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14 09 2009	PRAPeR Tele Conference 22	Ecotoxicology

REPORT OF PRAPeR EXPERT MEETING TC 21

CARBOSULFAN

Rapporteur Member State: BE

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
August 2009	BE	Carbosulfan Addendum_VOL3_B7 (August 2009).doc
2009-08-28	BE	Carbosulfan evaluation table rev 1-0 (2009-08-28).doc
August 2009	BE	Carbosulfan list of end points (August 2009).doc
2009-07-31	BE	Carbosulfan reporting table rev 1-1 (2009-07-31)

3. Documents tabled at the meeting:

Date	Supplier	File Name
none		

The conclusions of the meeting were as follows:

4. **Data on preparations:** Marshal 10G

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

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

7. **Reference List:** Not discussed.

Areas of concern: The intake assessment conducted in the additional report indicates a risk for the consumer. The experts' decision to include also the 3-keto-carbofuran free and conjugated in the residue definition for risk assessment is likely to exacerbate the situation.
With the data available, no refinement of the consumer intake / risk assessment is currently possible and thus further data and consideration is necessary on the residue levels of carbamate compounds in rotational crops and in refined sugar.

Appendix 1: Discussion table: CARBOSULFAN

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Carbosulfan (in)

3. Residues

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 0.1 The new template for the list of end points should be used. See reporting table 0(1)	It was confirmed that the new template should be used for the list of endpoints. Moreover, the list of endpoints should be updated in accordance with the decisions of the meeting.	Open point still open. Moreover, the list of endpoints should be updated in accordance with the decisions of the meeting.
	Open point: 3.1 RMS to check the raw data in the goat metabolism study in terms of the respective ratio between free and conjugated Carbofuran and 3-OH-carbofuran See reporting table 3(3)	Based on the goat metabolism study in the revised DAR (Curry S.J., Weintraub R.A., 1996) it is not possible to derive the proportion of conjugated and non-conjugated 3-OH-carbofuran, since metabolites identification was performed on the organosoluble fractions only. The radioactivity in the non organosoluble fractions were characterized as polar metabolites without any further metabolites investigation. If we assumed that the entire aqueous soluble phase were composed of conjugates it could effectively be possible to calculate a ratio. In the metabolism study in lactating goats (Hoffman and Robinson, 1994) from the JMPR 1997 report and presented in the addendum of August 2009 in some matrices, conjugates of 3-OH-carbofuran accounted for more than 50% and 70% in liver and kidney (i.e. at a significant proportion) of the total 3-OH-carbofuran residues recovered in these matrices. There are different types of conjugates (proteins/sulphates conjugates) recovered in animal matrices, and it is known that these different conjugates can be released in different proportion depending on the extraction procedure used (enzyme vs. acid hydrolysis or in combination). The efficiency may be different depending on the type of conjugates. In conclusion, the available studies make it difficult to derive a reliable ratio between free and conjugated 3-OH carbofuran. Moreover, this ratio is expected to differ between matrices (milk, liver etc.). It is however evident from the data that conjugated 3-OH carbofuran occurs in toxicologically significant amounts in animal matrices, even if the residues are calculated	Open point fulfilled. Based on the available data a reliable factor to describe the ratio between free and conjugated 3-OH-carbofuran cannot be established. It is therefore recommended to maintain the proposal for inclusion of conjugated 3-OH-carbofuran also in the residue definition for monitoring.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		to be very low (at non-detectable levels between 0.00005 and 0.003 mg/kg) considering the livestock dietary burden from the representative use in sugar beet. Consequently, the residue definition for animal matrices should be maintained as agreed for carbofuran: RA: 3-OH-carbofuran free and conjugates expressed as carbofuran Monitoring: preferably the same as above However, the efficacy of the analytical method to release the conjugates needs to be addressed.	
	Data gap: 3.1 The available method of analysis for monitoring to determine the residues of 3-OH-carbofuran and its conjugates in animal matrices includes a hydrolysis step. The efficiency of this step to release the 3-OH-carbofuran conjugates should be addressed. See reporting table 3(3)	The only way to address this point is to compare the extraction efficiency using the samples from the metabolism studies performed with the radio-labelled active substance. But for the time being there are no guidelines on how to tackle this issue. In addition, some types of conjugates existing in animal matrices (sulphate and protein conjugates) may not be totally released using acid hydrolysis. However, this point should be referred to the section on Phys-Chem. properties.	Data gap open. Requirement is referred to section 1 on Phys-Chem. properties.
	Open point: 3.2 Experts to discuss whether it would be necessary to consider the following issue for the consumer risk assessment of carbosulfan: DBA is certainly less toxic than	The recovered levels of DBA are very low (TRR 0.02 mg/kg in sugar beet leaves and roots after soil application at 1 kg a.s./ha). DBA was formed in large amounts in the rat and its toxicity is covered by the tox studies, but the concern is the potential for NDBA to be formed depending on the acidic and temperature conditions under processing (or under particular environmental conditions). The meeting considered to what extent the consumer could be exposed to NDBA. Due to the processing conditions (alkaline) during sugar refining it was considered unlikely	Open point fulfilled. Due to the processing conditions during sugar refining it was considered unlikely that NDBA will be present in refined sugar. New open point proposed, see

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	carbosulfan itself, but it may be a precursor of NDBA in acidic conditions and/or at higher temperature, conditions as present under crop processing. See reporting table 3(5)	that NDBA will be present in refined sugar. However, due to the microbiological activity in the soil it is necessary to check if NDBA is not formed in the environment and present in the ground water. RMS has to check if this point has been considered by the tox and fate section for the potential leaching of NDBA in the ground water.	below. RMS to check if the issue on NDBA has been considered by the tox and fate section (for the potential leaching of NDBA in the ground water).
	New open point: 3.7 RMS to check if the issue on NDBA has been considered by the tox and fate section (for the potential leaching of NDBA in the ground water).		Open point open.
	Open point: 3.3 For a toxicologically relevant compound consumer exposure (amounts occurring) should be considered to conclude whether it is relevant for consumer risk assessment. The issue to be discussed by experts. It was agreed in the first peer review on carbofuran that all metabolites with	In the previous meetings, based on a statement by the RMS, 3-keto carbofuran was assumed to be less toxic than carbofuran and 3-OH carbofuran, but this information was not confirmed by the toxicologists (it had been previously agreed that in analogy with 3-OH-carbofuran, the reference values of carbofuran should apply to 3-keto-carbofuran). We have now to reconsider the residue definition for RA in the light of 3-keto carbofuran being as toxic as 3-OH carbofuran and that the reference values for carbofuran should apply to both metabolites. 3-keto carbofuran was recovered in low levels in leaves (0,0045 mg/kg) and roots (0.0014 mg/kg) and in livestock matrices. The contribution to the total tox burden of this compound in comparison to carbofuran and the 3-OH-carbofuran already included in the residue definition is limited (increase by approx. 10% and 25% for sugar beet leaf and root residues). However, the exceedance of the tox reference value calculated for the sugar beet (425% ARfD) is significant. Although the 3-keto amounts in sugar beet are very low, due to its toxicity (classified with T, R25; lower tox reference values than for parent carbosulfan), its contribution might yet be significant, especially in the acute risk assessment.	Open point fulfilled. The meeting agreed to include 3-keto carbofuran in the residue definition for risk assessment.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	carbamate moiety (including the 3-keto) are toxicologically relevant. The 3-keto-carbofuran is classified with T, R25. Tox data for the metabolite are very limited, however it is very likely that the reference values of carbofuran will cover the toxicity of the metabolite. See reporting table 3(6)	Eventually, the meeting agreed to include 3-ketocarbofuran in the residue definition for risk assessment. It was noted that a respective revision of the residue definition will be necessary also for the uses of benfuracarb and carbofuran. Residue definition for risk assessment: 1) Carbosulfan 2) Carbofuran, 3-OH carbofuran and 3-keto-carbofuran, including their conjugates expressed as carbofuran	
	Data gap: 3.2 The efficiency of the hydrolysis step in the analytical method (plant matrices-supervised residue trials and monitoring) to release all the conjugates of carbofuran and 3-OH-carbofuran must be demonstrated. See reporting table 3(9)	In case it will not be possible to establish a conversion factor to take into account for residues of 3-keto carbofuran (see open point 3.6 below) the residue definition for monitoring will have to be reconsidered for inclusion of 3-keto carbofuran and conjugates. In this case the data gap should be amended to demonstrate also the efficiency of the hydrolysis step in the analytical method (plant matrices) to release all the conjugates of 3-keto carbofuran.	Data gap open. See data gap 3(1)
	Open point: 3.4 RMS to check analytical reports of the field trials 'Trial F006	These two trials were performed in the 1980ies and the information in the raw dossier is very limited. The new trials using HPLC-MS/MS show that carbosulfan is never detected in sugar beet at harvest, which is in line with the observations in metabolism studies on plants after soil application.	Open point fulfilled. The meeting agreed not to take into account these two trials in the

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	7903/2' and 'Trial F006 7907' (carbosulfan in roots) for validity / acceptability. See reporting table 3(11)	The meeting agreed not to take into account these two trials in the assessment (i.e. trials not acceptable).	assessment (i.e. trials not acceptable).
	Data gap: 3.3 Data to address residues in rotational crops, in particular further metabolite identification in the edible parts of the rotational crops is required. See reporting table 3(15)	See also discussion on carbofuran in PRAPeR 70 meeting of experts. The residue situation considered for rotational crops by PRAPeR 70 is also supported by rotational crop studies reported by the JMPR. Further clarification on the actual amount of relevant residues for RA (carbamate metabolites carbofuran, 3-OH-carbofuran and 3-keto-carbofuran and their conjugates) in succeeding crops is required. For the time being the TRRs recovered in succeeding crops were used in the chronic and acute consumer RA. See also discussion in open point 3.5 below.	Data gap open.
	Open point: 3.5 Experts may consider whether the approach as suggested by the applicant is justified to consider 10% TRR in rotational crops in the consumer risk assessment See reporting table 3(15)	The case made by the applicant that the residues of carbamate compounds are below 10% TRR cannot be supported. Cereals in rotation with sugar beet were found to be of low concern. A high concern was identified for leafy and root crops (exceedance of ARfD). Metabolism of carbosulfan was investigated in different plants, but the identification of the relevant metabolites was not performed in all studies. For root crops, a sufficient identification was only in potato tuber at harvest in the carbofuran dossier, but this information cannot be used in the carbosulfan evaluation (due to current legislation). In the carbosulfan dossier only information on soybean plant is available. In immature soybean plants 50% TRR at 30 days and 20% TRR at 60 days were identified as relevant carbamate compounds. These figures cannot support the 10% proposed by the applicant for leafy crops.	Open point fulfilled. The default 10% TRR for carbamate compounds in leafy, root and oilseed crops is not supported by the available studies.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		In conclusion, the available studies are not sufficient to support the 10% TRR value proposed by the applicant.	
	Open point: 3.6 Combined risk assessment should be conducted considering the same mode of action (cholinesterase inhibition) but the different tox potency of carbofuran (plus 3-OH carbofuran) and carbosulfan. See reporting table 3(18)	Carbosulfan is rapidly hydrolysed to carbofuran and its metabolites (3-OH and 3-keto) and a combined risk assessment has to be conducted. RMS will compile an overview table with the levels of the individual carbamate metabolites to be considered in the risk assessment. It should be checked whether sufficient data are available on 3-keto carbofuran to be used in the consumer RA.	Open point fulfilled. New open point proposed, see below.
	New open point: 3.8 raised by experts during PRAPeR TC 21 meeting: RMS to compile an overview table with the levels of the individual carbamate metabolites to be considered in the risk assessment. It should be checked whether sufficient data are available on 3-keto carbofuran to be used in the consumer RA.		Open point open.
	New open point: 3.9 raised by experts	Due to the LOQ of 0.01 mg/kg used in the studies, it is not possible to conclude on a no-residue situation for sugar beet roots for such a highly toxic compound. The LOQ needs to	Open point fulfilled.

No.	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	during PRAPeR TC 21 meeting: The presumed residue level of carbamate residues of “zero” (PRAPeR 70) in refined sugar has to be reconsidered. Is for sugar the use of a “zero” value for the risk assessment really justifed?	be lowered. The available processing study shows that significant residues of 3-keto-7-phenol were observed in molasse and sugar (0.02 to 0.03 mg/kg, indication for concentration) and it cannot be excluded that also residues of carbamate metabolites are present in sugar (<current LOQ). The “zero“ value used in the consumer risk assessment is thus questionable and the applicant has to address the residue level of carbamate metabolites in refined sugar in order to conduct a refined acute dietary risk assessment. Otherwise, it is not possible to conclude the actual consumer exposure to residues from the use of carbosulfan in sugar beets. Data to get a clear picture on the residue levels of the carbamates metabolites in sugar are required.	New data gap proposed, see below. Applicant to address the residue levels of the carbamate metabolites in sugar.
	New data gap: 3.4 identified at PRAPeR TC 21 meeting: Applicant to address the residue levels of the carbamate metabolites in sugar.		Data gap 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: ***6*** Points for clarification: ***0*** Data gaps: ***3***			Section 3 Open points: ***3*** Points for clarification: ***0*** Data gaps: ***4***
	Open point: 0.1 The new template for the list of end points should be used. See reporting table 0(1)			PRAPeR TC 21 (14 September 2009): Open point still open. Moreover, the list of endpoints should be updated in accordance with the decisions of the PRAPeR TC 21 meeting.
	Open point: 3.1 RMS to check the raw data in the goat metabolism study in terms of the respective ratio between free and conjugated Carbofuran and 3-OH-carbofuran See reporting table 3(3)	**NOT:** see comment data gap 3.1	**RMS 08.09:** In the goat metabolism study (Curry S.J. and Weintraub R.A., 1996), the extraction procedure showed that acid hydrolysis step was applied on the aqueous soluble phases. Enzymatic digestion and acid hydrolysis were also performed on the non extractable radioactive residues in order to release additional radioactivity. Muscle and fat were not further analysed for metabolites identification due to the very low levels of recovered	PRAPeR TC 21 (14 September 2009): Open point fulfilled. Based on the available data a reliable factor to describe the ratio between free and conjugated 3-OH-carbofuran cannot be established. It is therefore recommended to maintain the proposal for inclusion of conjugated 3-OH-carbofuran also in the residue definition for monitoring.

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
			residues (0.006 and 0.0105 mg/kg, respectively). Phenyl label treated milk, liver and kidney were analysed for metabolites identification. Both in the 3 matrices, Carbosulfan and Carbofuran were not detected or detected at a trace level (0.1-0.2 % of TRR). Based on the reported goat metabolism study in the revised DAR and the detailed extraction procedure outlined in the addendum to the DAR-August 2009, if it is assumed that in liver and kidney, the polar metabolites recovered in the non organo soluble phase are conjugates, a ratio between free and conjugated 3-OH-carbofuran can be approximately derived. A clear picture is given based on the available goat metabolism study ((Hoffman and Robinson, 1994a) reported in the JMPR 1997 report-see Addendum to the DAR-August 2009. Indeed, in this study, Carbofuran was detected at a trace level in milk only. 3-OH-carbofuran was recovered at a level around 10 % of TRR in milk and kidney and at a level of 4% TRR in liver. The information was given that in milk,	

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
			10 % of the TRR occurred as free 3-OH-carbofuran only. In liver, the 4 % of the total residues included 2.2% conjugated 3-OH-carbofuran, released by protease treatment. While in kidney, 11 % of the total residues included 8.2% conjugated 3-OH-carbofuran, released by protease treatment. There is no indication whether the aqueous fractions resulting from the mild/strong acid hydrolysis were further characterized.	
	Data gap: 3.1 The available method of analysis for monitoring to determine the residues of 3-OH-carbofuran and its conjugates in animal matrices includes a hydrolysis step. The efficiency of this step to release the 3-OH-carbofuran conjugates should be addressed. See reporting table 3(3)	**NOT:** In Curry and Weintraub, 1996, acid hydrolysis extraction was used as the last step to realese bound residue that could not be released by other means. The results indicate that less than 13% of the TRR remained unextracted. This indicates this high efficientcy of the acid hydrolysis to release conjugated residue.	**RMS 08.09:** RMS agrees that the efficiency of the hydrolysis step to release the 3-OH-carbofuran conjugates should be addressed. It is the RMS understanding that the extraction procedures used in the livestock metabolism studies should be compared to the extraction step in the analytical method for monitoring to determine the residues of 3-OH-carbofuran and its conjugates in animal matrices (see Vol 3 B(5)-&B.5.2.2) in order to determine the efficiency of the acid hydrolysis step.	PRAPeR TC 21 (14 September 2009): Data gap open. Requirement is referred to section 1 on Phys-Chem. properties.

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
			Based on the available goat metabolism study reported in the revised DAR, April 2009, -Milk/liver: Enzymatic hydrolysis with β-glucuronidase. No acid hydrolysis step. -Liver NER/kidney/kidney NER: Enzymatic digestion (pronase-E) and acid hydrolysis steps are combined. RMS proposes to discuss a general approach to define the efficiency of the hydrolysis step of an analytical method both in plants and animal matrices since a spiking with conjugated 3-OH-carbofuran standards to determine the recoveries is not possible and considering also that there are different types of conjugates (proteins/sulphates conjugates) recovered in animal matrices that might be quite resistant to acid hydrolysis.	
	Open point: 3.2 Experts to discuss whether it would be necessary to consider the following issue for the consumer risk assessment of carbosulfan: DBA is certainly less toxic than carbosulfan itself, but it may be a precursor of NDBA in acidic conditions and/or at	**NOT:** the crop metabolism study reveals that no DBA must be expected in the sugar beet roots	**RMS 08.09:** For the consumers, no major risk of Dibutylnitrosamine intake is expected from food ingestion. From the metabolism study in sugar beet (Robinson R.A., 1982), where the metabolic profile of the ^{14}C-Dibutylamine moiety was investigated (worst-case foliar application 1 kg a.s./ha, greenhouse conditions), it	PRAPeR TC 21 (14 September 2009): Open point fulfilled. Due to the processing conditions during sugar refining it was considered unlikely that NDBA will be present in refined sugar. New open point proposed, see below.

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
	higher temperature, conditions as present under crop processing. See reporting table 3(5)		appeared that no relevant residue level (0.014 mg/kg) was observed in the 30 - day sugar beet root sample. After soil incorporation at similar dose (1.1 kg a.s./ha), the total radioactive residues at harvest (130 days) accounted for 0.02 ppm in both sugar beet leaves and roots, indicating a very low potential exposure of the consumers to DBA residues when consuming sugar beet roots (mainly sugar after crystallization process). Drinking water is not expected to contain Dibutylnitrosamine after Carbosulfan application by soil incorporation since Dibutylamine has no leaching potential into the groundwater. RMS considers that no risk is expected for the consumers to both DBA and DBNA when carbosulfan is applied to the soil.	
	New open point: 3.7 RMS to check if the issue on NDBA has been considered by the tox and fate section (for the potential leaching of NDBA in the ground water).			PRAPeR TC 21 (14 September 2009): Open point open.
	Open point: 3.3 For a toxicologically relevant	**NOT:** the metabolism studies show that the formation of 3-keto-carbofuran	**RMS 08.09:** The available plant and animal	PRAPeR TC 21 (14 September 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
	compound consumer exposure (amounts occurring) should be considered to conclude whether it is relevant for consumer risk assessment. The issue to be discussed by experts. It was agreed in the first peer review on carbofuran that all metabolites with carbamate moiety (including the 3-keto) are toxicologically relevant. The 3-keto-carbofuran is classified with T, R25. Tox data for the metabolite are very limited, however it is very likely that the reference values of carbofuran will cover the toxicity of the metabolite. See reporting table 3(6)	in plants remains one order of manitude lower than carbofuran + 3-OH carbofuran. Furthermore, the residue d-base shows that no residue of carbofuran nor 3-OH carbofuran can be quantified at 0.005 mg/kg. Therefore, adding 3-keto-carbofuran to the residue definition would not add any valuable information. Carbosuran and 3-OH-carbofuran are effective tracers that demonstrate the absence of residue at harvest.	metabolism studies reported in the revised DAR, April 2009 showed that the metabolite 3-keto-carbofuran is not a relevant metabolite of the total residues occurring in the edible parts of the crops or in animal matrices after Carbosulfan soil application. -Sugar beet crop metabolism: 3-keto-carbofuran was recovered at a level of 0.0045 mg/kg in leaf (30 days after application) and at 0.0014 mg/kg in root (60 days after application). -Livestock matrices: 3-keto-carbofuran was recovered at a trace level considering the calculated dietary burden. RMS considers that including this metabolite in the residue definition for risk assessment won't contribute significantly to the toxicological burden.	Open point fulfilled. The meeting agreed to include 3-keto carbofuran in the residue definition for risk assessment. Residue definition for risk assessment: 1) Carbosulfan 2) Carbofuran, 3-OH carbofuran and 3-keto-carbofuran, including their conjugates expressed as carbofuran
	Data gap: 3.2 The efficiency of the hydrolysis step in the analytical method (plant matrices- supervised residue trials and monitoring) to	**NOT:** The acid hydrolysis step was used in all crop metabolism studies in order to realease residue that could not be fully extracted by solvent means. The results show that on the crop samples where parent and early	**RMS 08.09:** See data gap 3.1. RMS has some reserve regarding the determination of the efficiency of the hydrolysis step based on the available plant matrices from the metabolism	PRAPeR TC 21 (14 September 2009): Data gap open. See also data gap 3(1).

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
	release all the conjugates of carbofuran and 3-OH-carbofuran must be demonstrated See reporting table 3(9)	metabolites are expected, the % of TRR extracted is very high and concur with significant findings of carbofuran and 3-OH-carbofuran. This would not be the case if the acid hydrolysis step was unable to eficiently release the conjugated carbofuran and 3-OH-carbofuran.	studies. Can we assume that all the residues present in the plant samples at harvest will be under their conjugated form when Carbosulfan is applied at pre-planting ? The available data in the Benfuracarb/Carbofuran dossier showed that this was not the case. In the 1997 JMPR evaluation (reported in the Benfuracarb updated addendum to the DAR -January 2009) based on metabolism studies performed on corn, potato and soya plants using soil application, it was shown that carbofuran, 3-keto carbofuran, 3-OH carbofuran and the phenol metabolites and their conjugated forms were present at non negligible levels at longer sampling intervals and at harvest. This point should be discussed further.	
	Open point: 3.4 RMS to check analytical reports of the field trials 'Trial F006 7903/2' and 'Trial F006 7907' (carbosulfan in roots) for validity / acceptability. See reporting table 3(11)	**NOT:** We refer to RMS and notifier comments under point 3(11) of the Reporting tables.	**RMS 08.09:** RMS did not find the original analytical reports. These were asked to the applicant. An additional comment on these reports will be sent before the TC.	PRAPeR TC 21 (14 September 2009): Open point fulfilled. The meeting agreed not to take into account these two trials in the assessment (i.e. trials not acceptable).

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
	Data gap: 3.3 Data to address residues in rotational crops, in particular further metabolite identification in the edible parts of the rotational crops is required. See reporting table 3(15)	**NOT:** We refer to RMS and notifier comments under point 3(15) of the Reporting tables.	**RMS 08.09:** In the PRAPeR Expert Meeting 70 on Carbofuran, it was concluded that more than 10 % of the carbamate residues were expected in soil after 100 days in a number of available studies (considering the total Carbofuran, 3-OH-carbofuran and 3-keto-carbofuran). A confined rotational crop study was reported in the revised DAR, April 2009. TRR in green parts of the plants after 30 days exceeded 0.01 mg/kg but no data was provided on the nature of the residues. -In a confined Carbofuran rotational crop study (JMPR 1997 report) and reported in the addendum to the DAR-August 2009, Phenyl-^{14}C-Carbofuran was applied directly to the soil at a rate of 3.4 kg a.s./ha. Wheat, soya beans and sugar beet were sown in the treated soil 4 and 12 months after treatment. The phenolic metabolites (3-OH-7-phenol, 3-keto-7-phenol and 7-phenol) were the main degradation products recovered in the rotated crops while the carbamates (carbofuran, 3-OH-carbofuran, 3-keto-carbofuran) constituted less than 10 % of the TRR	PRAPeR TC 21 (14 September 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
			in any crop sown at 4 and 12 months. However, this study did not address the situation of short plant back intervals. -In the reported plant metabolism studies in the revised DAR, only in sugar beet root and in soya bean plants, the level of the carbamates metabolites was below 10 % of TRR. In rice and corn grains, no metabolite identification was investigated. RMS is of the opinion that the approach as suggested by the applicant to consider 10 % TRR as carbamates in the rotational crops for the consumer risk assessment calculation is border line. Considering the extremely low toxicological reference values of Carbofuran and 3-OH-carbofuran, the trigger value of 0.01 mg/kg is not applicable and further metabolite identification in the edible parts of the rotational crops is necessary. Nevertheless, it has to be noted that RMS performed a consumer risk assessment including the TRR values from the rotational crops (see Carbofuran Addendum –April 2009). Using such values, the ARfD was	

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
			significantly exceeded for leafy and root crops but not in succeeding cereals crops. A proposal to overcome the problem might be to restrict the crop rotation to cereals.	
	Open point: 3.5 Experts may consider whether the approach as suggested by the applicant is justified to consider 10% TRR in rotational crops in the consumer risk assessment See reporting table 3(15)	**NOT:** We refer to RMS and notifier comments under point 3(15) of the Reporting tables.	**RMS 08.09:** See Data gap: 3.3	PRAPeR TC 21 (14 September 2009): Open point fulfilled. The default 10% TRR for carbamate compounds in leafy, root and oilseed crops is not supported by the available studies.
	Open point: 3.6 Combined risk assessment should be conducted considering the same mode of action (cholinesterase inhibition) but the different tox potency of carbofuran (plus 3-OH carbofuran) and carbosulfan. See reporting table 3(18)		**RMS 08.09:** Under point B.7.11 in the revised DAR, April 2009, a combined dietary intake risk assessment was performed using the sum of the LoQs for Carbofuran and 3-OH-carbofuran, respectively. Carbosulfan was not included in this risk assessment calculation since the metabolism data showed that it was hydrolysed directly into carbofuran and Dibutylamine.	PRAPeR TC 21 (14 September 2009): Open point fulfilled. New open point proposed, see below.
	New open point: 3.8 raised by experts during PRAPeR TC 21 meeting: RMS to compile an overview			PRAPeR TC 21 (14 September 2009): Open point 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
	table with the levels of the individual carbamate metabolites to be considered in the risk assessment. It should be checked whether sufficient data are available on 3-keto carbofuran to be used in the consumer RA.			
	New open point: 3.9 raised by experts during PRAPeR TC 21 meeting: The presumed residue level of carbamate residues of “zero” (PRAPeR 70) in refined sugar has to be reconsidered. Is for sugar the use of a “zero” value for the risk assessment really justifed?			PRAPeR TC 21 (14 September 2009): Open point fulfilled. New data gap proposed, see below.
	New data gap: 3.4 identified at PRAPeR TC 21 meeting: Applicant to address the residue levels of the carbamate metabolites in sugar.			PRAPeR TC 21 (14 September 2009): Data gap open.

REPORT OF PRAPeR EXPERT MEETING TC 22

CARBOSULFAN

Rapporteur Member State: BE

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
August 2009	BE	Carbosulfan Addendum_VOL3_B9 (August 2009).doc
2009-08-28	BE	Carbosulfan evaluation table rev 1-0 (2009-08-28).doc
August 2009	BE	Carbosulfan list of end points (August 2009).doc
2009-07-31	BE	Carbosulfan reporting table rev 1-1 (2009-07-31)
August 2009	BE	Carbosulfan Revised AR_VOL3_B9_part 1 (August 2009).doc
August 2009	BE	Carbosulfan Revised AR_VOL3_B9_part 2 (August 2009).doc
August 2009	BE	Carbosulfan Revised AR_VOL3_B9_part 3 (August 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: Marshal 10G

5. Classification and labelling: R50/53

6. Recommended restrictions/conditions for use: Not discussed.

7. Reference list: Not discussed.

Areas of concern: Birds, mammals (both a.s. and metabolites) and earthworms.

Appendix 1: Discussion table: CARBOSULFAN

Appendix 2: Evaluation table

Appendix 1: Discussion Table, Carbosulfan (In)

5. Ecotoxicology

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Open point: 0.1 The new template for the list of end points should be used. See reporting table 0(1)	It was acknowledged that the most recent template for the list of endpoints (LOEP) has not been used for the environment section. It was considered not necessary to update the list of endpoints at this stage.	Open point closed.
	Open point: 5.1 RMS to amend in the DAR and the LoEP the long-term endpoint for the metabolite carbofuran in accordance with the outcome of the expert discussion on carbofuran (PRAPeR 68 in May 2009). (The LC10 (14d) = 0.64 was suggested to be used in the risk assessment together with an increased safety factor of 10). See reporting table 5(1)	The DAR and the list of endpoints have been updated to include an AF of 10. It should be specified in the LoEP for which substance (carbosulfan/carbofuran) the risk assessment was conducted.	Open point open. RMS to amend the LoEP with substance (carbosulfan/carbofuran) details.
	Open point: 5.2	The DAR and the LoEP have been updated.	Open point open.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	RMS to indicate in the LoEP that the PD/PT values suggested in the refined risk assessment are based on general considerations of diet composition and that they are not appropriate to be used in a quantitative risk assessment. See reporting table 5(2)	The conclusion of the previous expert meeting (PRAPeR 68) regarding the use of PD/PT for carbofuran is also valid for carbosulfan, i.e. they can only be used for illustrative purpose. A footnote should be added to the LoEP that the LD50 5th-percentile (5.32 mg a.s/kg bw) has been used in the risk assessment. The value is only used following the EPPO guidance.	RMS to add footnote to the LoEP that the LD50 5th-percentile (5.32 mg a.s/kg bw) has been used in the risk assessment.
	Open point: 5.3 RMS to update the evaluation of the residue trial with insects and earthworms as discussed in the expert meeting (PRAPeR 68, May 2009) in the context of the refined risk assessment for carbofuran. See reporting table 5(3)	The residue trial (carbosulfan) in sugar beet seedlings was made at both application rates (100 and 750 g a.s./ha) and measurements of carbosulfan, carbofuran and 3-OH-carbofuran were made. The residue trial (carbosulfan) in beetles and earthworms was made only at the application rate of 750 g a.s./ha and measurements of carbosulfan and carbofuran were made (no measurements of 3-OH-carbofuran). Residues in earthworms: There are still uncertainties regarding residues in the study (earthworms stored over night before analysis and earthworms void gut content). The DAR should be updated to explain that the residue studies with earthworms (Kölzer U., 2005a and Farrelly E., Hinchcliffe A., 2005) were not used in the risk assessment and why the studies were not accepted. Residue trials in sugar beet seedlings: RMS noted shortcomings that residues were measured in N. EU under protected conditions. This was not considered representative for the whole EU. Furthermore,	Open point open. RMS to update the DAR to explain that the residue studies with earthworms were not used in the risk assessment and why the studies were not accepted. RMS furthermore to update the DAR (Tabel B.9.1.12-13) to leave out the recommendation on residue measurement after BBCH 12.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
		residues of 3-OH-carbofuran were not measured. It was clarified that sugar beet production is also relevant to S EU. The 2-leave stage was considered appropriate for the residue measurements. At later stages residues were expected to be more diluted following plant growth. RMS to update the DAR (Table B.9.1.12-13) to leave out the recommendation on residue measurement after BBCH 12. RMS has reservations to reduce residues concentrations proportional to the application rate (see discussion of carbofuran). If uses at such a reduced rate should be further supported, new residue trials would be needed with reduced application rate (100 g a.s./ha). Member state experts agreed.	
	Open point: 5.4 RMS to update in an addendum to the DAR and in the LoEP the risk assessment for mammals and carbofuran with the NOAEL of 0.1 mg carbofuran/kg bw/d. See reporting table 5(5)	The DAR and LoEP have been revised accordingly. RMS to indicate the origin of the medium-term mammal endpoint (28 day NOAEL = 2.2 mg a.s./kg bw/day) in the LoEP.	Open point open. RMS to indicate the origin of the medium-term mammal endpoint (28 day NOAEL = 2.2 mg a.s./kg bw/day) in the LoEP.
	Open point: 5.5 RMS to indicate in an addendum to the DAR and in the LoEP that the suggested refinement of PD for hare and shrew are uncertain since they were not derived from	The DAR and the LoEP have been revised accordingly.	Open point fulfilled.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	targeted studies in sugarbeet fields. See reporting table 5(6)		
	Open point: 5.6 MSs to discuss in an expert meeting the probabilistic risk assessement for birds from uptake of granules as grit. See reporting table 5(13)	Probabilistic RA for carbosulfan was based on the same assumptions by the applicant as for carbofuran. The RMS had several concerns (many assumptions) regarding this approach for carbosulfan similarly as RMS also had for carbofuran. The probabilistic risk assessment is not needed to address the risk and the approach was not accepted for carbofuran. The risk from granules can be addressed following the EPPO approach. It was noted that the revised Bird and Mammal Guidance Document currently being developed have only very minor difference compared to the EPPO scheme. Calculations were performed based on the EPPO scheme, as in the proposals for carbofuran and benfuracarb. For carbosulfan 10.9 granules are needed to reach the LD50 (15g bird). For carbofuran 0.2 granules were needed to reach LD50 (15g bird). The EPPO guidelines state that the risk is considered high with one to a few granules, without further trigger. It was discussed whether the EPPO scheme would be considered in every case and particularly in the cases where substances are of high acute toxicity. However, for consistency reasons the meeting agreed on the need to provide calculation based on the existing guidance. In the case of carbosulfan, 10.9 granules do not represent a high number, and it was also pointed out that some of the a.s. may degrade to carbofuran on the granules before eaten by birds, which would make it more toxic. Also the fate of the a.s. in the granules would need to be considered further. Therefore, the meeting agreed to use the EPPO scheme as usual for a standard risk assessment and to include a comment that monitoring data being available in MS should be used for national registration to confirm/infirm the outcome of the assessment. EFSA should also highlight that the risk is potentially high and precautions are needed to avoid spill of granules.	Open point open. EFSA to highlight in the conclusion that the risk is potentially high and precautions are needed to avoid spill of granules.
	Open point: 5.7 MSs to discuss in an	According to the applicant house sparrow (considered relevant focal species by the applicant) metabolises carbosulfan fast or does not eat granules.	Open point fulfilled.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	expert meeting the applicability of the avoidance study with house sparrow and granules. See reporting table 5(16)	The RMS had concerns regarding the applicability of an avoidance study under field conditions. The RMS mentioned among others that in the avoidance study it was not recorded if birds did eat granules. Furthermore, it was noted that the cage study did not cover spill situations or end-of-row presence of granules. The cage study was not considered a worst case situation and was not accepted. Member state experts agreed with the RMS.	
	Open point: 5.8 MSs to discuss in an expert meeting the refined acute risk assessment based on body burden modelling according to the PPR opinion on pirimicarb. See reporting table 5(21)	The RMS highlighted that the parameters needed for the approach were not accepted for carbofuran (basically same input parameters used for carbosulfan and carbofuran) and the pirimicarb approach could not be used. Consequently, the approach was not considered valid for carbosulfan. See discussion of carbofuran. Member state experts agreed to the RMS' assessment The applicant was seeking clarification whether new ADME studies would be required to use the pirimicarb approach. There were concerns that AChE inhibition measurements in the blood would not reflect systemic effects.	Open point fulfilled.
	Open point: 5.9 RMS to update the aquatic risk assessment with the new PECsw values. See reporting table 5(29)	The DAR and LoEP have been updated with revised TER calculations based on FOCUSsw Step 3. The endpoint for Chironomus (for carbofuran) should be presented as mean measured value. This was discussed at PRAPeR 68. The LoEP should be updated accordingly.	Open point open. RMS to update Chironomus endpoint as mean measured value in the LOEP.
	Open point: 5.10 MSs to discuss in an expert meeting whether the aquatic risk assessment should be based on	At tier 1 there is a risk for *Daphnia* and *Ceriodaphnia* at FOCUSsw Step 3. The risk can be addressed by use of a mesocosm (NOAEC of 0.4 µg a.s./L). TER values were above the Annex VI trigger in 5 out of 6 scenarios. A NOEC of 0.1 µg a.s./L was derived from the mesocosm study.	Open point fulfilled.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	the NOAEC of 0.4 µg a.s./L together with an uncertainty factor of 4. The resulting EAC of 0.1 µg a.s./L would drive the aquatic risk assessment. RMS to update the LoEP accordingly. See reporting table 5(30)	It was mentioned that the reason for a AF of 4 used on the NOAEC should be explained or instead a NOEC should be used without an AF. (In both cases the RAC = 0.1 µg a.s./L) Some MSs prefer the NOEC endpoint from mesocosm studies to take account of effects on species with few individuals. Use of PRC to derive NOAEC may miss single (sensitive) species. Futher guidance on assessment of mesocosms is awaited from the revison of the aquaric guidance document. MS experts agreed on the RAC of 0.1 µg a.s./L based on the mesocosm study available.	
	Open point: 5.11 MSs to discuss in an expert meeting whether new studies with fish are necessary. See reporting table 5(32)	The validity of the acute fish toxicity study with the a.s. was questionable due to the lack of analytical measurements. However, the metabolite studies were acceptable. It's suggested to either delete the endpoint from the LoEP or add a footnote that the endpoint is based on nominal concentrations. MS experts agreed on a footnote "no analytical measurements were available which add some uncertainty".	Open point open. RMS to add the following footnote in the LOEP "no analytical measurements were available which add some uncertainty".
	Open point: 5.12 MSs to discuss in an expert meeting whether new studies with daphnids are necessary. See reporting table 5(33)	MS experts agreed on a footnote "no analytical measurements were available which provide some uncertainty" to be added in the LOEP.	Open point open. RMS to add the following footnote in the LOEP "no analytical measurments were available which provide some uncertainty".
	Data gap: 5.1 Applicant to submit the study of Broadbent and Tomlin (1982).	As no new information can be accepted following Commission Regulation EC No 33/2008 on resubmissions, the data gap is confirmed. How can broadcast application concentration be transformed to soil concentration	Data gap open.

	Subject	Discussion Expert Meeting	Conclusions Expert Meeting
	Please note that according to regulation 1095/2007 no new studies can be taken into account in the peer review. Therefore this point was identified as a formal data gap. See reporting table 5(36)	following drilling application? Is broadcast application more worst case than in forrow application? Information is needed to confirm that broadcast application is more worst case than in furrow application. Else field studies following the GAP would be required. New PECsoil calculations representing in furrow application are needed.	
	Open point: 5.13 RMS to correct in the LoEP the endpoints for *Hypoaspis* and *Folsomia* (they are inverted). See reporting table 5(37)	The LoEP has been revised accordingly.	Open point fulfilled.

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: ***13*** Points for clarification: ***0*** Data gaps: ***1***			Section 5 Open points: ***8*** Points for clarification: ***0*** Data gaps: ***1***
	Open point: 5.1 RMS to amend in the DAR and the LoEP the long-term endpoint for the metabolite carbofuran in accordance with the outcome of the expert discussion on carbofuran (PRAPeR 68 in May 2009). (The LC10 (14d) = 0.64 was suggested to be used in the risk assessment together with an increased safety factor of 10). See reporting table 5(1)	**NOT:** We agree with the selection of the LC10 (14d) of 0.64 mg/kg bw/day for the metabolite carbofuran. However, we stress that the use of the LC10 in itself contains already a safety factor. Besides, the residue declines rapidely, so that a continued exposure of 14 days represents a worst case scenario. Therefore increasing the Safety factor to 10 in the Risk assessment is very conservative.	**RMS (August 2009):** The updated DAR August 2009 (p. 94; p. 99-101) and the List of endpoints have been revised.	PRAPeR TC 22 (14 September 2009): Open point open. RMS to amend the LoEP with substance (carbosulfan/carbofuran) details.
	Open point: 5.2 RMS to indicate in the LoEP that the PD/PT values suggested in the refined risk assessment are based on general considerations of diet composition and that they are not appropriate to be used in	**NOT:** A PT of 1 represents a worst case estimate rather than a reasonable estimate for the long term risk assessment, since it is not possible to use a higher value. Residues in insects have been shown to decline very rapidly with time. Therefore, a PT value of 1 overestimates the number of	**RMS (August 2009):** The updated DAR August 2009 (p. 99) and the List of endpoints has been revised. In principle, we agree with the notifier that PT of 1 overestimates the risk. However, a quantification of the PT value is not possible based on the available information.	PRAPeR TC 22 (14 September 2009): Open point open. RMS to add footnote to the LoEP that the LD50 5th-percentile (5.32 mg a.s/kg bw) has been used in the 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
	a quantitative risk assessment. See reporting table 5(2)	contaminated insects likely to be found. With regard to moribund insects: (1) the non-target arthropod field trials show a rapid recovery of the surface dwelling insects (that will be part of the diet) indicating that toxic effects on this important guild of insects which make up the diet are not long lasting, i.e. only short-term duration; and (ii) as foliage density increases then any affected insects would become increasingly difficult to find in the crop. Both observations add weight to the argument that the portion of the diet from the treated area is only likely to be contaminated for a short period of time.		
	Open point: 5.3 RMS to update the evaluation of the residue trial with insects and earthworms as discussed in the expert meeting (PRAPeR 68, May 2009) in the context of the refined risk assessment for carbofuran. See reporting table 5(3)	**NOT:** we agree However note that 3-OH-carbofuran was not measured in these residue trials. However, as highlighted in the Environmental Fate Section of the DAR, 3-OH-carbofuran is a minor and transient metabolite in soil. Therefore, the contribution of 3-OH to the residue in earthworms and arthropods is expected to be modest. This conclusion is confirmed in practice by the earthworm/insect residue trials that were reported in the benfuracarb DAR, where 3-OH-carbofuran was measured and found to contribute only modestly to the overall residue.	**RMS (August 2009):** The residue trials in both dossiers are not the same. In the carbofuran DAR, residue trials were conducted with carbofuran; in the carbosulfan DAR, residue trials were conducted with carbosulfan. The residue trial (carbosulfan) in sugar beet seedlings was made at both application rates (100 and 750 g a.s./ha) and measurements of carbosulfan, carbofuran and 3-OH-carbofuran were made. The residue trial (carbosulfan) in beetles and earthworms was made	PRAPeR TC 22 (14 September 2009): Open point open. RMS to update the DAR to explain that the residue studies with earthworms were not used in the risk assessment and why the studies were not accepted. RMS furthermore to update the DAR (Table B.9.1.12-13) to leave out the recommendation on residue measurement after BBCH 12.

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
			only at the application rate of 750 g a.s./ha and measurements of carbosulfan and carbofuran were made. (no measurements of 3-OH-carbofuran). However, the same shortcomings as in the carbofuran dossier apply leading to an underestimation of the residues (p. 31 of updated DAR August 2009). The notifier has also submitted an "Updated and comparative risk assessment of the carbosulfan use on sugar beet at 100 g ai/ha versus 750 g ai/ha." RMS disagrees with the statement of the notifier that the residues will decline 7.5 times for the lower application rate of 100 g a.s./ha, compared to the applied 750 g a.s./ha. This extrapolation should be substantiated with data, e.g. residue trials conducted at 100 g a.s./ha. A copy of the statement of the notifier on the lowered dose rate of 100 g a.s./ha is included in the addendum (p. 10-15). RMS maintains its position on this issue.	
	Open point: 5.4 RMS to update in an addendum to the DAR and in the LoEP the risk assessment for mammals and carbofuran with the	**NOT:** We refer to our comment under point 5(5) of the Reporting Tables.	**RMS (August 2009):** The updated DAR August 2009 (p. 163-172) and the List of Endpoints have been revised.	PRAPeR TC 22 (14 September 2009): Open point open. RMS to indicate the origin of the medium-term mammal endpoint (28 day NOAEL =

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
	NOAEL of 0.1 mg carbofuran/kg bw/d. See reporting table 5(5)			2.2 mg a.s./kg bw/day) in the LoEP.
	Open point: 5.5 RMS to indicate in an addendum to the DAR and in the LoEP that the suggested refinement of PD for hare and shrew are uncertain since they were not derived from targeted studies in sugarbeet fields. See reporting table 5(6)		**RMS (August 2009):** The updated DAR August 2009 (p. 167 and 172) and the List of Endpoints have been revised.	PRAPeR TC 22 (14 September 2009): Open point fulfilled.
	Open point: 5.6 MSs to discuss in an expert meeting the probabilistic risk assessement for birds from uptake of granules as grit. See reporting table 5(13)	**NOT:** the proposed PRA meets the conclusion of the RA for granule intake as according to the EPPO subscheme. Indeed, both evaluations independently conclude that the chance for a bird to intake a few numbers of granules is very low. Hence to risk to birds is acceptable.	**RMS (August 2009):** The RMS has the same reservations for the probabilistic risk assessment with Marshal 10G (carbosulfan) as for Furadan 5G (carbofuran). The PRA for carbofuran was discussed in PRAPeR 68 and the meeting agreed with the RMS that too many uncertainties remained. For the PRA of carbosulfan, the RMS recalculated the annual mortality for a period of 2 weeks and found that the effect of carbosulfan could be equal to the normal mortality during 2 weeks (estimated exposure period to carbosulfan). Furthermore, it is unclear what caused the annual mortality. The timing of application should be	PRAPeR TC 22 (14 September 2009): Open point open. EFSA to highlight in the conclusion that the risk is potentially high and precautions are needed to avoid spill of granules.

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
			compared to the breeding season. The current PRA approach considers population effects, but should not individual deaths be of concern also? What is the protection goal? There might be a cumulative effect, while the PRA now only takes 1 visit per bird into account. The PRA is based on HD_5 = 3.179 mg a.s./kg b.w./day, with an uncertainty factor of 1 (no margin of safety even if an endpoint based on mortality is used).	
	Open point: 5.7 MSs to discuss in an expert meeting the applicability of the avoidance study with house sparrow and granules. See reporting table 5(16)	**NOT:** The initial assessment indicates that 11 carbofuran granules are sufficient to kill a small bird. Since sufficient granules to kill a bird were potentially available, then the results suggest that either (1) the birds quickly metabolised carbosulfan and suffered no harm, or most likely (2) the birds do not take the granule because, it is proposed, they do not resemble grit. The latter reduces exposure and is consistent with the results of the EPPO scheme risk assessment. Furthermore the notifier believes that the house sparrow is an appropriate species of choice for this study because the granule size range overlaps the grit size range for the species of interest. Best and Gionfriddo (1991) reported the mean	**RMS (August 2009):** The conclusion of the RMS on the acceptance study is on p. 19 of the updated DAR August 2009. RMS considers that the results of this study cannot be easily extrapolated to the actual field situation.	PRAPeR TC 22 (14 September 2009): Open point fulfilled. The cage study was not considered a worst case situation and was not accepted.

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
		gizzard grit size for house sparrows (*Passer domesticus*) to be 0.7 mm (range of 0.25 to 1.6 mm). Marshal® 10G granule size range is 0.3 to 1.0 mm (de Ryckel, 1999a), which overlaps the range for house sparrow. With house sparrows being a readily available granivore that has been used in laboratory settings, it was the most reliable species to evaluate the potential avoidance of Marshal granules to small granivores that would seek grit particles of the same size.		
	Open point: 5.8 MSs to discuss in an expert meeting the refined acute risk assessment based on body burden modelling according to the PPR opinion on pirimicarb. See reporting table 5(21)	**NOT:** the pirimicarb approach has the merit to consider the rapid metabolisation and the reversibility of the AChE inhibition – which are inherent properties of carbosulfan and carbofuran.	**RMS (August 2009):** The PPR panel approach for assessing pirimicarb was also used for the carbofuran dossier and discussed during PRAPeR 68. The parameters used in the carbosulfan dossier are the same as in the carbofuran dossier, except for the residues in arthropods and sugar beet seedlings. The conclusion of the PRAPeR 68 meeting was : For the yellow wagtail: $T_{1/2}$, AVT and AVD were not accepted; for woodpigeon: FPM, $T_{1/2}$, AVT and AVD were not accepted. The meeting concluded that, because of all the uncertainties identified, the pirimicarb-approach is not accepted.	PRAPeR TC 22 (14 September 2009): Open point fulfilled. The pirimicarb approach was not considered valid for carbosulfan.

<table>
<tr><th>No.</th><th>Column A
Conclusions from the Reporting Table</th><th>Column B
Comments from the notifier / applicant</th><th>Column C
Rapporteur Member State comments on the notifier / applicant comments</th><th>Column D
Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure</th></tr>
<tr><td></td><td>Open point: 5.9
RMS to update the aquatic risk assessment with the new PECsw values.

See reporting table 5(29)</td><td>NOT: New highest PECsw at max application rate of 750 g ai/ha for carbosulfan and its metabolite, carbofuran, are 0.0 and 0.0658 ug/L for the Run off and drainage respectively, in all simulated scenarios using FOCUS Step 3.
The revised aquatic TERs based on toxicity endpoint reported in the carbofuran Dossier are in the Table below.
<table>
<tr><td>Lepomis macrochirus</td><td>96 h</td><td>180 ug/L</td><td>2736</td></tr>
<tr><td>Cyprinodon variegatus</td><td>35 d</td><td>6 ug/L</td><td>91</td></tr>
<tr><td>Daphnia magna</td><td>48 h</td><td>2.05 ug/L</td><td>31</td></tr>
<tr><td>Ceriodaphnia dubia</td><td>7 d</td><td>0.16 ug/L</td><td>2.4</td></tr>
<tr><td>Chironomus riparius</td><td>28 d</td><td>4.0 ug/L</td><td>61</td></tr>
<tr><td>Pseudokirchneriell</td><td>72 h</td><td>6500 ug/L</td><td>98784</td></tr>
</table></td><td>RMS (August 2009):
The revised TER calculations (750 g a.s./ha) are presented in an addendum (p. 2-7) and the List of Endpoints has been revised.</td><td>PRAPeR TC 22 (14 September 2009):

Open point open.

RMS to update Chironomus endpoint as mean measured value in the LOEP.</td></tr>
</table>

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
		a subcapitata		
		All of the TERs represent an acceptable risk, except for *Ceriodaphnia dubia.*		
	Open point: 5.10 MSs to discuss in an expert meeting whether the aquatic risk assessment should be based on the NOAEC of 0.4 µg a.s./L together with an uncertainty factor of 4. The resulting EAC of 0.1 µg a.s./L would drive the aquatic risk assessment. RMS to update the LoEP accordingly. See reporting table 5(30)	**NOT:** We agree.	**RMS (August 2009):** The updated DAR August 2009 (p. 140, 144) and the List of Endpoints have been revised. The results of the mesocosm study can be used to refine the risk assessment for aquatic invertebrates : NOAEC = 0.4 µg carbosulfan/L EAC = 0.1 µg carbosulfan/L Complete recovery of the population of *Ceriodaphnia* occurred after 40 days at 0.4 µg carbosulfan/L. The refined risk assessment for *Daphnia magna* and *Ceriodaphnia dubia* is presented in an addendum (p. 7) and in the List of Endpoints.	PRAPeR TC 22 (14 September 2009): Open point fulfilled. MS experts agreed on the RAC of 0.1 µg a.s./L based on the mesocosm study available.
	Open point: 5.11 MSs to discuss in an expert meeting whether new studies with fish are necessary. See reporting table 5(32)	**NOT:** We refer to RMS and notifier comments under point 5(32) of the Reporting tables.	**RMS (August 2009):** Only the acute toxicity studies with carbosulfan were considered of low quality, not the studies with the metabolites. We agree with the view of the notifier. **NOT (reporting table):** A sufficient number of studies are available to	PRAPeR TC 22 (14 September 2009): Open point open. RMS to add the following footnote in the LOEP “no analytical measurements were available which add some uncertainty”.

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
			adequately determine risk to aquatic species including fish and invertebrates. The current risk assessment passes at Step 3 and generation of new data would not change the overall risk conclusions derived in the surface water risk assessments.	
	Open point: 5.12 MSs to discuss in an expert meeting whether new studies with daphnids are necessary. See reporting table 5(33)	**NOT:** We refer to RMS and notifier comments under point 5(33) of the Reporting tables.	**RMS (August 2009):** Only the acute toxicity studies with carbosulfan were considered of low quality, not the studies with the metabolites. We agree with the view of the notifier. **NOT (reporting table):** See comment in 5(32).	PRAPeR TC 22 (14 September 2009): Open point open. RMS to add the following footnote in the LOEP “no analytical measurments were available which provide some uncertainty”.
	Data gap: 5.1 Applicant to submit the study of Broadbent and Tomlin (1982). Please note that according to regulation 1095/2007 no new studies can be taken into account in the peer review. Therefore this point was identified as a formal data gap. See reporting table 5(36)	**NOT:** Addressed. This publication has been submitted to RMS in the meanwhile.	**RMS (August 2009):** The notifier submitted the publication and the RMS has evaluated this in an addendum (p. 8-9). The RMS has reservations towards this study due to several shortcomings (low number of earthworms found, measurements after 22 weeks when residues had fallen to 0 mg/kg). Therefore, based on this publication, RMS cannot conclude on the comparison of exposure via in-furrow or via broadcast application.	PRAPeR TC 22 (14 September 2009): Data gap open.
	Open point: 5.13 RMS to correct in the LoEP		**RMS (August 2009):** The List of Endpoints has been	PRAPeR TC 22 (14 September 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
	the endpoints for *Hypoaspis* and *Folsomia* (they are inverted). See reporting table 5(37)		revised.	Open point fulfilled.