 to the Additional Report for response	
	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 See reporting table 3(25)	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 RMS 17.06.09 See Addendum 2 to the Additional Report for response	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 Written procedure: Open point fulfilled
	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 Written procedure: Open point fulfilled
	Message from section 3 to section 2.			PRAPeR TC 11 (4 June 2009): Answer from section 2 to section 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
	MS to confirm a difference in the potency of malaoxon vs malathion.			New open point proposed in section 2: RMS to revise the difference in the potency of malaoxon and malathion based on the overall database.

4. Environmental fate and behaviour

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 4 Open points: ***5*** Points for clarification: ***0*** Data gaps: ***0***			Section 4 Open points: ***0*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 4.1 RMS to simulate and present FOCUS step 4 PECsw and sed for malathion which implements a 30m no spray buffer zone (equates to ca. 95% spray drift reduction) for simulations with 4 applications in an addendum to the additional report clearly reporting the model parameterisation used and also add this information to the LoEP. Step 4 values for a 40m no spray zone to be deleted from the LoEP. Consideration to be made of the comments of the applicant in column 3 of the reporting table when completing any new simulations. See reporting table 4(4)	Notifier: Our opinion remains that it is the responsibility of MS to decide which mitigation measures are appropriate and practical to achieve the needed reduction in exposure for their particular circumstances. For the scenarios identified the submitted PECsw values at Step 4 with 95% risk mitigation show that an acceptable risk assessment can be achieved.	RMS: In the addendum to the additional report it has been demonstrated that either a 30 m buffer zone (D6 ditch) or a 40 m buffer zone (R1, R2, and R3 stream) mitigate spray drift by less than 95%. New PECs have therefore been calculated with FOCUS STEP 4 for those scenarios/buffer zones, with an interval between applications of 10 days to properly reflect the proposed GAP. Open point addressed. RMS 17.06.09 End points now	EFSA consideration of the RMS addendum to B8 of the additional report dated May 2009. Open point fulfilled The new PECsw (FOCUS step 4) presented in the addendum and included in the updated LoEP dated May 2009 are appropriate and in line with the pertinent guidance (note in this (May) version of the endpoints the ecotox aquatic TER tables had not been updated but this was subsequently done in the June version)

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
			updated	
	Open point: 4.2 RMS to estimate and make a proposal for what the maximum number of treatments to ornamentals would be, that would ensure that the potential groundwater exposure would be within the available groundwater simulations in the original DAR and EFSA conclusion addenda in an addendum to the additional report. See reporting table 4(5)	Notifier: Agreed, no further comment necessary.	RMS: In the addendum to the additional report a comparison of the proposed rate of application to ornamentals has been made with the GAP modelled (6 x 2.16 kg a.s/ha to strawberries) in the original EU Review of malathion. It was calculated that even if a worst case of no interception was assumed, 45 applications could be made to ornamentals without exceeding the maximum total dose in the groundwater modelling. It is therefore proposed that it is not necessary to stipulate a maximum number of applications due to the large margins of safety demonstrated by the groundwater modelling to strawberries. Open point addressed.	EFSA consideration of the RMS addendum to B8 of the additional report dated May 2009. Open point fulfilled The calculations in the addendum indicate that the available groundwater exposure assessment would cover the requested use on ornamentals when up to 45 applications per year are made.
	Open point: 4.3 RMS to add to the LoEP the time of application for Step 1-2 for PECsw and PECsed for malathion. The information was already included for the metabolites. See reporting table 4(8)	Notifier: Agreed, no further comment necessary	LoEP updated. Open point addressed.	EFSA consideration June 2009 Open point fulfilled The LoEP was appropriately updated by the RMS in the vesion dated May 2009.
	Open point: 4.4 RMS to update the heading	Notifier: Agreed, no further comment necessary	LoEp updated.	EFSA consideration June 2009 Open point fulfilled

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	of the final column of the LoEP table for FOCUS modelling PECgw results to be headed 'Site specific Kfoc (ml/g)' See reporting table 4(9)		Open point addressed.	The LoEP was appropriately updated by the RMS in the vesion dated May 2009.
	Open point: 4.5 RMS to update the list of end points to include MMCA in the residues definition for groundwater that requires exposure assessment. See reporting table 4(10)	Notifier: MMCA should be included in the exposure assessment although the potential for groundwater contamination of MMCA above 0.1 µg/L is low (all scenarios <0.001 µg/L.	LoEP updated. Open point addressed.	EFSA consideration June 2009 Open point fulfilled The LoEP was appropriately updated by the RMS in the vesion dated May 2009.

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: ***0*** 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 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	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, i.e. insects (foliar dwelling invertebrates).	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
		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.	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	

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			key reason for the caution is the point 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.	

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
			It is proposed that the issue of appropriate RUD and associated DT50 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 Written procedure: Data gap still 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. RMS 17.06.09 end points have been updated	PRAPeR TC 13 (5 June 2009): Open point open: RMS to include in the LoEP all acute LC50 and NOEC values for fish. Written procedure: Open point fulfilled
	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	Notifier: Agreed, no further comment necessary	RMS: It is proposed that this point is addressed by the response in the Reporting Table. RMS 17.06.09 end points have been updated	PRAPeR TC 13 (5 June 2009): Open point open: RMS to recalculate the acute TER for frugivorous birds based on 90th percentile residue values Written procedure: 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
	additional report. See reporting table 5(6)			
	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	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
			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 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. RMS 17.06.09 end points have been updated	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 Written procedure: Open point fulfilled
	Open point: 5.8	Notifier: Agreed, using PECsw values	RMS has produced an Addendum to	PRAPeR TC 13 (5 June 2009):

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
	RMS to update the aquatic risk assessment in light of revised PECs that only mitigate spray drift by a maximum 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)	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 mitigation measures are appropriate and practical to achieve the needed reduction in exposure for their particular circumstances.	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. 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. RMS 17.06.09 end points have been updated	Open point open: PECsw values (and TERs) need to be updated with maximum 95% mitigation of entry of the a.s. in surface water. Written procedure: Open point fulfilled
	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. RMS 17.06.09 end points have been updated	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 Written procedure: Open point fulfilled
	Open point: 5.10 MSs to discuss in an expert	Notifier: Agreed, appropriate risk mitigation measures to reduce risk can	RMS: The risk to honeybees from the proposed use on strawberries is considered to be acceptable providing	PRAPeR TC 13 (5 June 2009): Open point fulfilled

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	meeting the risk to bees and the appropriate mitigation measures. See reporting table 5(21)	be set at MS level.	that risk mitigation is implemented at MS level.	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)	Notifier: Agreed, no further comment necessary	RMS: LoE will be updated after the Expert Meeting. RMS 17.06.09 end points have been updated	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 <0.0017%. Written procedure: Open point fulfilled