PEER REVIEW REPORT ON **CARBOFURAN** 22 06 2009

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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: ***1*** Points for clarification: ***0*** Data gaps: ***0***			Section 1 Open points: ***1*** Points for clarification: ***0*** Data gaps: ***3***
	Open point: 1.1 The acceptability of method A-17-05-13, validated by Battelle (Enriquez, 2006), and of the ILV study by Zietz (2008) to be discussed in a meeting of experts in light of the modifications described in the ILV claimed to be necessary for robustness of the method See reporting table 1(5)	**NOT**: we refer to RMS and applicant comment from the Reporting tables	**RMS:** The validation by Battelle shows lower recoveries in some cases (in comparison with ILV by Zietz); however, these are within the acceptable range.	PRAPeR 66 (21 – 24 April 2009): Open point fulfilled.
	New data gap 1.1 identified at PRAPeR 66 meeting: ILV for modified method (Zietz (2008)) is needed			PRAPeR 66 (21 – 24 April 2009): Data gap open. Written procedure Data gap remains
	New data gap 1.2 identified at PRAPeR 66 meeting Efficiency of hydrolysis step to be addressed			PRAPeR 66 (21 – 24 April 2009): Data gap open.

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				Written procedure Data gap remains
	New open point 1.2: EFSA to amend residue definition in conclusions after residue meeting			PRAPeR 66 (21 – 24 April 2009): Open point open. Written procedure: Open point fulfilled The residue definitions in conclusions after residue meeting were amended
	New data gap 1.3 identified at PRAPeR 70 meeting: The notifier to address the efficiency of the hydrolysis step to release the 3 OH-carbofuran conjugates in animal matrices in the method of analysis for monitoring.			PRAPeR 66 (21 – 24 April 2009): Data gap open. Written procedure Data gap remains

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: ***3*** Points for clarification: ***0*** Data gaps: ***0***			Section 2 Open points: ***0*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 2.1 MSs to discuss the AOEL values in an expert meeting. See reporting table 2(2)	**NOT:** We refer to our position paper on the setting of the ADI, ARfD and AOEL; to DE comment 2(3) from the reporting table; to applicant comment 2(5) from the reporting table and to JMPR views on the setting of carbofuran ADI, ARfD and AOEL. We maintain that ADI, ARfD and AOEL should be set at 0.001 mg/kg bw/day.	**RMS:** It is questionable whether PND11 rat brain development would be equivalent to that of human brain in the 3th trimester of human pregnancy. In open literature, estimates are not consistent. Some authors* estimate that the PND7 old pup is approximately equal to the human neonate in terms of brain growth rate, periventricular germinal matrix composition, neurochemical expression, EEG patterns and synapse formation. More relevant for the endpoint of AChE inhibition**, the timing of axonal outgrowth of AChE-positive nerve fibers was demonstrated just before birth in humans and perinatally (up to PND7) in the rat. On the contrary, in a more general neurodevelopmental model***, it was predicted that a PND14 old rat pup has a brain cortical development comparable to a human foetus 2 months before birth, possibly suggesting that human neonate neurodevelopment would be comparable to that in the weaned rat (however, the model is restricted to rat PND14 stage). In a recent paper****, it was considered reasonable that the 2nd half of the brain growth spurt in the rat (PND11-21) corresponds in developmental time to a portion of the human brain postnatal growth	PRAPeR 69 (4. – 8. May 2009): Open point fulfilled The AOEL is 0.0003 mg/kg bw/day

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			spurt. Inspection of all the study results on PND11 or PND17 ♂rats moreover shows that brain AChE inhibition at 0.1 mg/kg was overall of about the same magnitude (33-40%), indicating that the rat neonate PND11 and PND17 were of equivalent sensitivity, and represent merely a human perinatal, and not a “third trimester embryo” situation. In any case, from the risk assessment point of view, it is not realistic that women in late pregnancy (approximately last month) would be representative for operators loading and applying Carbofuran. Therefore, it is not relevant to establish an AOEL on a pup toxicity NOAEL (0.015 mkd), and the adult NOAEL (0.03 mkd) is considered preferable. *References:* **Am J Physiol Regul Integr Comp Physiol, 282, 55-63, 2002; **in: Bjorklund, A, Hokfelt,T (Eds.) Handbook of Chemical Neuroanatomy, Elsevier, A’dam, 33-62, 1991; ***Neuroscience, 105, 7-17,2001; ****Toxicol Appl Pharmacol, 196, 287-302, 2004.*	
	Open point: 2.2 MSs to discuss the dermal absorption value in an expert meeting. See reporting table 2(7)	**NOT:** We refer to RMS comments 2(7) and 2(8) from the reporting tables.	**RMS:** The refinement consisted in comparing the *in-vivo* and the *in-vitro* (first study) absorption value at 6h post-application (see addendum p 188). In both cases the absorption rate was about 1-2%. This equivalence is an essential condition to make a bridging from *in-vivo* to *in-vitro*. Then, the rat/human proportion (2×)	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. The dermal absorption value is 5 %

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			calculated on the data *in-vitro* was applied on the 24h absorption value (6%), leading to the 3% estimate. RMS considered it overly conservative to rely on an *in-vivo* value at >24h, as in a regular *in-vivo* study, the skin would have been swabbed to remove the excess of radioactivity. It is logic that extending the contact time without swabbing leads to a protracted skin absorption (although a plateau phase seems to be attained at 24h). In addition, using acetone to dissolve the a.s. is likely to enhance absorption, and a 80× more diluted substance was used *in-vivo* compared with *in vitro*. Thus, several parameters indicate that the *in-vivo* study approximated a worst-case condition. In conclusion, the 3% value was considered a reasonable approach, and not very different from the value proposed by NL (5%), taking into account the variation usually observed in this kind of studies.	

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	Open point: 2.3 Pending on the outcome of the discussion on the AOEL and dermal absorption values, RMS to provide new estimates of operator exposure risk assessment. MSs to discuss the model to be used in the operator exposure risk assessment in an expert meeting. See reporting table 2(9)		**RMS:** agreement to make a new estimation of the operator exposure in case of an altered reference dose (AOEL) or if skin absorption is revised upwards.	PRAPeR 68 (4. – 8. May 2009) Open point open. Written procedure Open point fulfilled

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: ***10*** Points for clarification: ***0*** Data gaps: ***0***			Section 3 Open points: ***4*** Points for clarification: ***0*** Data gaps: ***3***
	Open point: 3.1 The residue definition in plant commodities both for monitoring and risk assessment should be discussed in a meeting of experts. See reporting table 3(~~12~~ 11)	**NOT**: We refer to RMS and applicant comment 3(12) from the reporting tables. The residue definition in plant should be maintained as carbofuran + 3-0H carbofuran, both free and conjugated expressed as carbofuran.	**RMS 04.2009:** RMS agrees that the residue definitions for monitoring and RA in plant commodities must be consistent with the residue definitions established for Carbofuran in the framework of Benfuracarb dossier. The available plant metabolism studies showed that Carbofuran and 3-OH-carbofuran were the most predominant compounds of the total residues. Considering the limited characterization of the glycosides and other conjugates in the acid hydrolysis released radioactivity, the following residue definitions are proposed for sugar beet: -**Monitoring**: **carbofuran + 3-0H carbofuran expressed as carbofuran** **-Risk assessment: carbofuran + 3-0H carbofuran, both free and conjugated expressed as carbofuran.** There is no need to include other carbamates metabolites (3-keto-	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. Risk assessment: Sum of carbofuran + 3 OH-carbofuran both free and conjugated expressed as carbofuran Monitoring: Open (pending information on efficiency of the hydrolysis step in the analytical method) Preferably, the same as for risk assessment.

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			carbofuran) and phenolic metabolites that are less toxic than Carbofuran and 3-OH-carbofuran. RMS proposes to discuss this point during the Expert meeting considering the JMPR Carbofuran evaluation that is presented in the Addendum to the DAR-April 2009.	
	Open point: 3.2 The residue definition in animal commodities both for monitoring and risk assessment should be discussed in a meeting of experts. See reporting table 3(~~13~~ 12)	**NOT**: We refer to RMS and applicant comment 3(13) from the reporting tables. 3-0H carbofuran, both free and conjugated expressed as 3-OH-carbofuran would be the appropriate residue definition in animal commodities – if such residue definition is required.	**RMS 04.2009:** RMS also agrees that considering the available metabolism studies in livestock and the theoretical calculated dietary burden, no residue is expected in the animal matrices. -For ruminants'matrices, **3-OH-carbofuran** can be a valid indicator of the total residues in milk, liver and kidney and per default in muscle and fat characterized by extremely low levels of recovered radioactivity (0.01 µg/kg). Indeed, a non negligible fraction of the radioactivity consisted of aqueous soluble residues/polar residues in all the matrices. The available analytical methods for the determination of the carbamate metabolites (carbofuran, 3-OH-carbofuran and 3-keto-carbofuran) include an acid hydrolysis step to take into account the possible conjugates.	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. Risk assessment: 3 OH-carbofuran free and conjugates expressed as carbofuran Monitoring: Preferably the same (pending information on efficiency of the hydrolysis step in the analytical method) Data gap (see below): Notifier to address the amount of conjugates in the livestock metabolism studies Data gap for section 1 (transferred to section 1): The notifier to address the efficiency of the hydrolysis step to release the 3 OH-carbofuran conjugates in animal matrices in the method of analysis for monitoring.

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			HPLC-PCD methods were considered as suitable for the determination of the residues of Carbofuran, 3-OH-carbofuran and 3-keto-carbofuran in animal matrices with a LOQ for each analyte of 0.05 ppm (liver, muscle, eggs), LOQ of 0.025 ppm (whole milk). Concerning kidney, fat and milk cream, insufficient data were available to establish a LOQ unequivocally. For poultry matrices, no residue is expected in any matrices considering the calculated dietary burden that did not trigger a metabolism study. The metabolite 3-OH-metabolite was detected only in egg yolk. Therefore, a general residue definition is proposed for animal matrices: -**For monitoring: 3-OH-carbofuran** **-For risk assessment: 3-OH-carbofuran, free and conjugated expressed as 3-OH-carbofuran.**	
	New data gap 3.1 identified at PRAPeR 70 meeting: Notifier to address the amount of conjugates in the livestock metabolism studies			PRAPeR 70 (4 – 8 May.2009): Data gap open Written procedure: 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
	Open point: 3.3 It should be clarified whether in the data generation methods (residue trials) the efficiency of the hydrolysis step was validated? See reporting table 3(16)	**NOT:** We refer to the metabolism data which demonstrates that solven and acid hydrolysis extraction release any free and conjugated residue while enzyme extraction release the bound residue (compounds incorporated to natural plant constituents). Therefore, the hydrolysis extraction step is validated by the metabolism data for its efficiency at releasing conjugated 3-OH-carbofuran.	**RMS 04.2009:** The efficiency of the hydrolysis step in the analytical method referenced A-17-05-13 was validated through the validation data package of this method under chapter B.5.2.1, Table B.5.2.1-9b regarding the recovery and precision of the analytical method for 3-OH-carbofuran. Indeed at fortification levels of 0.005 and 0.05 mg/kg with this metabolite, the recoveries accounted for 107 % and 92 %, respectively. The complete validation data package for the analytical method No A-17-05-13 is reported in the Addendum to the DAR-April 2009.	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. Data gap (see below): The notifier to address the efficiency of the hydrolysis step to effectively release the carbofuran and 3 OH-carbofuran conjugates in the methods of analysis used in the supervised residue trials.
	New data gap 3.2 identified at PRAPeR 70 meeting: The notifier to address the efficiency of the hydrolysis step to effectively release the carbofuran and 3 OH-carbofuran conjugates in the methods of analysis used in the supervised residue trials.			PRAPeR 70 (4 – 8 May.2009): Data gap open Written procedure: Data gap open
	Open point: 3.4 Upon a plant residue definition for risk assessment has been agreed, the available residue data should		**RMS 04.2009:** A complete residue database covering North and South of Europe on sugar beet was provided in the frame of the resubmission and showed a non-	PRAPeR 70 (4 – 8 May.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
	be reviewed and the appropriate data should be selected. (Consider also open point in comment 3(16)) See reporting table 3(19)		residue situation both in roots and leaves with tops. The analytical method was completely validated at a Limit of Quantification of 0.005 mg/kg for each analyte.	Written procedure: Open point open
	Open point: 3.5 The available processing data (nature and level) should be discussed by experts in terms of their suitability to conclude on residue behaviour under sugar beet processing/ sugar raffination See reporting table 3(22)	**NOT:** For recall, the processing study was run at exaggerated dose rate (4.48 g ai/ha) and showed 0.02 – 0.03 mg/kg of 3-keto-7-phenol in molasses and sugar while no carbamates residue was recovered. This confirms that any carbamate residue would convert to phenolic metabolite through the processing of roots to sugar. We believe that this data could support a 3 x residue degradation factor in processing, considering the worst case assumption that 0.03 mg/kg of carbamate degraded to 0.02 mg/kg of phenoilic metabolite and 0.01 mg/kg of carbamate (0.01 mg/kg being the LOQ of carbamates residue in the processing study).	**RMS 04.2009:** The first study (El-Naggar S.F., Reynolds J.L., 1982) was not conducted according to the representative hydrolytic conditions of processing according to the current guideline. In fact, the study was conducted at room temperature (T°: 25°C) and at pH values of 5.0, 7.0 and 9.0. Processing operations typically involve higher T° but for much shorter periods and for more extreme pH values. Moreover, this study performed with Carbosulfan did not investigate the hydrolysis of Carbofuran and 3-OH-carbofuran. Although the second study (Alvarez M., 1989b) was considered as acceptable (see Carbofuran DAR-Vol 3 B(2), point B.2.1.14), this study cannot be considered as valid to describe the fate of Carbofuran and its metabolites under the different processing conditions.	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. The experts do not expect any new metabolites other than that recovered in the plant metabolism. A processing factor could not be derived from the sugar beet processing study.

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			With regard to the residue levels in processed sugar beet commodities, the study (Stearns J.W., 1986) consisted of a soil treatment at an exaggerated dose rate of 4.48 kg as/ha. No residues of carbamates metabolites were recovered in the roots, cossettes, molasses and sugar (<0.01 mg/kg). It is therefore not possible to calculate a processing factor. Only low residue levels of 3-keto-7-phenol (0.02-0.03 mg/kg) were recovered in molasses and sugar suggesting that all the carbamates have been degraded totally in to the phenolic metabolites through sugar processing.	
	Open point: 3.6 Asssessment of residues in animal matrices, considering information available from all animal studies, to be submitted in an addendum and reviewed by the meeting of experts See reporting table 3(25)	**NOT:** We refer to applicant comment 3(28) from the Reporting table.	**RMS 04.2009:** RMS agrees that the available ruminants' feeding study presented in the DAR (point B.7.8.1) was not suitable to perform a robust dietary intake risk assessment with LoQs of 0.025 mg/kg and 0.05 mg/kg in whole milk and tissues, respectively provided the extremely low toxicological reference values of Carbofuran. Therefore, assuming linearity in dose and recovered residue levels in all the matrices, RMS proposed to carry out the consumer risk assessment	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. New open point (see below): Estimates of residue levels in animal products to be reconsidered in the light of the conjugates issue (see Open point 3.2).

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			considering the recovered residue values in the carbofuran metabolism studies performed on lactating goats and laying hens. To be consistent with the residue definition proposed for animal matrices (open point 3.2), the residue levels of 3-OH-carbofuran that would be expected are listed as follows considering the **120 N** and **2500 N** rates for ruminants and poultry, respectively and the recovered residue levels in the different animal matrices (see tables B.7.2.1-3 and B.7.2.2-3 in the DAR): -0.3 µg/L in milk, -0.3 µg/kg in kidney, -0.05 µg/kg in liver , -0.01µg/kg in muscle and fat, -0.01µg/kg in eggs. The assessment of the residue levels in the animal matrices were reported in the Addendum to the DAR-April 2009. These values were considered as inputs in the EFSA PRIMo and UK model to carry out the dietary risk assessment.	
	New open point 3.11 Estimates of residue levels in animal products to be reconsidered in the light of			PRAPeR 70 (4 – 8 May.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
	the conjugates issue (see Open point 3.2).			Written procedure: Open point open
	Open point: 3.7 The issue of residues in rotational crops should be discussed in a meeting of experts, taking into account the conclusion drawn on benfuracarb with regard to carbofuran residues and the interim results obtained in the new confined study (2008). See reporting table 3(26)	**NOT:** We refer to applicant comment 3(26) from the Reporting table. If a consumer risk assessment for succeeding crops should be considered, we then propose to consider that 10% of the TRR in succeeding crop expressed carbofuran + 3-OH-carbofuran (both free and conjugated). This would still be an extreme worst case assumption (1) since all metabolism data show that less than 10% of the TRR in consumable parts – at harvest – accounts for carbofuran and + 3-OH-carbofuran (both free and conjugated); and (2) since it does not takes into account the degradation of carbofuran to phenolic metabolites happening in the soil in the time interval between 2 crops.	**RMS 04.2009:** DT_{50} lab Carbofuran: 1.3-27 days. DT_{90} Carbofuran field (Netherlands, Spain, Italy) on bare soil: 4.4-91 days. . DT_{50} lab 3-OH-carbofuran: 0.22-0.3 days DT_{50} lab 3-keto-carbofuran: 1.54-8.12 days DT_{50} lab carbofuran-phenol: 0.3 day RMS disagrees on the conclusions that were drawn on Benfuracarb to require additional rotational crops since the longest DT_{90} (field) is 91 days for Carbofuran. The 2 other metabolites containing the carbamate moiety have DT_{90} ranging between 1 and 26 days. It is therefore obvious that less than 10% of the total relevant residue (carbofuran and carbamate metabolites) can be found in soil at 100 days. In the new confined rotational crop study (Rosenwald J., 2008), the uptake of Carbofuran by all plant parts at all ageing periods was very low and the level of total radioactive residues did	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. New data gap (see below): Data on further identification of residues in rotational crops has to be provided.

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			not exceed the trigger value of 0.01 mg/kg, except for spinach leaves at 30-day interval (0.031 mg/kg at harvest). The notifier mentioned that no further investigation of the TRR in spinach leaves will be undertaken because of the low levels of total recovered residues. In order to perform the dietary risk assessment, the total radioactive residues values reported for the edible parts of the rotated crops at the 30-day interval were used as inputs in the EFSA PRIMo although these residue levels are largely overestimated with regards to the most valid indicators of the total residues in crops, i.e. Carbofuran and 3-OH-carbofuran. Moreover, this approach is rather conservative as it does not consider the further degradation of these carbamate metabolites into the phenolc compounds occurring into the soil before the rotated crop is sown. These inputs in the EFSA PRIMo were : -0.006 mg/kg fort the root vegetables rotated crops, -0.001 mg/kg for the small grain rotated crops, -0.03 mg/kg for the leafy rotated crops.	

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	New data gap 3.3 identified at PRAPeR 70 meeting: Data on further identification of residues in rotational crops has to be provided.			PRAPeR 70 (4 – 8 May.2009): Data gap open Written procedure: Data gap open
	Open point: 3.8 Consumer intake assessment for sugar beet and whether any refinement is possible with the available data should be discussed in a meeting of experts. See reporting table 3(27)	**NOT:** we refer to RMS and applicant comment 3(30) from the reporting tables. The use of refine sugar consumption intake from the UK model is appropriate to reflect impact of the sugar beet use of carbofuran. See also Open point 3.5 for another refinement on the basis of the processing study.	**RMS 04.2009:** EFSA PRIMo: The maximum food intake reported at the 97.5th percentile for the UK 4-6 year old child (20.5 kg bw) and for the UK adult (76 kg bw) accounted for 1309 g/day and 1971 g/day of sugar beet root, respectively. If we assume that the sugar beet root contains approximately 16 % of sugar, the actual sugar consumption can be estimated to raise 209 g/day for the UK 4-6 year old child and 315 g/day for the UK adult. The recommended maximum sugar intake for an adult and a 4-6 year old child are 50 g/day and 40 g/day of sugar, respectively. In addition, when taking into account the no-residue situation in sugar beet root characterized by an extremely low Limit of Quantification (0.005 mg/kg for each analyte), the soil DT_{90} values	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. The majority of the experts were of the opinion that it would be acceptable to use the input value “0” for sugar beet/sugar in the intake assessment.

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			respectively for Carbofuran and 3-OH-carbofuran and assuming that any residue that may be left in the roots is substantially reduced during production of sugar, the outcome of this model can be considered as clearly conservative. With regard to the rotational crops, the input values in the EFSA PRIMo corresponded to the amount of TRR found in the succeeding crops after 30 days (simulating a crop failure). This approach is rather conservative since the residue levels of Carbofuran and 3-OH-carbofuran are lower than the TRR values (see available plant metabolism studies performed with Carbosulfan and Carbofuran) considering the $DT_{50/90}$ values of Carbofuran and 3-OH-carbofuran and also the metabolisation of Carbofuran into its other carbamate and phenolic metabolites that occurs in soil before planting the succeeding crops. RMS presented the consumer risk assessment considering all the sources of exposure to carbofuran according to the EFSA PRIMo. UK model was also used since the refined sugar consumption data is more appropriate to refine the impact of the sugar beet use of carbofuran on	

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			the consumer safety.	
	Open point: 3.9 The consumer risk assessment should be discussed in a meeting of expert, considering all relevant sources of exposure to carbofuran residues with respect to the notified use See reporting table 3(28)	**NOT:** See our comments under Open points 3.6, 3.7 and 3.8.	**RMS 04.2009:** The consumer dietary risk assessment including all means of consumer dietary exposure (animal products, rotated crops) was performed according to EFSA PRIMo and the UK model and is presented in the Addendum to the DAR-April 2009.	PRAPeR 70 (4 – 8 May.2009): Open point fulfilled. The provisionally estimated intakes, considering all relevant sources of exposure to carbofuran residues indicate a risk for consumers.
	Open point: 3.10 At the end of the discussion on carbofuran the meeting of experts may consider the MRLs (plants, animals) that should be proposed to risk managers See reporting table 3(30)		**RMS 04.2009:** RMS agrees.	PRAPeR 70 (4 – 8 May.2009): Open point open. For the time being, no MRLs can be proposed for plant and animal commodities Written procedure: Open point open
	New open point 3.12 The list of endpoints to be updated in accordance with the decisions of the meeting of experts PRAPeR 70			PRAPeR 70 (4 – 8 May.2009): Open point open. Written procedure:

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				Open point open

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: ***15*** Points for clarification: ***0*** Data gaps: ***0***			Section 4 Open points: ***5*** ***0*** Points for clarification: ***0*** Data gaps: ***0***
	Open point: 4.1 MS experts to discuss whether is there any need for DegT50 value for carbofuran-phenol for the exposure assessment or the available estimations using DisT50 are supported; and discuss moreover the vapour pressure used in the PEC calculations. Notes for the discussion: - carbofuran-phenol is regarded as minor metabolite in aerobic soil, but major in water/sediment system - carbofuran-phenol does not contain the carbamate moiety - the definition of residue regarding carbofuran-phenol might be changed - an open point is set for the discussion of the input parameters for modelling,		The RMS has requested the QSAR calculations in a later stage in the procedure. The RMS has considered, taking into account the properties of 7-phenol (metabolite without the carbamate moiety, very high Koc,…) that the discrepancy for the vapour pressure (0.28 of 1.3) was not important enough to request new PEC calculations	PRAPeR 67 (20 -24 April.2009): Open point fulfilled.

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	however the degradation parameters and adsorption parameters were already agreed by the meeting of PRAPeR 62 - another Vp value for carbofuran-phenol is reported in B.8.4.6 of the addition report of carbofuran (0.28 Pa) See reporting table 4(6)			
	Open point: 4.2 RMS to update the List of Endpoints by indicating the actual temperature or range of temperature used in the soil photolysis studies in the box of soil photolysis. See reporting table 4(11)	**NOT:** As mentioned previously, soil photolysis is not a major route of carbofuran degradation.	The listing of endpoints has been amended.	PRAPeR 67 (20 -24 April.2009): Open point fulfilled.
	Open point: 4.3 RMS to include the evaluation of the PEC calculations, which considers the soil DT50 value of 14 days and the supported application rate in an addendum. Include in the addendum all the input parameters used, all the relevant results and		**RMS:** We consider that a detailed argumentation has been given in the DARs of benfuracarb and carbofuran to exclude the studies by Saxena and Schocken. The RMS disagrees with the conclusions of the PRAPER 62 meeting on this point and would like that his argumentation is taken on board in the conclusions of carbofuran.	PRAPeR 67 (20 -24 April.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
	examples of the output files of the models as well. Note that an open point is set for discussion of the input parameters for modelling in 4(39) of the reporting table. See reporting table 4(13)		**Study by Saxena**: - In this study two soils were used, called as acidic and alkaline soil. The alkaline soil was prepared by adding lime to the collected sandy loam soil (acidic), by this the pH was modified from 5.7 to 7.7. - The soil indeed seems to be dry if compared with e.g. the FOCUS default values for sandy loam, but the moisture holding capacity of the soil was determined in this GLP study and the actual moisture content was set for this (75% of 1/3 bar=4.05%) in accordance with EPA guidelines (Very often, degradation determined according EPA guideline is slower). - The microbial biomass was checked several times throughout the study and the results show that both soils were viable at the end of the study. - According to the RMS, one soil has been tested in this study (same soil properties, except pH, same microflora). It is therefore not valid to derive 2 DT50 in order to artificially increase the mean or the median DT50.	

No.	Column A Conclusions from the Reporting Table	Column B Comments from the notifier / applicant	Column C Rapporteur Member State comments on the notifier / applicant comments	Column D Recommendations of the PRAPeR Expert Meeting / Conclusions from the written procedure
			Study by Schocken: - The pH of this sandy loam soil was also modified by lime from 5.8 to 7.1. The microbial activity of the soil was checked by measuring the evolved $^{14}CO_2$ from ^{14}C labelled glucose up to 57 days in a parallel experiment. The evolved CO_2 was continuously increasing and reached 62.3% by the end of this term. It was stated in the DAR that the carbofuran degradation in this study is occurring through a chemical rather than a microbial process (similar degradation rates under sterile and non-sterile conditions). Absence of mineralization is observed in this study The degradation of carbofuran has been determined under aerobic laboratory conditions with carbofuran, benfuracarb or carbosulfan as test substance (14 studies with DT50 ranging between 5.7 and 22.7 days) and under field conditions (5 studies with DT50 ranging between 1.3 and 27 days). Under anaerobic laboratory	

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
			conditions, the DT50 in one soil is 7.6 days. The RMS considers that there are sufficient arguments that are indicating that the DT50 of 381, 174 days (actually one soil tested in Saxena 1994) and 444 days (one soil in Schocken, 1989) are not valid. The new PECgw and PECsw have been included in the addendum.	
	Open point: 4.4 MS experts to discuss the need of the correction for degradation/recovery of the Kdoc of 43 L/kg of the metabolite 3-hydroxy-carbofuran (sandy loam soil, Speyer 2.3) or alternatively should this value completely be excluded from the exposure calculations. Note that Kdoc of 55 L/kg for 3-hydroxy-carbofuran was agreed to be used in modeling by the meeting of PRAPeR 62.	**NOT:** The 3'OH-carbofuran metabolite is not the driver for the groundwater or surface water risk assessment. The notifier will refine assessment as necessary based upon outcome of expert meeting – should this be requested.	It has been shown in the original submission that the metabolites of carbofuran were clearly not major (never at level above 5% at 2 sampling points): 3-OH-carbofuran (max 0.8%, once in 1 out of 5 soils), 3-keto-carbofuran (once at maximum level of 6.2% AR, in 1 out of 5 soils), carbofuran-phenol (=7-phenol) (max 2.1%, once in 1 out of 5 soils) (Arysta, FMC) However EPCO 31 agreed that 3-OH-carbofuran and 3-keto-carbofuran need to be further assessed as carbofuran metabolites containing the active carbamate moiety. Carbofuran-phenol does not contain the carbamate	PRAPeR 67 (20 -24 April.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 4(15)		moeity. The notifer has provided DT50 (the 3 metabolites are not persistent) and Koc (Koc for modelling has been chosen according to a worst case approach) for the metabolites. Despite the choice of worst case input parameters assumptions, the PEC gw for the metabolites are clearly below the trigger of 0.1 µg/L. The RMS considers that the change of the Koc figure has no impact on the final risk assessment.	
	Open point: 4.5 RMS to cancel all the values, which were not considered as valid by the previous peer review from the LoEP. For modeling KFoc of 22 with 1/n of 0.96 has to be used for carbofuran. See reporting table 4(19)		The mean Koc and mean 1/n factor have been recalculated considering the 3 acceptable adsorption/ desorption studies (Daly, 1988; Brandau,1976; Mamouni, 2000). The Koc values derived by Baumann (2002) were anomalously high and were withdrawn. There was no discussion in the previous PRAPER on the derivation of the Koc of 23.3 as proposed in the DAR of carbofuran. The RMS considers that the choice of the 3 studies (Daly, 1988; Brandau,1976; Mamouni, 2000) results in a worst case Koc. No discussion has taken place on the fact that the last study could be	PRAPeR 67 (20 -24 April.2009): Open point still open. The list of end points still needs to be amended. Written procedure (May 2009): Open point closed.

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
			acceptable.	
	Open point: 4.6 EFSA to emphasize in the EFSA conclusion that the leachate samples were collected in every 14 days in both studies and this might enhance the degradation in the leachate samples. See reporting table 4(25)	**NOT:** The notifier does not expect an impact to the resulting lysimeter study concentrations as carbofuran metabolites were also analyzed in the study.	The lysimeter studies have not been considered in the final risk assessmemnt	PRAPeR 67 (20 -24 April.2009): Open point closed. New open point proposed, see below.
	New open point 4.16: RMS to update the list of end points by deleting all information on the lysimeters and stating: no reliable information available.			PRAPeR 67 (20 -24 April.2009): Open point open. Written procedure (May 2009): Open point closed.
	Open point: 4.7 EFSA to emphasize in the EFSA conclusion that the lysimeter studies were performed under similar experimental conditions and these conditions were dry (very low percolation). See reporting table 4(27)	**NOT:** The lysimeter studies were conducted under observed environmental conditions in Germany. This dry conditions do not discredit the validity of the study. The lower amounts of leachate water would potentially lead to slower degradation and higher observed average concentrations both of which did not occur. In all cases, concentrations were below the 0.1 ug/L trigger for relevant metabolites.	The lysimeter studies have not been considered in the final risk assessmemnt	PRAPeR 67 (20 -24 April.2009): Open point closed, see open point 4.6

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: 4.8 RMS to state and explain why they agree or disagree with the argumentation given in the position paper by Shaaban F. Elnaggar, 2005 in an addendum. See reporting table 4(30)		The argumentation points that were available in the DAR have been repeated in an addendum Degradation studies of carbofuran and 7-phenol show that 7-phenol is a short-lived degradation product in/on soil/sediment environment. Carbofuran-phenol does not contain the carbamate moiety. Carbofuran-phenol is 4 orders of magnitude less toxic than carbofuran to aquatic organisms. This compound does not pose a risk to aquatic organisms.	PRAPeR 67 (20 -24 April.2009): Open point redundant. New open point proposed, see below.
	New open point 4.17: RMS to recalculate STEP 1 with formation fraction derived from the maximum observed sum of water and sediment % AR indicate with a footnote in the LoEP that the formation of 12 % should be replaced with 23.5 % for the sum of the water and sediment compartments.			PRAPeR 67 (20 -24 April.2009): Open point open. Written procedure (May 2009): Open point redundant. The calculation for carbofuran-phenol is not needed as the PRAPeR 67 meeting proposed to use the parent Step 3 PECs to cover the potential exposure.
	Open point: 4.9 For completeness, RMS to include in the LoEP those whole system DT50 values		In order to avoid as much as possible confusion about data ownership and data protection between the 3 carbamates dossiers, the RMS has carefully tried to present each study at	PRAPeR 67 (20 -24 April.2009): Open point still 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
	those come from the benfuracarb dossier and indicate that these values were derived from studies with benfuracarb. Indicate moreover that Millstream (A) and Millstream (D) is the same system, but different application rates were used in the experiments. See reporting table 4(31)		its right place and to avoid to mix up studies of different origins. The application rates in the Millstream systems have been added.	Written procedure (May 2009): Open point closed. Done partly by the RMS. Finalised by EFSA.
	Open point: 4.10 RMS to include in an addendum that which metabolites have toxicological relevance and which one has not. See reporting table 4(32)	**NOT:** It is the Notifer's position that carbofuran and 3'OH carbofuran are the molecules of toxicological relevance as they have been identified in soil, water, and plant studies. 3'keto carbofuran is observed infrequently and at very low levels to be relevant.in the residue definition. 7-OH carbofuran phenol is not a relevant metabolite due to the absence of a carbamate moiety.	The relevance of the metabolites has been discussed in the addendum	PRAPeR 67 (20 -24 April.2009): Open point fulfilled.
	Open point: 4.11 RMS to amend the soil incorporation depth for PECgw to 7 cm in the LoEP. See reporting table 4(38)		The incorporation depth has been changed in the listing of endpoints	PRAPeR 67 (20 -24 April.2009): Open point fulfilled.
	Open point: 4.12 MS experts to discuss the input parameters to be used		MS experts to discuss the input parameters to be used for the modelling (PECgw, PECsw)	PRAPeR 67 (20 -24 April.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
	for the modelling (PECgw, PECsw), taking into consideration that the degradation and the adsorption parameters were already discussed and agreed at the meeting of PRAPeR 62. For formation fraction of 3-keto-carbofuran and 3-hydroxy-carbofuran in soil 0.1 was accepted. See reporting table 4(39)			
	Open point: 4.13 RMS to amend the vapour pressure data of the metabolites in the relevant boxes of the LoEP. Notes: The use of 5 times higher Vp. value in the modeling can have a significant effect on the outcome in the higher range of Vp. The set of the other Vp. data (including the value of 1.32 Pa) originates from other QSAR estimations (see benfuracarb evaluation).		The RMS has requested the QSAR calculations in a later stage in the procedure. The RMS has considered, taking into account the properties of 7-phenol (metabolite without the carbamate moiety, very high Koc,…) that the discrepancy for the vapour pressure (0.28 of 1.3) was not important enough to request new PEC calculations	PRAPeR 67 (20 -24 April.2009): Open point still open. Written procedure (May 2009): Open point closed. This was not done by the RMS. EFSA performed this

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 4(41)			
	Open point: 4.14 MS experts to discuss the definition of residue. See reporting table 4(44)	**NOT:** It is the Notifer's position that carbofuran and 3'OH carbofuran are the molecules of toxicological relevance as they have been identified in soil, water, and plant studies. 3'keto carbofuran is observed infrequently and at very low levels to be relevant.in the residue definition. 7-OH carbofuran phenol is not a relevant metabolite due to the absence of a carbamate moiety.	See residue definition proposal in the DAR.	PRAPeR 67 (20 -24 April.2009): Open point fulfilled.
	Open point: 4.15 RMS to amend the list of end points in line with the discussion of the meeting of experts on carbofuran. See reporting table 4(45)		-	PRAPeR 67 (20 -24 April.2009): Open point still open. Written procedure (May 2009): Open point closed. This was not done by the RMS. EFSA performed this.
	Message from section 4 to section 5: The PECsurface water (and sediment) for carbofuran-7-phenol should be derived from the STEP 3 PEC values			PRAPeR 67 (20 -24 April.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
	for carbofuran as calculated in addendum B.8 of March 2009, which might be corrected for molar weight and maximum occurrence (if required).			

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: ***21*** Points for clarification: ***1*** Data gaps: ***0***			Section 5 Open points: ***6*** Data gaps: ***6***
5.1	Point of clarification: Applicant to provide more detailed information on the size of the granules. See reporting table 5(10)	**NOT:** **Size of granule:** the particle size distribution of Furadan 5G granule was determined by de Ryckel (2001) and reported already in the original DAR. The particle size distribution ranges from 0.4 – 0.85 mm. See point B2.2.26b in Vol. 3 of the new DAR. **Weight of granule:** Whilst 0.37 mg was mentioned in the original DAR, it is correct that FMC does not have data superseding the measurement from Knäbe *et al*. (2008), which indicates a weight of 0.87 mg per granule.	**RMS (April 2009):** No further comment.	PRAPeR 68 (4. – 8. May 2009) Point of clarification not addressed and changed into a data gap: Applicant to provide more detailed information on the size and weight of the granules.
	Open point: 5.1 MSs to discuss in an expert meeting whether the risk assessment covers also bigger granules (0.6-0.85 mm). See reporting table 5(10)		**RMS (April 2009):** The calculations for the probabilistic risk assessment have been performed for a size range of 0.4 to 0.85 mm.	PRAPeR 68 (4. – 8. May 2009) Open point closed, see point of clarification 5.1
	Open point: 5.2	**NOT:**	**RMS (April 2009):**	PRAPeR 68 (4. – 8. May 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
	MSs to discuss in an expert meeting which residue values in seedlings should be applied in the refined risk assessment for birds. Note: open points 5(14) and 5(42) should be discussed together. See reporting table 5(14)	From the study of Zietz, E. (2008) there was a 10-fold difference in residues between applications at 600 g a.s./ha and 60 g a.s./ha (see Table B.9.1.8-2 from the revised assessment report). Levels of the metabolites were also reported.	1) RMS disagrees with the statement of the notifier that the residues will decline 10 times for the lower application rate of 60 g a.s./ha, compared to the applied 600 g a.s./ha. This extrapolation should be substantiated with data, e.g. residue trials conducted at 60 g a.s./ha. 2) For the same reason, extrapolation of the factor 2.5 from the dossier of benfuracarb (cabbage) cannot be done to the dossier of carbofuran (sugar beet). 3) The RMS indicated in the DAR (Table B.9.1.12-11) why the 3-OH-carbofuran residues were not taken into account in the calculations of the RMS. "RMS considers that too much uncertainty remains on the conversion factor and has therefore presented a TER assessment based on the measurement of carbofuran alone. This element must be taken into account in the interpretation of the final risk assessment. A copy of the statement of the notifier on the lowered dose rate of 60 g a.s./ha is included in the addendum. RMS maintains its position on this issue.	Open point fulfilled. New data gaps 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
	New data gap 5.1 identified at PRAPeR 68: Further trials at the correct application rate, according to GAP and at different field conditions (N and S-Eur) are necessary in which 3-OH should be included and measurements on carbofuran and 3-OH on different timepoints should be done.			PRAPeR 68 (4. – 8. May 2009) Data gap open.
	New data gap 5.2 identified at PRAPeR 68: Further arthropod residue studies are necessary at the right application rate and GAP, in which the issue of rainfall is addressed, with behavioural observations, also including residues on dead arthropods, and at different field conditions (N and S-Eur), in which 3-OH is measured, and carbofuran and 3-OH are followed over time.			PRAPeR 68 (4. – 8. May 2009) Data gap open.
	New data gap 5.3 identified at PRAPeR 68: Further residue trials with			PRAPeR 68 (4. – 8. May 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
	earthworms are necessary at the correct application rate and GAP, in which the issue of rainfall is addressed, 3-OH is measured, and carbofuran and 3-OH are followed over time, and at different field conditions (N and S-Eur).			
	Open point: 5.3 MSs to discuss in an expert meeting the refined risk assessment for birds (3rd tier) based on the approach suggested for pirimicarb. It should also be discussed if the provided data are robust enough to support such a risk assessment approach. See reporting table 5(16)	**NOT:** We refer to our comments in 5(16).	**RMS (April 2009):** The RMS would welcome discussion in the expert meeting: Does the expert meeting consider that the “Opinion on pirimicarb” can be used to refine the risk assessment for other active substances? Under which conditions?	PRAPeR 68 (4. – 8. May 2009) After the discussion the meeting concludes that because of all the uncertainties identified, the pirimicarb-approach is not accepted. Open point fulfilled.
	Open point: 5.4 RMS to provide in an addendum a risk assessment for birds for the uptake of contaminated drinking water from puddles in line with the suggestion of the PPR opinion on the science behind the GD on risk assessment for birds and mammals (EFSA Journal,	**NOT:** It should be noted that granules are buried to a depth of ≥ 40 mm when applied in furrow with the seed. Stewardship of the product requires that exposed granules should be buried or removed. Therefore the presence of granules in drinking water puddles and the subsequent risk assessment may, when stewardship in line with the requirements of	**RMS (April 2009):** A calculation for the drinking water according to EFSA Journal is presented in an addendum (acute TER = 1.41). RMS agrees with the statement of the notifier that these calculations possibly overestimate the risk.	PRAPeR 68 (4. – 8. May 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
	July 2008) See reporting table 5(19)	authorisation is undertaken, lead to a possible overestimate of the risk.		
	Open point: 5.5 RMS to indicate in the corrected DAR and in the LoEP that the long-term reproductive NOEC for birds of 10 ppm includes only reproductive effects but not parental mortality which was observed at concentrations of 2, 5 and 10 ppm. See reporting table 5(20)		**RMS (April 2009):** The DAR and the List of Endpoints are corrected accordingly.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled.
	Open point: 5.6 MSs to discuss the long-term endpoint to be used in the risk assessment for birds. See reporting table 5(21)	**NOT:** See comment 5(21)	**RMS (April 2009):** The RMS is of the opinion that the adult mortalities observed in the reproduction study are not relevant for the risk assessment (12 weeks exposure period is an overestimation of the exposure in the field).	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. New open point proposed, see below.
	New open point 5.22: RMS to recalculate the risk with the trigger of 10. The long-term NOEC of 1.5 ppm will be removed from the LoE and the reproduction study from the list of studies		**RMS (May 2009):** The DAR and the List of Endpoints are corrected accordingly.	PRAPeR 68 (4. – 8. May 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
	relied on. The LC10 of 0.64 will be included in the LoE also as reproductive endpoint.			
	Open point: 5.7 MSs to discuss in an expert meeting whether the quantitative refinement of PT and PD values are sufficiently supported by data. See reporting table 5(23)	**NOT:** We believe that we are using appropriate values from the guidance document (see 5(23)).	**RMS (April 2009):** The calculations with PD = 1 are already performed in the first tier. The RMS would welcome discussion in the expert meeting. As RMS, we consider that EFSA and MS have discarded our proposals for PD/PT factors, however without proposing acceptable ways for refinement: According to our last information, the new guidance opinion on risk assessment is not yet in application. We therefore invite EFSA to propose its own evaluation and to explain clearly how to perform the risk assessment for birds and mammals on the basis of the available database. - Is the guidance document SANCO/4145/2000 (Sept 2002) still acceptable? - What are acceptable PD and PT values for relevant bird species in	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. 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
			sugar beet crop? How would you use the bird/mammal diet information that is proposed in the "bird/mammal bible – Crocker *et al*., 1998)"? - How to address the determination of an acute PD factor for an acutely toxic compound? - Which interesting results can be expected from a radio-tracking study? How many replicates? How to perform this study?	
	New open point 5.23: RMS should indicate in the LoE that the PT and PD values used in the TER calculations are only for illustrative purposes.		**RMS (May 2009):** The List of Endpoints is corrected accordingly.	PRAPeR 68 (4. – 8. May 2009) Open point open.
	Open point: 5.8 MSs to discuss the risk assessment for birds for the uptake of granules. See reporting table 5(24)	**NOT:** See comments at 5(24)	**RMS (April 2009):** The RMS would welcome discussion in the expert meeting. Is the EPPO scheme for calculations of risk to granules still valid? Does the meeting whish to apply a supplementary safety factor in the calculations?	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. New data gap proposed, see below.
	New data gap 5.4 identified at PRAPeR 68: Notifier to address the risk to			PRAPeR 68 (4. – 8. May 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
	birds from exposure to granules, considering all comments of RMS and PRAPeR meeting. Concerns were raised in the meeting about the possibility to address the risk considering the high risk to birds after intake of only one granule.			
	Open point: 5.9 MSs to discuss in an expert meeting the risk assessment for mammals for the uptake of granules. See reporting table 5(31)	**NOT:** We agree with the comments of the RMS (5(31))	**RMS (April 2009):** According to the theoretical calculations based on the EPPO scheme, the risk to mammals *accidentally* ingesting Furadan 5G granules when seeking food, would be acceptable: ETR are 0.049, 0.010 and 0.039 respectively for the short-term, medium-term and long-term risk assessment. Where the ETR < 1, the risk is considered to be low. These ETR are equivalent to TER values of respectively 21, 95 and 26 showing acceptable acute and long-term risk to mammals. The RMS considers the risk to mammals acceptable since they do not consume grit.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled.
	Open point: 5.10 MSs to discuss the PD/PT values suggested in the	**NOT:** The feeding behaviour of mammals may show differences between MS	**RMS (April 2009):** The RMS would welcome discussion in the expert meeting.	PRAPeR 68 (4. – 8. May 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
	refined risk assessment for mammals. See reporting table 5(32)	due to different habitats because of differences in agronomic practices. For an Annex I inclusion of a representative use however, it appears appropriate to initially use robust representative values, e.g. the 'Mammal Bible', which may be refined within MS should an Annex I inclusion follow.	- What are acceptable PD and PT values for relevant bird species in sugar beet crop? How would you use the bird/mammal diet information that is proposed in the "bird/mammal bible – Crocker *et al*., 1998)"? - How to address the determination of an acute PD factor for an acutely toxic compound?	New data gap proposed, see below.
	New data gap 5.5 identified at PRAPeR 68: The risk to mammals needs to be addressed further.			PRAPeR 68 (4. – 8. May 2009) Data gap open.
	Open point: 5.11 MSs to discuss in an expert meeting the refined risk assessment for mammals based on the approach suggested for pirimicarb. It should also be discussed if the provided data are robust enough to support such a risk assessment approach. See reporting table 5(35)	**NOT:** See comment at 5(35)	**RMS (April 2009):** The RMS would welcome discussion in the expert meeting: Does the expert meeting consider that the "Opinion on pirimicarb" can be used to refine the risk assessment for other active substances? Under which conditions?	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled.
	Open point: 5.12 MSs to discuss in an expert meeting the endpoint to be		**RMS (April 2009):** The long-term risk resulting from the use of carbofuran is not the most	PRAPeR 68 (4. – 8. May 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
	applied in the long-term risk assessment for mammals. See reporting table 5(40)		ecologically relevant: Main toxicological effects are related to the acute effects of cholinesterase inhibition. The exposure through crop seedlings or invertebrates is short-lived as indicated in the residue trials. The RMS would welcome discussion in the expert meeting to decide on the appropriate NOAEL.	New open point proposed, see below.
	New open point 5.24: the relevant long-term endpoint for mammals has to be determined.		**RMS (May 2009):** RMS included its position in the addendum (update May 2009) on the relevant long-term endpoint for mammals (NOAEL = 0.1 mg a.s./kg b.w./day).	PRAPeR 68 (4. – 8. May 2009) Open point open.
	Open point: 5.13 MSs to agree on the residues in sugar beet seedlings used in the refined risk assessment for mammals. See reporting table 5(42)	**NOT:** See comment under open point 5.2.	**RMS (April 2009):** 1) RMS disagrees with the statement of the notifier that the residues will decline 10 times for the lower application rate of 60 g a.s./ha, compared to the applied 600 g a.s./ha. This extrapolation should be substantiated with data, e.g. residue trials conducted at 60 g a.s./ha. 2) For the same reason, extrapolation of the factor 2.5 from the dossier of benfuracarb (cabbage) cannot be done to the dossier of carbofuran (sugar beet).	PRAPeR 68 (4. – 8. May 2009) Open point closed., see open point 5.2

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
			3) The RMS indicated in the DAR (Table B.9.3.2-18) why the 3-OH-carbofuran residues were not taken into account in the calculations of the RMS. "RMS considers that too much uncertainty remains on the conversion factor and has therefore presented a TER assessment based on the measurement of carbofuran alone. This element must be taken into account in the interpretation of the final risk assessment. A copy of the statement of the notifier on the lowered dose rate of 60 g a.s./ha is included in the addendum. RMS maintains its position on this issue.	
	Open point: 5.14 RMS to provide in an addendum a risk assessment for mammals for the uptake of contaminated drinking water from puddles in line with the suggestion of the PPR opinion on the science behind the GD on risk assessment for birds and mammals (EFSA Journal, July 2008)	**NOT:** See comment under open point 5.4.	**RMS (April 2009):** A calculation for the drinking water according to the EFSA Journal is presented in an addendum (acute TER = 20).	PRAPeR 68 (4. – 8. May 2009) Open point closed, see open point 5.4

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	See reporting table 5(47)			
	Open point: 5.15 RMS to present in an addendum the TER calculations for *C. riparius* based on refined PECsed values (FOCUS step2 and step3). See reporting table 5(50)		**RMS (April 2009):** The risk for sediment dwelling organisms is considered acceptable since the calculations in surface water (TER = 155 in Table B.9.2.16.2-6) demonstrate acceptable risk. Moreover, the TER of 2.11 in sediment is based on a worst-case endpoint (FOCUS step 1: maximum concentration achieved in sediment). The notifier provided new PECsw FOCUS step 3 calculations. The TER calculations of the RMS based on these new PECsw values are presented in an addendum. The risk of 7-phenol to sediment dwelling organisms is acceptable (TER > 680000).	PRAPeR 68 (4. – 8. May 2009) Open point still open for RMS to check final PECs. **RMS (May 2009):** The List of Endpoints is corrected accordingly.
	Open point: 5.16 MSs to discuss in an expert meeting whether a new acute toxicity study with 3-keto-carbofuran and *Ceriodaphnia dubia* is necessary. See reporting table 5(51)	**NOT:** We agree with the RMS	**RMS (April 2009):** The RMS considers that a new study is not required and that the margin of safety is sufficient (TER values between 9608 and 81667 based on FOCUS step 3 calculations). There was a calculation error which is corrected in the updated DAR. The notifier provided new PECsw FOCUS step 3 calculations. The TER calculations of the RMS based on	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. New open point proposed, see below.

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			these new PECsw values are presented in an addendum. The risk of 3-keto-carbofuran to aquatic invertebrates is acceptable (TER > 6203).	
	New open point 5.24: RMS to add a footnote to the LoE explaining why the study was accepted.		**RMS (May 2009):** The List of Endpoints is corrected accordingly.	PRAPeR 68 (4. – 8. May 2009) Open point open.
	Open point : 5.17 RMS to include the mean measured concentrations from the studies with sediment dwellers and carbofuran 7-phenol and carbofuran in the LoEP and in an addendum and to provide a revised risk assessment in an addendum and to update the LoEP See reporting table 5(52)		**RMS (April 2009):** For the study with 7-phenol, the nominal concentration of 10 mg/L corresponds to the mean measured concentration of 5.34 mg/L. For the study with carbofuran, the nominal concentration of 0.004 mg a.s./L corresponds to the mean measured concentration of 0.0032 mg a.s./L. The TER calculations based on mean measured concentrations are presented in an addendum. The List of endpoints is corrected accordingly. The outcome of the risk assessment remains unchanged.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. New open point proposed, see below.
	New open point 5.25: I the Step 1 calculation for 7-phenol, the carbofuran		**RMS (May 2009):** The List of Endpoints is corrected accordingly.	PRAPeR 68 (4. – 8. May 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
	endpoint was used instead of 7-phenol endpoint, RMS should revise this in the list of end points.			
	Open point: 5.18 MSs to discuss in an expert meeting whether the studies with Rove Beetle (Schmuck R., 1993, p. 194-195 and Schmuck R., 1993, p. 201-203) and the study on Carabid Beetles (Schmuck, 1993, p 198-200) are acceptable since no positive control was tested See reporting table 5(55)	**NOT:** In the absence of suitable information the studies may provide supplementary information to identify which terrestrial organisms may be at a potential risk following application of carbofuran granules in furrow. We agree with the RMS that should the studies not be acceptable the outcome of the risk assessment would not change because of the availability of field studies.	**RMS (April 2009):** An extensive database containing laboratory studies on numerous organisms and field studies has been evaluated. The RMS believes that the 3 studies are acceptable. However, if the meeting would consider these 3 studies as not acceptable, this would not change the outcome of the risk assessment.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled.

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	Open point: 5.19 MSs to discuss in an expert meeting whether the field study performed with a capsule suspension preparation (Strömel C. *et al*., 2002) can be used to address the risk from the granular formulation suggested in the representative use. See reporting table 5(62)	**NOT:** We agree with the RMS that analytical measurements from the study demonstrated exposure of the test organisms to carbofuran at a higher concentration than that predicted following application in line with the proposed GAP (in-furrow application at 60 – 600 g a.s./ha).	**RMS (April 2009):** The position paper of the notifier is presented on p. 240-241 in the DAR. The average actual concentration in the soil at day 0 was 2.8 mg carbofuran/kg wet soil. This test concentration covers the maximum PECsoil of 0.8 mg carbofuran/kg soil.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled. New data gap proposed, see below.
	New data gap 5.6 identified at PRAPeR 68: Notifier to provide further details on this study (Broadbent and Tomlin) to support the use of the field study.			PRAPeR 68 (4. – 8. May 2009) Data gap open.
	Open point: 5.20 RMS to include a statement in the updated DAR or in an addendum that the risk to other soil dwelling macro-organisms is not addressed for the use rate of 0.6 kg a.s./ha.		**RMS (April 2009):** The statement is included in the updated DAR on p. 246.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled.

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	See reporting table 5(63)			
	Open point: 5.21 RMS to correct in the LoEP the interchanged TER values for *Hypoaspis aculeifer* and *Folsomia candida.* See reporting table 5(68)		**RMS (April 2009):** The List of Endpoints is corrected accordingly.	PRAPeR 68 (4. – 8. May 2009) Open point fulfilled.
	Vol. 1, Level 4 Data gaps in ecotoxicology	**EFSA:** The refined risk assessment for birds and mammals resulted in TERs below the triggers. The data gap identified in level 4 states that more information is needed on residue levels in feed items. However it is not clear if such a refinement would be sufficient to demonstrate a low risk. Further refinement may be necessary. Therefore it is suggested to broaden the wording of the data gap to “further refinement of the risk assessment to birds and mammals for the uptake of carbofuran residues in feed items is needed”.	**Comment of the reporting table added by RMS (April 2009):** The RMS would welcome discussions in the expert meeting: As RMS, we consider that EFSA and MS have discarded our proposals for PD/PT factors, however without proposing acceptable ways for refinement: According to our last information, the new guidance opinion on risk assesment is not yet in application. We therefore invite EFSA to propose its own evaluation and to explain clearly how to perform the risk assessment for birds and mammals on the basis of the available database. - Is the guidance document SANCO/4145/ 2000 (Sept 2002) still applicable?	PRAPeR 68 (4. – 8. May 2009) ??? **RMS (May 2009):** The discussions on these issues were integrated in the points above.

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			- What are acceptable PD and PT values for relevant bird species in sugar beet crop? How would you use the bird/mammal diet information that is proposed in the "bird/mammal bible – Crocker *et al*., 1998" - How to address the determination of an acute PD factor for an acutely toxic compound? - Which interesting results can be expected from a radio-tracking study? How many replicates? How to perform this study? - Is it necessary to request additional residue trials in beet seedlings, earthworms and arthropods (which GAP, in-furrow, at the plant hole, or seed treatment)? Is the EPPO scheme for calculations of risk to granules still valid? Does the meeting whish to apply a supplementary safety factor in the calculations? We would welcome a discussion in the expert meeting on the applicability of probabilistic risk assessment. Does the expert meeting consider that the "Opinion on pirimicarb" can be	

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			used to refine the risk assessment for other active substances? Under which conditions? The RMS would welcome discussion in the expert meeting to decide on the appropriate NOAEL for the long-term risk to mammals. **NOT:** We believe that the evaluation should consider the RA at the application rate of 60 g ai/ha (see also Article 15 1b of regulation 33/2008/EC), and the experts should define what refinement route is acceptable. For example, how could the reversibility of the carbamates AChE depression be considered in the RA?	
	Message from section 4 to section 5: The PECsurface water (and sediment) for carbofuran-7-phenol should be derived from the STEP 3 PEC values for carbofuran as calculated in addendum B.8 of March 2009, which might be corrected for molar weight and maximum occurrence (if required).			PRAPeR 68 (4. – 8. May 2009) noted.