CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance carbosulfan[1]

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SUMMARY

Carbosulfan is one of the 52 substances of the second stage of the review programme covered by Commission Regulation (EC) No 451/2000[i3] as amended by Commission Regulation (EC) No 1490/2002[4]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

Belgium being the designated rapporteur Member State submitted the DAR on carbosulfan in accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, which was received by the EFSA on 11 August 2004. Following a quality check on the DAR, the peer review was initiated on 17 August 2004 by dispatching the DAR for consultation to the Member States and the sole applicant FMC Chemical sprl. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed in an evaluation meeting on 18 May 2005. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in September 2005.

Following the Commission Decision of 16 June 2007 (2007/415/EC)[5] concerning the non-inclusion of carbosulfan in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the notifier FMC made a resubmission application for the inclusion of carbofuran in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the areas of concern identified in the review report as follows: the consumer exposure, the risk to ground water, operator exposure, risk to birds and mammals, risk to aquatic organisms, risk to bees, earthworms, non target arthropods and non-target micro-organisms and plants.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, Belgium, being the designated rapporteur Member State, submitted an evaluation of the additional data on Carbosulfan in the format of an Additional Report (Belgium, 2009a). The Additional Report was received by the EFSA on 13 May 2009. In accordance with Article 19, the EFSA distributed the Additional Report to the Member States and the applicant

1 On request from European Commission Question No EFSA-Q-2009-00730, issued on 16 October 2009.
2 Correspondence: praper@efsa.europa.eu
3 OJ No. L 53, 29.02.2000, p.25
4 OJ No. L 224, 21.08.2002, p. 25
5 OJ No L 156, 16.06.2007, p.30
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for comments on 18 May 2009. The EFSA collated and forwarded all comments received to the Commission on 16 June 2009. At the same time the collated comments were forwarded to the rapporteur Member State for compilation in the format of a Reporting Table.

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

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

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

The original conclusion from the review was reached on the basis of the evaluation of the representative use as an insecticide on sugar beet. The use on maize in the original conclusion has not been supported in the resubmitted dossier under Commission Regulation (EC) 33/2008. Full details of the GAP can be found in the list of end points. Carbosulfan can be used as an insecticide and nematicide. It should be noted that during the peer review process only the use as an insecticide was evaluated. The representative formulated product for the evaluation was "Marshal 10G", a granule (GR), registered in some Member States of the EU. It should be noted that the applicant no longer supports the second formulation, presented in the dossier and DAR ("Marshal 25CS"). Consequently also the uses on citrus and cotton are no longer supported. In the resubmitted dossier the applicant proposed a reduced application rate on sugar beet. This was rejected by the RMS as it was not considered a representative use.

There are methods available to monitor all compounds given in the respective provisional residue definitions for food of plant and animal origin, body fluids and tissues, however data gaps were identified for additional validation data for the hydrolysis step of the monitoring methods for plant matrices and for an ILV. If MRLs are to be set for animal products in the future then validation of the hydrolysis step in the methods would be needed. For the environmental matrices sufficient methods are available for soil, for water the LOQ is not low enough for drinking water and also the method does not analyse for 3-keto-carbofuran for drinking and surface water. For air there is no method for carbofuran available (see data gap). Published multi-residue methods allowing determination of all compounds included in the proposed residue definitions in all matrix groups are not available.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Carbosulfan is toxic if swallowed and should be classified as T, R25 "Toxic if swallowed". It is of low toxicity via dermal route and toxic via inhalation (classification as T, R23 "Toxic by inhalation" is proposed). Carbosulfan is not a skin or eye irritant but is a skin sensitiser and should be classified R43 "May cause sensitisation by skin contact". Carbosulfan gave negative results in the *in vitro* and *in vivo* genotoxicity tests and did not show any carcinogenic potential. In the three-generation rat study, the relevant parental and reproductive NOAEL was 1.2 mg/kg bw/day. In developmental toxicity studies in rats and rabbits, the relevant maternal and developmental NOAEL was 2 mg/kg bw/day. Carbosulfan displayed no potential for induced delayed neurotoxicity. In acute and subchronic neurotoxicity studies in rat decreased brain acetylcholinesterase activity was the critical finding, being the acute NOAEL 0.5 mg/kg bw and the subchronic NOAEL 1.2 mg/kg bw/day. All three reference values are based on the acute neurotoxicity study: ADI, AOEL and ARfD are 0.005 mg/kg bw/day, applying a safety factor of 100. According to the PHED model calculations, operator exposure is below the AOEL when operators use gloves during the loading and application operations. It is considered that bystander and worker exposure is likely to be negligible under the supported conditions of use.

Based on all available data the metabolic pathway of carbosulfan in soil applied uses can be considered as sufficiently investigated. Carbosulfan on one hand and the sum of carbofuran, 3-hydroxy-carbofuran and 3-keto carbofuran and their conjugates on the other hand were considered the relevant residues to assess consumer

exposure and consumer risk. However, a need to fully address residues and in particular their identity in succeeding crops was identified.

Supervised residue trials in sugar beet, indicated that residues were very low (between LOQ and LOD) and in all submitted trials below the LOQ. However, data to demonstrate the analytical method used in the residue trials has efficiently determined conjugated residues is still necessary in order to validate the residue data.

In livestock, carbosulfan undergoes an extensive metabolisation. 3-hydroxy-carbofuran and 3-keto-carbofuran free and conjugated were considered the relevant residue in animal matrices to assess consumer exposure and consumer risk. On the basis of available data the ratio of free and the conjugated residues in animal matrices could not be established, and therefore it was proposed to include the conjugates of 3-hydroxy carbofuran in the animal residue definition for monitoring. It has to be elaborated whether residues of 3-keto carbofuran (free and conjugated) can be taken into account by a conversion factor, or need to be included in the residue definition for monitoring.

The RMS has provided a comprehensive dietary exposure and risk assessment for consumers using both the EFSA PRIMo and the UK model for a review by the experts, which can be considered being indicative.

The sum of intakes of carbofuran and 3-hydroxy carbofuran from the primary crop, rotational crops and food of animal origin was estimated and compared to the toxicological reference values for carbofuran. An **exceedance of the ADI** was noted for UK toddlers. Moreover, the acute consumer risk assessment indicates the **ARfD is significantly exceeded** for a number of crops, mainly succeeding crops, consumed by children and by adults/the general population. The results highlight the importance of further residue data on succeeding crops to enable refinement of the dietary risk assessment for consumers.

In order to further refine the risk assessment a data gap was identified for the applicant to address the residue levels of the carbamate structured metabolites in sugar. To mitigate the identified risk it was moreover suggested to restrict crop rotation to cereals only, but further data and assessment of the proposed scenario will be necessary. Based on the available data no further refinement of the consumer risk assessment is currently possible.

EFSA notes that significant contribution to the acute and chronic exposure might be expected through drinking water derived from groundwater if any restrictions that might be considered to mitigate leaching of residues of carbofuran were not effective.

In soil under laboratory aerobic conditions, carbosulfan yields carbofuran (max. 48.7 % - 69.3 % AR after 3-7 d). Also 3-keto-carbofuran is produced in significant amounts (max. 5.3 % - 6.6 %) and needs to be further assessed as it contains the active carbamate moiety, as the minor transient metabolite 3-OH-carbofuran. The mineralization was very limited and bounded residues increased up to maximum of 90 % AR after 100 d. In a study performed with ^{14}C-dibutylamine labelled carbosulfan, dibutylamine was found as a major aerobic soil metabolite. No valid degradation study of carbosulfan in soil under anaerobic conditions is available. Also photolysis in soil was not investigated. Metabolite carbofuran was considered stable to photolysis in soil in its DAR. Evaluation meeting agreed that a re-evaluation of the degradation kinetic in degradation studies had to be performed. Reassessments and new degradation studies for the metabolites are available in the additional report. Carbosulfan exhibited very low to low persistence, while carbofuran exhibited low to high persistence. Metabolite carbofuran-phenol (another minor soil metabolite, but major in water/sediment systems) and 3-OH-carbofuran exhibited very low persistence, while 3-keto-carbofuran and dibutylamine exhibited very low to low persistence. Summaries of some field dissipation studies in EU are available. Half life of carbosulfan in these trials ranges between 0.35 to 9.8 d, half life of carbofuran is between 1.3 to 27 d and half life of dibutylamine is between 2.2-54 days. EFSA notes that, in the context of the carbofuran discussion, the meeting of MS experts was not able to determine the reliability of these studies. PEC in soil were calculated in the additional report for carbosulfan, carbofuran and dibutylamine based on the field worst case half lives and the representative uses in sugar beet. Based on new studies that are evaluated in the additional report, carbosulfan is classified as immobile compound. 3-hydroxy-carbofuran exhibits very high to high mobility and 3-keto-carbofuran exhibits very high to low mobility in soil, while carbofuran-phenol exhibits medium to low mobility. For the metabolite carbofuran an acceptable study (from a different notifier Dianica) is available in its dossier as active substance. Carbofuran is classified as very high mobile compound. A lysimeter study is available. However, annual average concentrations and detailed characterization of the residue are missing. Two new lysimeter studies performed with carbofuran were submitted and assessed, but were regarded as non-conclusive studies. Carbosulfan hydrolyses with half lives lower than 1 d at pH 5 and 7 and of 7 d at pH 9. Main products are carbofuran and

dibutylamine. Carbofuran degrades to carbofuran-7-phenol. Photolysis may contribute to the environmental degradation of carbosulfan in water. Two regions of polar degradation products (66.7 % AR) were found but not characterized. The formation of these unidentified polar products in natural water bodies is assumed to be low, as long as furrow application is used. Carbosulfan is not readily biodegradable. Carbosulfan was low persistent in aerobic water/sediment systems. Main metabolites formed were carbofuran (max. 34.7 % AR in water; max. 20.1 % AR in sediment) and carbofuran-phenol (max. 23.2% AR in water; max. 6.22% AR in sediment). A non characterized metabolite (Unknown 3) appears at levels above 10 % AR in the sediment of some systems (max. 20.11 % AR after 7 d). This compound has been tentatively identified as a structure that contains the carbamate moiety and may be expected to produce carbofuran when degraded. It is unlikely that this compound can occur in surface water in significant level, as long as carbosulfan is used via furrow application. The amount of bound residues increased steadily up to 30.5 – 43.0 % AR at the end of the experiments (102 d). No half lives are reported in carbosulfan DAR for metabolites carbofuran and carbofuran-7-phenol in the water / sediment systems.However for the resubmission, the residues of carbosulfan and the metabolites carbofuran and carbofuran-phenol were refitted and degradation endpoints were (re)calculated. Degradation endpoints from water / sediment studies summarized in the carbofuran DAR were also recalculated. Available water sediment studies under alkaline conditions (from carbofuran applicant Dianica) showed faster degradation of carbofuran and the formation of carbofuran-7-phenol at higher levels. For the resubmission, FOCUS PECSW/SED were calculated for all the relevant metabolites. The applicant presented an estimation of the potential for ground water contamination based on the FOCUS GW scheme.

The potential for groundwater exposure from the representative uses by the parent carbosulfan or the metabolite dibutylamine above the parametric drinking water limit of 0.1 µg/L, was concluded to be low in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. However it is noted that some parameters of the metabolite dibutylamine used in the simulations are uncertain. The main metabolite carbofuran was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations >0.1µg/L in case of 8 out of the 9 modelled FOCUS scenarios with the range of 0.22-4.09 µg/L using the PEARL model, and 7 out of the 9 modelled FOCUS scenarios with the range of 0.32-0.73 µg/L using the PELMO model, when annual applications were simulated. Only the Porto (PEARL) or Porto and Thiva (PELMO) FOCUS scenarios resulted in a PECgw value <0.1µg/L (0.023 µg/L, 0.009 µg/L and 0.004 µg/L, respectively). When triennial applications were simulated by FOCUS PEARL, 7 out of the 9 modelled FOCUS scenarios exceeded the 0.1µg/L parametric drinking water limit with the range of 0.24-1.11 µg/L, and again Porto and Thiva FOCUS scenarios resulted in a PECgw value <0.1µg/L (0.012 µg/L and 0.069 µg/L, respectively). When FOCUS PELMO was used for the simulation of triennial applications, 5 out of the 9 modelled FOCUS scenarios exceeded the 0.1µg/L parametric drinking water limit with the range of 0.15-0.30 µg/L. The Kremsmünster, Porto, Sevilla and Thiva FOCUS scenarios resulted PECgw <0.1µg/L (0.002 – 0.099 µg/L). The PECgw for the metabolites 3-keto-carbofuran and 3-hydroxy-carbofuran exceeded the 0.1µg/L parametric drinking water limit only in a few cases of FOCUS simulations when annual applications were simulated. When triennial applications were simulated, 3-keto-carbofuran exceeded this trigger only in one case (FOCUS PEARL, Piacenza scenario) of the simulations. However, it is noted that the simulations for the metabolites were regarded as worst case, as 100 % formation was assumed (which would be expected to be lower in reality). On the other hand it is also noted that another parameter (DT_{50} of the parent molecule) used in these simulations is regarded as favourable for all the metabolites. In summary, the potential for groundwater exposure from the representative uses by carbofuran, as a metabolite of the parent carbosulfan, above the parametric drinking water limit of 0.1 µg/L, was concluded to be very high in geo-climatic situations that are represented by 8 out of the 9 FOCUS groundwater scenarios.

Even at the drinking water limit of 0.1 µg/L that is applied to groundwater, consumer exposure would be greater than 10% of the toxicological reference values for vulnerable consumer groups (toddlers and infants). Therefore a drinking water limit <0.1 µg/L is needed for the carbamate structured metabolites according to uniform principles. However, a method with a validated LOQ < 0.1 µg/L for each analyte is not available.

It is not expected that either carbosulfan or its transformation product carbofuran (from data in carbofuran dossier) may contaminate the air compartment or be prone to long range transport through air.

The risk to birds and mammals from uptake of granules was assessed as acceptable provided that spills are avoided and the product is incorporated in soil. A high risk to birds and mammals was identified from residues in contaminated food items. The risk to birds and mammals needs to be further addressed. The risk to aquatic organisms was assessed as low for environmental conditions represented by the FOCUS scenarios D3, D4(stream), R1 and R3. A high risk was indicated for the scenario D4 (pond). Severe adverse effects were

observed in laboratory studies with non-target arthropods. No statistical significant effects on non-target arthropods were observed in a field study indicating a low risk to non-target arthropods. No valid laboratory studies were available with earthworms. The risk assessment was based on a field study with broadcast application. In order to draw a final conclusion on the risk to earthworms it would be necessary to demonstrate that exposure in the field study is representative also for the in-furrow application of the granules. Alternatively a new field study where the representative use is simulated is needed.

The risk to bees, soil non-target micro-organisms, non-target plants and biological methods of sewage treatment was assessed as low.

KEY WORDS

Carbosulfan, peer review, risk assessment, pesticide, insecticide, nematicide

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BACKGROUND

Commission Regulation (EC) No 451/2000 laying down the detailed rules for the implementation of the second and third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC, as amended by Commission Regulation (EC) No 1490/2002, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Carbosulfan is one of the 52 substances of the second stage covered by the amended Regulation (EC) No 451/2000 designating Belgium as rapporteur Member State.

In accordance with the provisions of Article 8(1) of the amended Regulation (EC) No 451/2000, Belgium submitted the report of its initial evaluation of the dossier on carbosulfan, hereafter referred to as the draft assessment report, to the EFSA on 11 August 2004. In accordance with Article 8(5) of the amended Regulation (EC) No 451/2000 the draft assessment report was distributed for consultation on 17 August 2004 to the Member States and the main applicant FMC Chemical sprl as identified by the rapporteur Member State.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed in an evaluation meeting on 18 May 2005 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level. A representative of the notifier attended this meeting.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings organised on behalf of the EFSA by the EPCO-Team of the Pesticide Safety Directorate (PSD) in York, United Kingdom in September 2005. The reports of these meetings have been made available to the Member States electronically.

A discussion of the outcome of the consultation of experts took place with representatives from Member States on 8 June 2006 leading to the conclusions as laid down in the EFSA conclusion issued on28 July 2006 (EFSA Scientific Report (2006) 90).

Following the Commission Decision of 16 June 2007 (2007/415/EC)[6] concerning the non-inclusion of carbosulfan in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the notifier FMC made a resubmission application for the inclusion of carbofuran in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the areas of concern identified in the review report as follows: the consumer exposure, the risk to ground water, operator exposure, risk to birds and mammals, risk to aquatic organisms, risk to bees, earthworms, non target arthropods and non-target micro-organisms and plants.

Belgium, being the designated rapporteur Member State, submitted the additional report (Belgium, 2009) on carbosulfan to the EFSA on 13 May 2009. In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA dispatched the additional report to Member States and the notifier for consultation. The comments received were subsequently submitted to the Commission for evaluation. In accordance with Article 20 of Commission Regulation (EC) No. 33/2008, the Commission subsequently requested the EFSA, by letter received on 20 July 2009 to arrange a peer review of the evaluation, i.e. the additional report provided by the rapporteur Member State, and to deliver its conclusion on the risk assessment within 90 days.

[6] OJ No L 156, 16.06.2007, p.30

The peer review was initiated on 18 May 2009. The comments received on the additional report were dispatched to the rapporteur Member State for examination. The rapporteur provided a response to the comments in the reporting table, which was subsequently evaluated by the EFSA to identify the remaining issues to be further considered in a series of scientific meetings with Member State experts in September 2009.

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

The original conclusion from the review was reached on the basis of the evaluation of the representative use as an insecticide on sugar beet and Maize. The use on maize in the original conclusion has not been supported in the dossier submitted under the Commission Regulation No, (EC) 33/2008. Full details of the GAP can be found in the list of end points. It should be noted that the applicant no longer supports the second formulation, presented in the dossier and DAR ("Marshal 25CS"). Consequently also the uses on citrus and cotton are no longer supported. Carbosulfan can be used as an insecticide and nematicide. It should be noted that during the peer review process only the use as an insecticide was evaluated. The representative formulated product for the evaluation was "Marshal 10G", a granule (GR), registered in some Member States of the EU. In the resubmitted dossier the applicant proposed a reduced application rate on sugar beet This was rejected by the RMS as it was not considered a representative use.

The documentation developed during the peer review was compiled as **a peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

the comments received (initial and resubmission)

the resulting reporting table (rev. 1-1 of 08 June 2005) and (rev. 1-1 of 31 July 2009)

the consultation report (initial review)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

the reports of the scientific expert consultation (initial review and resubmission)

the evaluation table (rev. 2-1 of 19 June 2006) and (rev. 2-1 of 12 October 2009)

Given the importance of the draft assessment report including its addendum (compiled version of May 2006 containing all individually submitted addenda), the additional report including its addenda (compiled version of October 2009) and the peer review report with respect to the examination of the active substance, these documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Carbosulfan is the ISO common name for 2,3-dihydro-2,2-dimethylbenzofuran-7-yl (dibutylaminothio)methylcarbamate (IUPAC).

Carbosulfan belongs to the class of benzofuranyl methylcarbamate insecticides such as benfuracarb and carbofuran. It belongs also to the class of carbamate nematicides. Carbosulfan is a systemic insecticide with contact and stomach action. The biological activity is based on a cleavage of the S-N-carbamate bond, which leads to the formation of carbofuran. Carbofuran inhibits the cholinesterase in the nervous system.

The representative formulated product for the evaluation is "Marshal 10G", a granule (GR), registered in some Member States of the EU. It should be noted that the applicant no longer supports the second formulation, presented in the dossier and DAR ("Marshal 25CS"). Consequently the uses on citrus and cotton are no longer supported.

The evaluated representative uses as insecticide comprise incorporation into soil (at drilling) to control soil insects, where maize and sugar beet will be grown. The application rate is 0.75 kg carbosulfan per hectare. Carbosulfan can be used as insecticide and nematicide. It should be noted that during the peer review process only the use as insecticide was evaluated.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. IDENTITY, PHYSICAL/CHEMICAL/TECHNICAL PROPERTIES AND METHODS OF ANALYSIS

The minimum purity of carbosulfan as manufactured should not be less than 890 g/kg (before adding the stabilizer), which is in compliance with the FAO specification 417/TC/S/F (1991).

The technical material contains three impurities which have to be regarded as relevant: carbofuran, 5-chlorocarbofuran and N-nitrosodibutylamine. The maximum content in the technical material should not be higher than 20 g/kg for carbofuran and 0.3 g/kg for 5-chlorocarbofuran and 1 mg/kg for N-nitrosodibutylamine. Only carbofuran is mentioned in the FAO specification.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of carbosulfan or the respective formulation. However, the following data gap was identified:

- Shelf life study with analysis of 5-chlorocarbofuran and N-nitrosodibutylamine.

Furthermore, it should be noted that the data on the tap density is not in line with the FAO specification 417/GR/S/F (1991)[7]. Data for carbofuran are available and demonstrate that the content of carbofuran is within the limits of the FAO specification (417/GR/S/F; 1991).

The content of carbosulfan in the representative formulation is 100 g/kg (pure).

The main data regarding the identity of carbosulfan and its physical and chemical properties are given in appendix A.

7 The applicant indicated that activities have been initiated to adapt the FAO specification.

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of carbosulfan and impurities in the technical material. Methods are available for carbosulfan and the relevant impurities in the representative formulation.

However, sufficient test methods and data relating to physical, chemical and technical properties and analytical methods are available to ensure that quality control measurements of the plant protection product are possible.

A HPLC-MS/MS method is available that claims to monitor both free and conjugated carbosulfan, carbofuran and 3-hydroxy carbofuran in food of plant origin (uses with soil application) with LOQs of 0.005 mg/kg for each analyte in maize kernel, and with LOQs of 0.001 mg/kg for each analyte in sugar beet respectively, however, the experts at PRAPeR 66 meeting April 2009 (meeting on carbofuran which is applicable to this active) , identified data gaps for the validation of the efficiency of the hydrolysis step in the method and for an ILV for the monitoring method.

Sufficient methods are available for soil, the methodology used is GC with PN- or MS detection, HPLC with post column derivatisation and fluorescence detection and HPLC-MS-MS. A multi-residue method like the Dutch MM1 or the German S19 is not applicable to due the nature of the residues.

Validated methods using HPLC-MS or HPLC with post column derivatisation and fluorescence detection are available for the determination of residues of carbosulfan, carbofuran, 3-hydroxy-carbofuran and carbofuran-7-phenol in water with a LOQ for each analyte of 0.1 µg/L. However, for groundwater/drinking water the LOQ is not sufficient because of the risk to consumers.In addition to this a validated method for monitoring residues of 3-keto-carbofuran in water is not available.

A method for the determination of carbosulfan in air is available but no method is available for carbofuran and this is a data gap.

An analytical method for food of animal origin is not required due to the fact that no MRLs are proposed (see 3.2). However it should be noted that a method is available but the validation is not complete.

Acceptable methods are available for body-fluids and tissues.

The discussion in the meeting of experts (EPCO 35, September 2005) on identity, physical and chemical properties and analytical methods was limited to the physical and chemical properties of carbosulfan, certain properties of the representative formulation, the analytical methods and the relevance of two impurities.

2. Mammalian toxicology

Carbosulfan was discussed at EPCO experts' meeting for mammalian toxicology (EPCO 33) in September 2005. During the resubmission application of carbosulfan, no further discussion was needed and the additional information provided in the additional report was included in this conclusion.

During the first review of carbosulfan, no analytical data on the impurity profile of the batches used in the toxicological studies was available. The toxicological studies were mainly performed with unstabilised technical carbosulfan, for which only the purity was stated. During the resubmission, some toxicity studies were performed with the new specification (acute toxicity – with the unstabilised technical carbosulfan and *in vitro* mutagenicity studies – with stabilised carbosulfan). No change in the acute toxicity or genotoxicity was found between the former and the recent batches in the studies. The presence of the relevant impurity N-nitrosodibutylamine has been lowered to acceptable levels; the other relevant impurity (5-chlorocarbofuran) was no longer detected in the new batch specification.

Overall, it was considered that the batches used in the toxicological studies represent the (new) technical specification (as proposed in the additional report – Belgium, 2009).

2.1. Absorption, distribution, excretion and metabolism (toxicokinetics)

Oral absorption after single low dose exposure was > 70 % of the dose based on urinary excretion, exhaled air, tissues, and carcass. Carbosulfan was widely distributed, mainly in excretory organs and carcass. Excretion was rapid and extensive within 24 hours, mainly via urine (63-78 %); faecal excretion amounted to 13-22 % and an additional 10-12 % of the dose was eliminated as expired CO_2. No accumulation was evident. Metabolism was extensive (> 80 %): carbosulfan mainly undergoes hydrolysis at the C7 ester bond to form carbofuran-7-phenol and at the N-S bond to form carbofuran and dibutylamine, which can be further metabolised. Both carbofuran-7-phenol and carbofuran can undergo oxidation to generate 3-hydroxy-carbofuran and 3-keto-carbofuran, which are conjugated and eliminated via urine.

2.2. Acute toxicity

The acute oral toxicity of carbosulfan has been evaluated in rats, rabbits and mice. Carbosulfan oral LD_{50} is 42.7 mg/kg bw in rabbit, 46.1 mg/kg bw in mouse and 101-180 mg/kg bw in rat, therefore classification as **T, R25 "Toxic if swallowed"** is proposed. Carbosulfan is of low toxicity via dermal route (dermal LD_{50} 3700 mg/kg bw in rats) and **"Toxic via inhalation"** (LC_{50} 0.61 mg/L air/1 hour): classification as **T, R23** is proposed. Carbosulfan is not a skin or eye irritant but is a skin sensitiser according to a patch test similar to the Buehler test and classification as **R43 "May cause sensitisation by skin contact"** is proposed.

2.3. Short term toxicity

Brain AChE is the most sensitive parameter following carbosulfan exposure, not always accompanied by overt clinical signs of toxicity.

In dogs, after a six-month exposure in diet, haematological parameters were altered and spleen relative weight decreased at doses lower than the ones inducing brain and plasma cholinesterase inhibition. The NOAEL in dogs was 1.6 mg/kg bw/day. In rats, death and inhibition of the brain, erythrocytes and plasma cholinesterase activity were the critical effects observed at the LOAEL of 500 ppm. The rat NOAEL of 20 ppm, equivalent 2 mg/kg bw/day, was agreed to be the relevant short term NOAEL during the EPCO experts' meeting.

The inhalation study showed a NOAEL of 0.15 mg/m^3; the NOAEL for systemic toxicity in rabbits after 21-day dermal exposure is 5 mg/kg bw/day. The experts' meeting concluded that no classification was required resulting from the repeated inhalation study, and noted that carbosulfan is classified as toxic by inhalation already.

EFSA note: The rapporteur Member State confirmed the oral NOAEL of 20 ppm, but the company did not provide the conversion to mg/kg bw/day and the Rapporteur Member State applied a conversion factor of 10 resulting in a NOAEL of 2 mg/kg bw/day. Taking into account the measured food intake, the conversion led to the new value of 1.2 mg/kg bw/day. This approach has not been discussed during the EPCO meeting; however it has been confirmed in the subchronic neurotoxicity study presented upon resubmission under point 2.7, where 20 ppm corresponds to 1.2 mg/kg bw/day.

2.4. Genotoxicity

During the first review, carbosulfan gave negative results in *in vitro* tests. *In vivo*, carbosulfan was tested in a number of studies; however, the shortcomings of many of these studies make a scientific evaluation of the results difficult. In addition, results from the open literature did not add further information. An *in vivo* chromosomal aberration test in mice giving clearly negative results was submitted and discussed during the EPCO meeting. The experts noted that carbosulfan technical has a proposed minimum purity of 89 %. A stabiliser was added to the material used in toxicity studies, and

as a result contained less impurities. The batches used in toxicity studies had reported purities of 90.8-94.7 %. The rapporteur Member State indicated that the toxicological properties of the impurities carbofuran and dibutylamine were known. It was noted that the test material used in the *in vivo* chromosomal aberration study was 84 %, and was assumed to be technical material (non stabilised). The issue was referred to the physical-chemical properties meeting in order to determine major differences in manufacturing process; and whether the impurity profile and five batch analysis justifies low purity.

The notifier was required to submit data on the presence of nitrosamine at concentration of 10-26 mg/kg in the technical active substance in the batches of carbosulfan used in genotoxicity studies. During the resubmission application, the applicant proposed a new specification with lower levels of nitrosamine (refer to point 1) and provided new *in vitro* genotoxicity studies conducted with stabilised carbosulfan. The results were negative in a bacterial reverse mutation assay using *Salmonella typhimurium* and *Escherichia coli*, in a mammalian cell gene mutation study (HGPRT locus) on Chinese hamster ovary (CHO) cell line and in a chromosomal aberrations test in CHO cells. It could therefore be concluded that carbosulfan has no genotoxic potential.

2.5. Long term toxicity

One long-term study in rats and one in mice were provided. Target effect was the inhibition of brain and erythrocytes acetyl cholinesterase. In the rat study, focal iris atrophy and degenerative retinopathy observed were ascribed to exposure to carbosulfan. This effect was not observed in mice. The lowest relevant NOAEL was 1 mg/kg bw/day from the 2-year study in rats. In mice, the NOAEL was 2.5 mg/kg bw/day. Carbosulfan did not show carcinogenic potential.

During the first review, the notifier was required to submit data on the presence of nitrosamine at concentration of 10-26 mg/kg in the technical active substance in the batches of carbosulfan used in carcinogenicity studies; this requirement was found obsolete during the resubmission due to the new specification proposed, where nitrosamine is specified at a maximum content of 1 mg/kg.

2.6. Reproductive toxicity

In the three-generation rat study, parental toxicity consisted of decreased body weight and food consumption. Body weight of females was altered during gestation and lactation but not during the growing phase at high doses. At the highest dose, clear signs of foetotoxicity were seen in different litters (decreased body weight, body weight gain, and in some litters, number pups born alive and survival were significantly decreased). The relevant parental, reproductive and offpring's NOAEL was 1.2 mg/kg bw/day.

Carbosulfan administered to rats by gavage produced an incomplete ossification at maternally toxic doses (≥ 10 mg/kg bw/day); the relevant maternal and developmental NOAEL was 2 mg/kg bw/day. (The EPCO meeting confirmed the proposal of the rapporteur Member State to decrease the maternal NOAEL from 10 mg/kg bw/day to 2 mg/kg bw/day due to the consistent reduction in the number of pups born alive, pup weight and pup survival in the presence of maternal toxicity).

In the rabbit developmental study, an increase in the incidence of major vessel variations was observed, however, it was noted that the left carotid arised from the innominate, observations were sporadic and showed no dose response. This effect was therefore not considered treatment-related, and the developmental NOAEL in the rabbit study was increased from < 2 mg/kg bw/day to 10 mg/kg bw/day, while the maternal NOAEL was 5 mg/kg bw/day due to body weight decrease and deaths.

A proposal for a classification was discussed since effects were noted, but not considered sufficient to warrant classification.

2.7. Neurotoxicity

Carbosulfan displayed no potential for development of clinical signs or morphologic changes associated with organophosphorus induced delayed neurotoxicity. The experts at the EPCO meeting set a new data requirement for the notifier to submit acute and subchronic neurotoxicity studies that were submitted to the JMPR. These studies were provided after the expert's meeting and were included in the additional report. In the acute neurotoxicity study, the NOAEL was 0.5 mg/kg bw, based on decreased brain and erythrocyte acetylcholinesterase activity observed at 5 mg/kg bw. In the subchronic neurotoxicity study, clinical signs of neurotoxicity, effects on body weight and reduced food consumption were noted at 64.8 mg/kg bw/day (1000 ppm) and the NOAEL was 1.2 mg/kg bw/day (20 ppm).

2.8. Further studies

Metabolites and impurities

Dibutylamine (DBA) is harmful (LD_{50} 205 mg/kg bw) by ingestion. An Ames test was wrongly provided on a different substance, whose results were considered positive. The EPCO meeting concluded that the genotoxicity of dibutylamine had not been adequately addressed, and a new data requirement was set: a full *in vitro* data package was required.

During the resubmission, the correct study was submitted and evaluated. The *in vitro* bacterial reverse mutation assay in *Salmonella typhimurium* conducted with DBA showed negative results; data from the open literature indicated that the rabbit dermal LD_{50} is 1010 mg/kg bw, the LC_{50} is 1.15 mg/L air, no skin sensitisation was found in a mouse swelling test and an *in vivo* micronucleus assay was negative. In the Annex I of Directive 67/548/EEC, DBA is classified for human health as Xn; R20/21/22 (harmful by inhalation, in contact with skin and if swallowed).

A particular concern is that DBA may be metabolised into N-nitrosodibutylamine (DBNA). However, it was agreed that dibutylamine is not a relevant metabolite as it is less toxic than the parent; being a precursor of a relevant impurity does not make it relevant.

EFSA notes: The EPCO expert's meeting noted that *N*-nitrosodibutylamine exceeded the acceptable maximum concentration of 1 mg/kg (specified in the equivalence of the former technical materials document). The meeting noted that the structurally related *N*-nitrosodimethylamine was classified as very toxic, and that at concentrations of 0.001 %-0.01 % had the risk phrase [R45] 'May cause cancer'. The rapporteur Member State indicated that assuming *N*-nitrosodibutylamine was of comparable toxicity to *N*-nitrosodimethylamine, carbosulfan would be classified. Furthermore, IARC considered *N*-nitrosodibutylamine a category 2B carcinogen, and it was carcinogenic in all categories tested. It was noted that the level of *N*-nitrosodibutylamine in batches used in genotoxicity and carcinogenicity studies was not known, and a new data requirement was set for the notifier to provide this data.

According to the new specification presented during the resubmission, N-nitrosodibutylamine does not exceed any longer the acceptable limit of 1 mg/kg, therefore the concerns of the EPCO meeting over this impurity can be considered as addressed.

Carbofuran

Two studies were submitted by the notifier on carbofuran: an AChE inhibition in neonates, weanling and adult rats and an evaluation of the safe exposure levels to carbamates to healthy adult volunteers.

Human studies In human volunteers, symptoms attributed to cholinesterase inhibition were seen at 0.25 mg carbamate/kg. Symptoms occurred in conjunction with a substantial reduction in red blood cell cholinesterase activity which was dose-related. The study has a limited scientific value due to the absence of important information (e.g. purity).

The experts considered during the EPCO meeting that data requirement for specific toxicological data on carbofuran was addressed in the carbofuran dossier. Carbofuran is very toxic by inhalation and if swallowed; the ADI and ARfD for carbofuran[8] are set at 0.00015 mg/kg bw/day, based on the LOAEL of 0.03 mg/kg bw from the acute neurotoxicity study (with carbofuran) and a safety factor of 200 applied.

3-hydroxy-Carbofuran

This metabolite of carbofuran was addressed in the carbofuran dossier: 3-hydroxy-carbofuran is very toxic if swallowed (rat oral LD_{50} = 8.3 mg/kg bw); it gave positive results in an Ames test and in a TK locus in L5178Y mouse lymphoma cells assay. It was considered that carbofuran's reference values could be applied to this metabolite.

3-keto-Carbofuran

This carbofuran's metabolite was addressed in the carbofuran dossier: 3-keto-carbofuran is toxic if swallowed (rat oral LD_{50} = 107 mg/kg bw). It was considered that the reference values of carbofuran could be applied to this metabolite.

For the impurity **5-chlorocarbofuran** no toxicological data was submitted. This impurity is no longer detected in the specification revised for the resubmission.

2.9. Medical data

Symptoms of poisoning include excessive sweating, headache, chest tightness, weakness, giddiness, nausea, vomiting, stomach pain, salivation, blurred vision, slurred speech and muscle twitching. Paresthesia and mild skin reactions have also been reported. Annual medical surveillance exams of workers at the technical manufacturing plant and at two formulating plants did not indicate unexpected or unusual health effects since the 1990s, up to 2005.

2.10. Acceptable daily intake (ADI), acceptable operator exposure level (AOEL) and acute reference dose (ARfD)

Provisional reference values were set at the EPCO expert's meeting due to the number of data gap identified during the process. The role of nitrosamines in determining health effects was to be assessed with regard to their level in toxicological batches, and their intrinsic properties had to be regarded as of concern, possibly leading to an increase of the safety factors applied. Also the missing acute and subchronic neurotoxicity studies were identified as having an impact on some of the reference values, in particular AOEL and ARfD.

ADI:

EPCO outcomes: A NOAEL of 1 mg/kg bw/day from the 2-year rat study was identified as relevant based on eye toxicity and AChE inhibition; a safety factor of 100 was applied, to give an ADI of 0.01 mg/kg bw/day.

2009 resubmission: The rapporteur Member State proposed a new **ADI of 0.005 mg/kg bw/day** in the additional report and the Member States. The ADI is based on the new acute neurotoxicity study with a NOAEL of 0.5 mg/kg bw for brain acetylcholinesterase inhibition, which is the most sensitive endpoint for carbosulfan, and applying a safety factor of 100. It is noted that this approach is in line with the one previously agreed for the ADI for carbofuran.

[8] refer to the EFSA Scientific Report (2009) 310, 1-132: Conclusion regarding the peer review of the pesticide risk assessment of the active substance carbofuran, issued on 16 June 2009

AOEL:

EPCO outcomes: A provisional systemic AOEL was derived from a NOAEL of 2 mg/kg bw/day resulting from the 90-day feeding study in rats. A safety factor of 100 was considered adequate. The meeting considered that no correction was necessary to account for the oral resoprtion. The proposed systemic AOEL was set at 0.02 mg/kg bw/day. The meeting decided that the AOEL had to be confirmed upon receipt of other data (acute and repeated dose neurotoxicity data) from the notifier.

2009 resubmission: The rapporteur Member State proposed a new **AOEL of 0.005 mg/kg bw/day** in the additional report. The AOEL is based on the new acute neurotoxicity study with a NOAEL of 0.5 mg/kg bw and applying a safety factor of 100.

ARfD:

EPCO outcomes: No acute neurotoxicity study in rats was provided. The 2-year study in rat was considered, applying a SF of 100. The ARfD was provisionally set at 0.01 mg/kg bw/day, to be confirmed after evaluation of the neurotoxicity studies, which were requested to the applicant.

2009 resubmission: The rapporteur Member State proposed a new **ARfD of 0.005 mg/kg bw/day** in the additional report. The ARfD is based on the new acute neurotoxicity study with a NOAEL of 0.5 mg/kg bw and applying a safety factor of 100.

2.11. Dermal Absorption

It is noted that the notifier did not support Marshal 25 CS at EU level any longer.

A comparative dermal absorption study, *in vitro*, conducted with the representative formulation "Marshal 10G" using rat and human skin was provided during the resubmission procedure. As some shortcomings were found in the human dermal absorption results, and no *in vivo* study was available, it was agreed to use the rat's dermal absorption value as proposed by the rapporteur Member State for the exposure risk assessment. As the formulation (granular) is not intended to be diluted, this value corresponds to the in-field use. The dermal absorption was found to be 0.16 %; it was rounded to **0.2 %.**

2.12. Exposure to operators, workers and bystanders

Operator exposure

Marshal 10G is a granular formulation: an operator exposure estimate using the PHED model was provided by the applicant as the UK-POEM and German Model are not applicable to assess exposure to such a type of formulation and application.

PHED:

The rapporteur Member State presented new calculations in the additional report (Belgium, 2009) based on the AOEL of 0.005 mg/kg bw/day, dermal absorption of 0.2 %, inhalation rate of 100 %, work rate of 15 ha/day, application rate of 0.75 kg carbosulfan/ha, and the total amount handled of 11.25 kg/day (for sugar beet). The body weight for operators was assumed to be 70 kg.

Operator exposure was calculated in the absence and in presence of a half-mask with P2 filter possessing an assigned protection factor of 10x. The RPE was assumed during the tasks of loading of the product, but not during the application of the granules. When Marshal 10G is applied using tractor-mounted/drawn equipment it is estimated that the total systemic operator exposure to carbosulfan is 10 % of the AOEL of 0.005 mg/kg bw/day (considering gloves worn during loading and application and a

respirator mask worn during loading operations). When gloves only are worn, operator exposure is 70 % of the AOEL of 0.005 mg/kg bw/day.

Estimated operator exposure presented as % of the AOEL (0.005 mg/kg bw/day) for an application rate of 0.75 kg carbosulfan/ha and a work rate of 15 ha/day, according to calculations with the PHED model.

Model	No PPE/RPE	With PPE:	With PPE and RPE:
PHED (75th percentile values)	-	70 %	10 %

PPE (personal protective equipment): gloves,
RPE (respiratory protection equipment) used during loading operations only

Worker exposure

As Marshal 10G is applied to the soil at the time of planting/transplanting and incorporated, workers entering treated are not likely to be exposed to dislodgeable foliar residues of carbosulfan.

Bystander exposure

Marshal 10G: No established models are available to estimate the level of bystander exposure likely to arise during granule application. It can be assumed that bystanders may be present during the field use of Marshal 10G. The applicant considered that bystander exposure to vapour or airborne particles at the time of application is likely to be negligible. This was agreed by the rapporteur Member State. The EPCO meeting asked the rapporteur Member State to present the estimated bystander exposure in an addendum with revised values. In the additional report (Belgium, 2009), the rapporteur Member State expressed the opinion that the use of granular applicators distributing granules by drilling eliminates bystander exposure.

3. Residues

The initially proposed representative uses for inclusion of carbosulfan in Annex I of 91/414/EEC were an in-furrow granular application to maize and sugar beet and a foliar spray application to citrus and cotton. The uses involving a foliar spray application were withdrawn by the applicant during the first EU review process in 2004/2005 (i.e. not further supported with respect to Annex I inclusion). Therefore the peer review for these uses stopped after the first evaluation meeting in May 2005, however for the sake of transparency the evaluation of residue data related to these uses are presented below as far as possible.

Carbosulfan was discussed in the experts' meeting for residues in September 2005 (EPCO 34). It is noted that the addendum of September 2005 was distributed during the discussion of carbosulfan in EPCO 34. The experts tried to consider the information in the addendum as good as possible. However due to the very late submission a detailed consideration of the presented information was not possible. Therefore, the addendum of September 2005 was not considered as peer reviewed.

The assessment of data in a resubmitted dossier of carbosulfan was discussed in the expert teleconference meeting on residues in September 2009 (PRAPeR TC21) on the basis of the additional report (revised DAR) of April 2009 and the Addendum of August 2009, considering the notified use in sugar beet with granular application at drilling.

3.1. Nature and magnitude of residues in plant

With the resubmission dossier of carbosulfan no new studies on plant metabolism became available.

It is however noted that, to assess the notified use, data and information submitted on the active substances benfuracarb and carbofuran as well as publicly available evaluation reports on carbofuran,

carbosulfan and benfuracarb were included in the peer review conducted on carbosulfan, if these data and information were considered to be appropriate but more critical or adverse.

3.1.1. Primary crops

Metabolism of carbosulfan was studied in sugar beet, soybean, maize and rice plants following a soil application; in oranges, alfalfa and sugar beet following a foliar treatment and in rice following a direct treatment of the ear heads with carbosulfan. In the studies material radio-labelled at either the phenly-ring or the dibutylamine-group was used. Based on the available studies the metabolic pathway of carbosulfan in plants can be considered as sufficiently investigated. In all cases, metabolism of carbosulfan was initiated by the cleavage of the S-N bond into carbofuran and dibutylamine. Carbofuran was further metabolised by subsequent hydroxylation on the furane ring to 3-hxdroxy-carbofuran. Numerous other metabolites were generated from carbofuran by successive hydroxylation or hydrolysis and oxidation steps, amongst them 3-keto-carbofuran and phenol derivates of carbofuran such as carbofuran-7-phenol, 3-hydroxy-7-phenol and 3-keto-7-phenol, (phenol metabolites hereafter) which were further conjugated. Dibutylamine was slowly degraded to minor levels of mostly unidentified products; however, the dibutylamine derivates N-formyldibutyl amine and acetyl-dibutylamine were identified in plant material.

With the exception of sugar beet, carbosulfan, carbofuran and 3-hydroxy-carbofuran (together ca 30-80% TRR) and dibutylamine (40-60% TRR) were found to be the major components of the total residue in plants having received a direct treatment (oranges, alfalfa, rice) at sampling times between 15 to 45 days after application. In sugar beet leaves, however, at comparable sampling times 3-hydroxy-carbofuran, 3-hydroxy-7-phenol and 3-keto-7-phenol were major compounds, accounting for up to ca 17%, 14% and 23% of the total residue, respectively, whereas the level of carbosulfan and carbofuran was minor (together < 3% TRR). Dibutylamine (up to 47% in leaves) and N-formyl-dibutylamine (up to 31% in leaves and 12% in roots) made up a major part of the residue in sugar beet treated with carbosulfan labelled at the dibutylamine -group. No metabolite identification was performed in the roots of plants treated with the phenyl-ring labelled carbosulfan. In crops grown following a soil application of carbosulfan the metabolic pattern was similar as in directly treated crops, with the exception, that carbosulfan was hardly detected in these crops. Carbofuran and 3-hydroxy carbofuran made up the majority of the total residue with their ratio depending on the sampling time, and were predominant primarily at early sampling stages. With time, the level of phenol-compounds increased, and besides 3-hydroxy-carbofuran the phenol metabolites appeared to be predominant metabolites identified in the mature crops (maize, soybean). Dibutylamine was as well a major metabolite found in crops grown following a soil treatment (immature maize and rice plants, silage, stalks and leaves at harvest). Dibutylamine was present up to 30% TRR and was only slowly decreasing with time. Very few data are available on the occurrence of dibutylamine in edible plant parts. Dibutylamine wasn't analysed for in the mature roots, grains and seeds in the metabolism studies with soil treatment.

Dibutylamine was under discussion concerning its potential genotoxicity, however this concern could be addressed by new toxicology data in the resubmission procedure (see 2.8) Even though dibutylamine is not specific to carbosulfan metabolism it is a predominant residue of carbosulfan metabolism. The rapporteur Member State raised a concern that dibutylamine might be also a precursor of *N*-nitrosodibutylamine, a category 2B carcinogen, however data underpinning this assumption has not been available.

Carbofuran, another main carbosulfan metabolite, is an active substance itself. It has a higher toxicity than carbosulfan. Also 3-hydroxy-carbofuran and 3-keto-carbofuran are of higher toxicity than carbosulfan. The phenol metabolites were tested regarding their acute toxicity and considered of lower toxicity than carbosulfan, carbofuran and 3-hydroxy-carbofuran. (Refer to 2.8 and to EFSA conclusion on carbofuran)

The experts' meeting for residues EPCO 34 had agreed on the need to further evaluate the dibutylamine residues in plant matrices and to consider dibutylamine as a component potentially to be

included in the residue definitions for risk assessment. The rapporteur Member State proposal in the addendum of February 2006, not to include dibutylamine in the plant residue definition for risk assessment, was neither peer reviewed nor discussed by experts. EFSA notes that in crops with foliar treatment (oranges and in alfalfa) dibutylamine was a major residue at harvest. Due to the limitation of the available data on dibutylamine in the edible parts of soil applied crops it is difficult to say whether or not dibutylamine would be also present in these plant parts. It could be assumed from the data on non-edible plant parts of those crops that dibutylamine residues, if present, might be in the same order of magnitude as carbofuran residues.

In the resubmission procedure for carbosulfan in 2009 the experts in mammalian toxicology meeting concluded that dibutylamine per se is not a relevant metabolite as it is less toxic than the parent carbosulfan (see 2.8). However, concerns remained in terms of dibutylamine being a precursor of nitroso dibutylamine that could be formed depending on acidic and/or temperature conditions under crop processing.

Due to the processing conditions during sugar refining the experts considered it unlikely that nitroso dibutylamine will be present in refined sugar.

EFSA fate and behaviour experts considered that it was unlikely that nitroso dibutylamine would be formed in soil from the soil metabolite dibutylamine. Thus, leaching of nitroso dibutylamine to groundwater would not be expected. The groundwater leaching assessment for dibutylamine indicates a low potential for groundwater contamination (see 4.2.2), consequently, formation of nitroso dibutylamine in cases where groundwater is treated to produce drinking water is unlikely.

It can be concluded that the qualitative metabolic pattern observed in plants treated with carbosulfan was independent from the mode of application whereas significant quantitative differences were noted, mainly with regard to the rate (percentage) of carbosulfan found in the crops. In terms of the representative uses with foliar application some aspects on applicability of the submitted metabolism studies still need to be clarified at MS level if foliar uses are reinstated in the future. (Refer to open points 3.3 and 3.5 in the evaluation table of the first peer review conducted in 2004/2005)

To assess the notified representative use in sugar beet treated in-furrow in the resubmission dossier, the experts in the teleconference meeting 21 (TC21) focussed their considerations on data in crops / crop groups relevant to the scenario currently under evaluation. Reference was made to the experts' discussion on the active substances benfuracarb and carbofuran that took place in experts' meetings earlier in 2009.

In TC21 the experts agreed that due to the similarity of the scenario and data considered for the benfuracarb and carbofuran applications the residue definition for risk assessment should be the same for the use of all the three compounds benfuracarb, carbofuran and carbosulfan. However, in the earlier discussions based on a statement by the RMS, 3-keto carbofuran was assumed to be less toxic than carbofuran and 3-hydroxy carbofuran, but this information was not confirmed by the mammalian toxicologists. As for its toxicological properties, the reference values of carbofuran should apply to 3-keto-carbofuran.

3-keto carbofuran was recovered in low levels in sugar beet leaves (0.0045 mg/kg; 30 day interval) and roots (0.0014 mg/kg; 60 day interval). The total toxicological burden of carbamate structured compounds in the residue definition for risk assessment will increase by approx. 10% and 25% for sugar beet leaf and root residues if 3-keto carbofuran is included. The experts considered that, due to its toxicity (classified with T, R25; lower toxicological reference values than for parent carbosulfan), its contribution might be significant, especially in the acute risk assessment.

Hence, the meeting agreed to include 3-ketocarbofuran in the residue definition for risk assessment, and defined the relevant residues as follows:

1) Carbosulfan and 2) Carbofuran, 3-hydroxy carbofuran and 3-keto-carbofuran, including their conjugates expressed as carbofuran.

It was noted that a respective revision of the residue definition will be necessary also for the uses of benfuracarb and carbofuran.

In the expert meeting on carbofuran (PRAPeR 70) the necessity was discussed to also include the conjugates in the residue definition for monitoring, however, currently it is unclear if and to what extent the analytical methods for monitoring determine conjugated residues. Taking into account that the efficiency of the analytical method to release the conjugates of carbofuran and 3-hydroxy carbofuran still has to be demonstrated, the experts could not conclude on a definite residue definition for monitoring. In addition, it might be necessary to also consider the inclusion of 3 keto carbofuran and its conjugates if it will not be possible to establish a conversion factor to take into account for these residues. However, for the moment a proposal on the residue definition for monitoring is open and a data gap in terms of the analytical method for monitoring has been identified.

Already for the first peer review in 2004/2005, residue trial data under field conditions had been submitted on cotton and citrus from Southern Europe and on maize and sugar beet from both European regions. Carbosulfan, carbofuran and 3-OHcarbofuran were the residues determined with a LOQ of 0.05 mg/kg per compound. It is noted that for the uses with foliar application i.e. cotton seed and citrus the data set of trials is incomplete and further data will be needed if foliar uses are reinstated in the future. Despite the submission of one further trial for the representative use in maize EPCO 34 concluded that the data base of residues trials in accordance with the cGAP is still incomplete and permits only a provisional assessment. After the meeting the rapporteur Member State indicated its disagreement with the EPCO 34 decision and considers the requirement of further residue trials is not necessary. Available trial data indicate residues being below the respective LOQ for all analytes in maize kernels, whereas in whole plants with cobs residues of carbofuran and 3-OH-carbofuran up to 0.14 mg/kg were determined.
In sugar beets a complete data set was submitted for N-EU and limited data have been available for S-EU. Even though residues in roots were mainly below the respective LOQ, residues might reach or exceed the LOQ. EPCO 34 considered that it was a ‘low residue’ situation as opposed to a ‘no residue’ situation in sugar beet. The potential residues in the root could not be discounted. The uptake of residues into sugar beet was supported by positive results found in carbosulfan residue trials with a higher application rate than the proposed rate for the representative use. It is noted that the rapporteur Member State did not agree with the EPCO 34 conclusion and considered the residue situation in the sugar beet is a ‘no residue situation’. EPCO 34 felt that for further considerations it would be necessary to check the validity of, and that the minimum number of trials is presented to support the proposed uses. Furthermore, it could not be concluded whether the residue trials are supported by sufficient storage stability data that cover all components included in the residue definition (data only available for orange matrices).

In the resubmission procedure, new residue data in sugar beet (and fodder beet) were submitted. 3 trials were conducted at the notified application rate (0.75 kg a.i./ha) and 4 trials at a slightly higher application rate (1 kg a.i./ha). Carbosulfan, carbofuran and 3-hydroxy carbofuran were analysed with an LOQ of 0.005 mg/kg for each compound. In none of the trials residues above the LOQ were found.

In addition, residues detected between LOQ and LOD (0.0008 mg/kg) were evaluated. The results confirmed that in both, beet leaves and roots carbosulfan, carbofuran and 3-hydroxy carbofuran can be found at low levels (between LOQ and LOD).

However, it is referred to the expert’s discussion on carbofuran in PRAPeR 70 in terms of the analytical method used in the residue trials, and whether this method has also determined residues according to the established residue definition for risk assessment for carbofuran including conjugated residues of carbofuran and 3-hydroxy carbofuran. On the basis of the available method validation data this could not be confirmed. Hence, a data gap was identified for the applicant to address the

efficiency of the hydrolysis step to effectively release the carbofuran and 3-hydroxy carbofuran conjugates in the methods of analysis used in the supervised residue trials.

Also in terms of the carbosulfan use the experts agreed that, as long as the efficiency of the analytical method to analyse the conjugates is unknown, the acceptability of the residue trial results in sugar beet is pending. A reliable consumer risk assessment can not be performed, since the submitted residue trial data may underestimate exposure if the results were not covering the residue definition for risk assessment.

To address the issue on 3-keto carbofuran residues in crops, the experts asked the RMS to compile an overview table with the levels of the individual carbamate structured metabolites to be considered in the risk assessment in order to elaborate whether sufficient data are available on 3-keto carbofuran that could be used in the consumer risk assessment and to establish a conversion factor for the residue definition for monitoring to risk assessment. Following TC 21 the RMS has provided such overview table (not peer reviewed). It would have to be discussed whether a reliable factor to account for 3-keto carbofuran residues could be established on the basis of the information provided.

In terms of the uses notified for the first peer review in 2004/2005, the investigation of effects of industrial or household processing on the nature of the residue was triggered for the representative use on citrus (not further supported with respect to Annex I inclusion). A position paper of the applicant for non-submission of those data was assessed by the rapporteur Member State in the addendum of February 2006 and was therefore not peer reviewed nor discussed by experts. In a citrus processing study, the effects on the level of carbosulfan, carbofuran and 3-hydroxy-carbofuran in processed citrus products were investigated. The data indicate high concentration of carbosulfan and carbofuran in citrus oil and of 3-OH-carbofuran in dried pulp, whereas no residues about the respective LOQ (0.05 mg/kg) were found in citrus juice. Whether other degradation products or metabolites were present at significant levels was not investigated.

To further address the nature and level of residues upon household and industrial processing the applicant has submitted data on a hydrolysis study performed with carbosulfan at pH 5, 7 and 9 at room temperature (25°C) (Belgium 2009a). These tests are not in compliance with the guidelines for generation of residue processing data. The study had already previously been discussed in the meeting PRAPeR 70 in terms of the carbofuran assessment. Even though sugar beet processing is conducted at merely alkaline conditions, the experts considered the submitted hydrolysis data as not acceptable since sugar beet processing operations comprise steps at much higher temperatures and up to pH 11. However, the experts expected under these conditions a more rapid degradation of residues to occur but not any novel metabolite to be formed.

In a submitted processing study on sugar beet no residues above the LOQ of 0.01 mg/kg for carbofuran, 3-keto carbofuran and 3-hydroxy carbofuran, respectively, were recovered in neither the raw commodity nor in the processed products. A processing factor could not be derived from the study and therefore its value to refine consumer risk assessment is limited.

While in the meeting PRAPeR 70 the majority of experts presumed that, due to the harsh conditions in sugar beet processing and the crystallisation steps, virtually no residues would occur in refined sugar, the experts in the meeting TC 21 challenged this position on the basis of the available data. The processing study shows that significant residues of 3-keto-7-phenol were observed in molasses and sugar (0.02 to 0.03 mg/kg), and thus, it cannot be excluded that also very low residues (< LOQ of 0.01 mg/kg) of carbamate structured compounds could be present in sugar.

The experts in TC 21 agreed that, in order to conduct a refined acute dietary risk assessment the applicant should address the residue level of carbamate structured metabolites in refined sugar (data gap). Otherwise, it will not be possible to refine the current risk assessment and to determine the actual consumer exposure to residues from the use of carbosulfan in sugar beets.

3.1.2. Succeding and rotational crops

During the first peer review on carbosulfan , the rapporteur Member State considered studies in succeeding crops or a waiting period for planting succeeding crops are not necessary since carbosulfan is degraded very rapidly in soil. However, also in soil carbosulfan is largely degraded to the more toxic carbofuran and to dibutylamine. Carbofuran appears more persistent in soil than carbosulfan and no degradation parameters were available for dibutylamine. Thus the experts' meeting for residues agreed that there is a need to address residues in succeeding crops following the application of carbosulfan to primary crops. It is noted that the rapporteur Member State did not agree with the experts' meeting decision. However, EFSA supported the EPCO 34 decision.

In a position paper (Belgium 2009a) the applicant argued that such data is not required since the DT90 for carbofuran would not trigger rotational crop studies. In the context of the assessment of benfuracarb the DT90 of carbofuran was re-discussed in the meeting of experts in environmental fate and behaviour (PRAPeR 62) in January 2009. The DT90 for carbofuran in field studies was 91 days, however it was concluded that more than 10% of carbamate residues were present in soil after 100 days in a number of available studies (considering the total carbofuran, 3-hydroxy carbofuran and 3-keto carbofuran in field studies, or extractable radioactivity lab incubations). Therefore already in the meeting TC05 on benfuracarb the experts reconfirmed the conclusion of the previous EPCO 34 meeting that rotational crop data according to current guidelines (intervals of 30, 120 days and 1 year on leafy crop, small grain crop and root crop) are necessary to address potential uptake of carbofuran residues in rotational crops.

With the resubmission dossier an interim report of a confined crop rotation study with phenyl ^{14}C carbofuran has been made available by the applicant. The interim results were presented in the additional report (Belgium 2009a).

Upon application of carbofuran to the soil at a rate (0.6 kg a.s./ha) equivalent the recommended field rate for carbosulfan the soil was aged for up to 30, 60 and 365 days. A leafy vegetable crop (spinach), a root crop (radish) and a grain crop (maize or winter wheat for the 30-day and 60-day interval, respectively) were planted.

The final report is not available; however from the interim report there is indication that TRR in green parts of plants (spinach, radish leaves, cereal forage) at 30 and 60 days plant back interval exceeded 0.01 mg/kg.

Since data is not complete for all crops and plant back intervals, and moreover no information was provided on the nature of the residues, a final conclusion can not be drawn. A data gap was identified for identification of residues in rotational crops. Considering the very low toxicological reference values for carbofuran (to be applied also to 3-hydroxy and 3-keto carbofuran) the experts agreed that the usual trigger values for identification of residues in food / feed could not be applied.

For the time being the RMS has performed the consumer dietary risk assessment with the total residues presented by the applicant in the rotational crop study interim report.

A case made by the applicant to only consider 10% of the TRR in rotational crops in the consumer risk assessment could not be supported by the experts in TC 21 on the basis of the available data and information.

3.2. Nature and magnitude of residues in livestock

Livestock animal metabolism was studied in lactating goats and laying hens orally dosed with carbosulfan radio labelled at either the phenyl-ring or the dibutylamine group. Carbosulfan was rapidly metabolised and excreted by livestock animals. Numerous metabolites identified in the animal tissue, organs, eggs and milk, respectively, are reflecting the existence of multiple degradation pathways in the animal body. Based on the radioactivity characterised in animal matrices it was concluded that the degradation of carbosulfan in livestock animals proceeds via the following pathways: Hydrolytic cleavage of the N-S bond of carbosulfan into carbofuran and dibutylamine with subsequent oxidation of the methyl group of the carbamate or of the methyl group of the furane ring and hydrolysis of the carbamate moiety followed by further oxidations. The phenyl portion of the molecule was converted into the carbamate and phenolic derivatives, while the dibutylamine moiety was oxidized into compounds containing the amine fragment and incorporated into natural products such as fatty acids, triglycerides, carbohydrates and proteins. Many metabolites were present as conjugated compounds (lipid or amino acids conjugates). All the metabolites identified in livestock animals have been found in the rat metabolism. Even though the relevant residues on potential feeding stuff are besides carbosulfan also carbofuran and 3hydroxy- carbofuran and 3-keto carbofuran including theire conjugates the available metabolism studies can be considered appropriate, since the referred to metabolites are generated in livestock animals, too.

Levels of recovered radioactivity in animal matrices strongly depended on the administered label. In tissues and organs of animals dosed with phenyl-labelled carbosulfan radioactive residues were highest in liver of poultry and goat, in goat kidney and in poultry muscle and skin. In matrices of animals dosed with dibutylamine-labelled carbosulfan highest residue levels were found in goat fat and in egg yolk followed by the liver of both species. The significant higher residues of the dibutylamine-label found in fatty matrices could be explained by the cleavage of the fat soluble dibutylamine side chain of carbosulfan. Characterisation and identification of radioactivity was carried out depending on the level of the recovered total residues in only some of the edible matrices. Carbosulfan per se was, if detected at all, only present at very low levels (less than 2% TRR). 3-hydroxy-carbofuran presented a major part of the residue in poultry muscle (37% TRR) and goat milk (up to 34% TRR) and kidney (22%TRR) whereas carbofuran residues were always below 10% TRR in all analysed matrices. Dibutylamine was the predominant metabolite in poultry muscle (22% TRR) and liver (37% TRR). In poultry fat and eggs only *ca* 4%TRR was identified as dibutylamine, whereas more than 85% TRR in these matrices remained unidentified. In goat matrices dibutylamine was either not radio-detected or found at very low levels. However, characterization of the radioactivity in fat showed that 82% of the TRR were recovered as fatty acids and a non negligible fraction of radioactivity was characterised as non conjugated and conjugated amines susceptible to contain the metabolite dibutylamine

The experts meeting for residues EPCO 34 agreed on the need to propose a residue definition for livestock . Based on the data and knowledge available at the time of the meeting EPCO 34 proposed to provisionally define the relevant residues in animal products as 3-OH-carbofuran. However the experts agreed on the need to further evaluate livestock animal data, in particular unidentified residue in fat and the dibutylamine residues in animal matrices, and to consider dibutylamine as a component to be included in the residue definitions for risk assessment. In the addendum of February 2006 the rapporteur Member State partially addressed the EPCO 34 request, however the provided evaluation was not peer reviewed.

Livestock may be exposed to residues as defined in the plant residue definition for risk assessment through the primary crop sugar beet and/or through rotational crops (see paragraph 3.1.2 above). The RMS conducted in the additional report a livestock dietary intake assessment on the basis of the LOQ of carbosulfan, carbofuran and 3-hydroxy carbofuran in sugar beet in supervised residue trials. Though residues in rotational crops relevant in animal diet have not been considered, the available estimates are expected to slightly increase. It should however be noted that the validity of the used residue values for sugar beet is still pending confirmation on whether or not conjugates of carbofuran and 3-hydroxy carbofuran were included in the reported results.

Reference is made to the discussion of livestock dietary intake and nature and level of residues in livestock matrices, in particular in the light of the very low toxicological reference values for carbofuran and its metabolites 3-hydroxy and 3-keto carbofuran.

No new data on livestock metabolism were submitted. It is however evident from the available data that conjugated 3-hydroxy carbofuran occurs in toxicologically significant amounts in animal matrices, even if the residues are calculated to be very low considering the livestock dietary burden from the representative use in sugar beet. In ruminant and poultry liver 3-keto carbofuran is present in higher amounts than 3-hydroxy carbofuran.

On the basis of the available data the following residue definition for animal matrices was agreed for risk assessment: 3-hydroxy carbofuran and 3-keto carbofuran, free and conjugated expressed as carbofuran. Residues of dibutylamine were not considered relevant for the consumer risk assessment.

For monitoring the experts suggested as residue definition 3-hydroxy carbofuran free and conjugated, since available data make it difficult to derive a reliable ratio between free and conjugated 3-hydroxy carbofuran (Belgium 2009a). Moreover, this ratio is expected to differ between matrices (milk, liver etc.). In terms of 3-keto carbofuran residues in animal matrices, the experts asked the RMS to compile an overview table with the levels of the individual carbamate structured metabolites to be considered in the risk assessment in order to elaborate whether sufficient data are available on 3-keto carbofuran that could be used in the consumer risk assessment and to establish a conversion factor for the residue definition for monitoring. Following TC 21 the RMS has provided such overview table (not peer reviewed). It would have to be discussed whether a reliable factor to account for 3-keto carbofuran residues could be established on the basis of the information provided.

It is moreover noted that the efficiency of the analytical method for monitoring to release the conjugates will have to be addressed to decide on the applicability of the proposed definition for monitoring.

3.3. Consumer risk assessment

In the additional report (Belgium 2009a) the RMS has provided a comprehensive dietary exposure and risk assessment for consumers using both the EFSA PRIMo and the UK model.

The estimated dietary intake of carbosulfan was in those calculations significantly below (<5%) the allocated carbosulfan ADI of 0.005 mg/kg bw/day for all considered consumer groups.

The sum of intakes of carbofuran and 3-hydroxy carbofuran from the primary crop, rotational crops and food of animal origin was considered and compared to the toxicological reference values for carbofuran (ADI and ARfD, both 0.00015 mg/kg bw /day). This approach is deemed to be appropriate as the metabolite 3-hydroxy-carbofuran is assumed to be of comparable toxicity as carbofuran based on acute toxicity studies. It is noted that the assessment does not yet consider the revised residue definition for risk assessment (including free and conjugated residues of 3-keto carbofuran), and the establishment of appropriate conversion factors to take into account for residues of 3-keto carbofuran is still pending.

An **exceedance of the ADI** was noted for UK toddlers in the EFSA PRIMo 173% ADI and the ADI was almost reached for toddlers in the UK model (98% ADI).

The acute consumer risk assessment indicates the **ARfD is significantly exceeded** for a number of crops consumed by children and by adults/the general population. A great exceedance of the ARfD was observed for leafy (up to 1800% ARfD) and root/tuber crops (up to 615% ARfD). These results highlight the importance of residue data on succeeding crops to enable further refinement of the dietary risk assessment for consumers.

In the light of the results the experts in PRAPeR 70 (carbofuran discussion) proposed to consider a restriction for following crops to cereals only, as the interim results in the rotational crop study indicate the transfer of residues in a succeeding cereal crop up to mature harvest might be limited. However, data on cereals have only been reported for one plant back interval, and further data and assessment of the proposed scenario will be necessary.

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.

Finally, it was noted by the expert meeting in fate and behaviour that, if there were no use restrictions imposed to mitigate groundwater exposure, the level of carbofuran in groundwater is expected to exceed 0.1 µg/L in 7 out of 9 scenarios (refer to 4.2.2.). In some of the scenarios the trigger of 0.1µg/L may also be exceeded for the toxicologically relevant metabolites 3-hydroxy carbofuran and 3-keto carbofuran.

In the consumer risk assessment performed by the rapporteur Member State the possible intake of carbofuran through drinking water derived from groundwater has not been considered. EFSA notes that significant contribution to the acute and chronic exposure might be expected if any restrictions that might be considered were not effective.

To assess this situation EFSA estimated consumer exposure (not peer reviewed) with regard to carbofuran residues in ground water used as drinking water on the basis of the predicted PEC groundwater levels (annual average, FOCUS PEARL) in order to reflect the worst case. The estimates are based on the default assumptions laid down in the WHO Guidelines for drinking- water quality[9] for the consumer groups of adults (weighing 60 kg), toddlers (10 kg) and bottle-fed infants (5 kg) with a daily per capita consumption of 2 L, 1 L and 0.75 L, respectively.

As advised by the section of toxicology the toxicological reference values of carbofuran are also applicable to 3-hydroxy carbofuran and 3-keto carbofuran. Therefore the sum of all 3 compounds leaching into groundwater was expressed as carbofuran equivalents and considered in the consumer risk assessment.

The predicted concentrations of carbofuran toxicological equivalents in the most vulnerable scenarios may lead to the exceedance of the toxicological reference values ADI and ARfD for toddlers and infants. In terms of the acute assessment it is noted that the used daily consumption figures might rather reflect a mean consumption than a high consumption that is normally considered for acute intake estimates, and thus the actual acute consumer exposure (single day event) might be even higher than estimated.

Estimated intakes of carbofuran toxicological equivalents (Cf equ) through drinking water derived from groundwater expressed in µg/kg bw and as percent of the toxicological reference values (ADI and ARfD, both 0.00015 mg/kg bw/day)

FOCUS Scenario	PEC_{GW} (µg/L) simulated by FOCUS PEARL			Estimated consumer intake					
				Adult		Toddler		Infant	
	Cf	3-OH Cf	3-keto Cf	µg Cf equ / kg bw	% tox. ref. val.	µg Cf equ / kg bw	% tox. ref. val.	µg Cf equ / kg bw	% tox. ref. val.
Chateaudun	1.2254	0.0351	0.0882	0.045	29.8	0.134	89.4	0.201	**134**

[9] Guidelines for drinking-water quality. 3rd edition, Volume 1: Recommendations. World health organisation (2006)

Hamburg	1.0283	0.0327	0.1465	0.040	26.6	0.120	79.8	0.179	**120**
Jokioinen	0.8212	0.0229	0.0438	0.029	19.6	0.088	58.9	0.133	88.4
Kremsmuenster	0.7044	0.0207	0.0672	0.026	17.5	0.079	52.9	0.118	78.7
Okehampton	0.8787	0.0266	0.0857	0.033	21.9	0.098	65.6	0.148	98.4
Piacenza	1.6247	0.0516	0.2888	0.065	43.2	0.194	**130**	0.292	**194**
Porto	0.0234	0.0006	0.0010	0.001	0.6	0.002	1.7	0.004	2.5
Sevilla	4.0895	0.1089	0.1657	0.145	96.6	0.435	**290**	0.652	**435**
Thiva	0.2250	0.0067	0.0200	0.008	5.6	0.025	16.7	0.038	25

3.4. Proposed MRLs

Separate MRLs for carbosulfan and carbofuran have been proposed resulting from the uses of carbosulfan in sugar beets

Carbosulfan 0.005 * mg/kg

Carbofuran : For the time being no MRLs can be proposed.

A new review has been conducted, leading to substantial changes in the assessment of carbofuran residues. Amongst others, the residue definition for monitoring could not be agreed due to outstanding data and information (for details refer to 3.1.1 and 3.2 above).

4. Environmental fate and behaviour

Carbosulfan fate and behaviour into the environment was discussed in the meeting of MS experts EPCO 31 (September 2005) on the basis of DAR (July 2004), the carbosulfan Reporting and Evaluation tables and the updated List of End Points (August 2005). An addendum to the fate and behaviour chapter was provided on 18 May 2006. When reported, the information in the addendum had been summarized too briefly to draw any conclusion on its reliability. Studies or reports presumably submitted by the applicant were not adequately referenced. Therefore, studies submitted by the applicant after the DAR was submitted were considered neither evaluated nor peer-reviewed in the original conclusion (July 2006).

For the resubmission, the RMS prepared an additional report (Belgium 2009) including new data and information and the summaries of those studies which had been available, but had not been regarded as peer-reviewed for the first peer review in 2006. Additionally, a final addendum was prepared for the additional report in July 2009 after the comments made by MS and EFSA were available for the RMS. Both the additional report (Belgium 2009a) and this addendum (Belgium 2009b) contain all the information originating from the original DAR and the information added later during the peer-review on the resubmission, but highlighted with different colours. These documents with the Reporting table (rev 1-1, 2009-07-31) were the bases of the second peer review on the fate and behaviour of carbosulfan in the environment. Additionally, some expert discussion on the metabolite carbofuran and its metabolites' fate and behaviour in the environment took place during the peer reviews on benfuracarb (PRAPeR 62, January 2009) and carbofuran (PRAPeR 67, April 2009). These discussions and expert's conclusions were taken into consideration in this conclusion, where these were relevant.

4.1. Fate and behaviour in soil

4.1.1. Route an rate of degradation

The route of degradation of carbosulfan was investigated under dark aerobic conditions at 20 ºC and 40 % MWHC in one study (Baumann 2002) with four soils (pH 5.8 – 7.3; OC 0.78 – 3.89 %; clay 8.2 – 23.3 %) and ^{14}C-phenyl labelled carbosulfan as test substance. In this study, only **carbofuran** (max.

48.7 % AR after 7 d) was found as a major transformation product of carbosulfan in soil. Several minor metabolites were identified being 3-keto-carbofuran (max. 5.3 % AR after 14 d) among them.

The meeting of MS experts (EPCO 31, September 2005) considered that this metabolite needs to be further assessed because it contains the active carbamate moiety. It is noted that the metabolite 3-hydroxy-carbofuran, which is another minor metabolite of carbofuran in soil, contains the active carbamate moiety, as well. The expert meeting for carbofuran and benfuracarb (also EPCO 31, September 2005) considered that this metabolite needs to be further assessed, as well. Although the side chain was not labelled, amounts of dibutylamine (max. 5.4 % of the initial molar amount) were also quantified in these experiments. The mineralization was very limited (max. CO_2 2.3 % AR) and bounded residues increased up to maximum of 90 % AR after 100d. In a separated study (Markle 1981a) aerobic (for 28 d) and anaerobic degradation of ^{14}C-phenyl labelled carbosulfan is compared in two soils (pH 6.1 – 7.0; OC 2.96 – 4.58 %; clay 25 %) incubated at 22 ºC and 60 % of MWHC (aerobic incubations). In this study maximum level of carbofuran formed was 69.3 % AR after 3 d and **3-keto-carbofuran** reached levels of 6.6 % AR after 28 d (end of the aerobic study). An analogous study (Markle 1981b, same soils and experimental conditions) was performed with ^{14}C-dibutylamine labelled carbosulfan. **Dibutylamine** (max 21.5 % AR after 3 d) was found as a major aerobic soil metabolite in these experiments. The anaerobic part of these studies was not considered acceptable by the rapporteur Member State.

No valid degradation study of carbosulfan in soil under anaerobic conditions is available. Also photolysis in soil was not investigated. Two soil photolysis studies are available for the main metabolite carbofuran in the corresponding DAR. On basis of these studies, carbofuran has been considered stable to photolysis in soil.

4.1.2. Persistence of the active substance and its metabolites, degradation or reaction products

Rate of degradation of carbosulfan in soil under dark aerobic conditions was calculated in the samestudies provided to investigate the route of degradation. Evaluation meeting agreed that a re-evaluation of the degradation kinetic in degradation studies, including assessment of the goodness of fit, needs to be performed by the applicant. Reassessment was provided to the rapporteur Member State in June 2005 but was not assessed and peer-reviewed in 2005. Therefore, it was not possible to agree during the first Peer Review on the laboratory degradation end points for carbosulfan.

In a separated non radio labelled study, rate of degradation of carbosulfan was also measured under

dark aerobic conditions in one soil (pH 7.1, OC 3.89 %, clay 16.5 %) at 10 ºC and 40 % MWHC. It is noted that the soil used in this study is one of the soils used in the experiments conducted at 20°C (mentioned above).

For the resubmission, the notifier reanalysed and normalised (to FOCUS reference conditions) all of the available data for carbosulfan, carbofuran and for benfuracarb, since benfuracarb is another precursor of carbofuran, according to the FOCUS kinetic guidance document.

In this reanalysis of the data, the residues of carbosulfan from the experiments regarded as valid by the previous peer review of carbosulfan were refitted by SFO (single first order) and also by FOMC (first order multi compartment) kinetics. Where the fit by the FOMC model was found to be better, the resulting degradation endpoints of these FOMC fits were used further. In these cases, for modelling purposes, pseudo SFO DT_{50} values were calculated by dividing the FOMC DT_{90} values by the factor of 3.32 as recommended by the FOCUS kinetic guidance document (FOCUS 2005) These pseudo SFO DT_{50} values were then combined with DT_{50} values derived from SFO fits (from experiments where SFO fits gave better fit than FOMC). For one soil two DT_{50} values from 20°C studies were available. The geomean of these two values were considered in the calculation of the overall geomean for carbosulfan. The resulting range of these DT_{50} values was 0.53 –11.43 days (normalized to FOCUS reference conditions, n=6) and the geometric mean was 4.81 days. Kinetic formation fractions

for carbofuran could be derived from five of these experiments. These formation fractions ranged from 0.47 to 1, with the arithmetic mean of 0.68.

The DT_{50} of carbosulfan (not normalised) derived from the experiment conducted at 10°C was 21.7 days.

Regarding the main metabolite carbofuran, the reanalysis of the experiments of degradation (considering all the accepted experiments from the dossiers of carbofuran, carbosulfan and benfuracarb) was already available for the meeting of experts of PRAPeR 62 (January 2009) when benfuracarb was discussed, except the three experiments that indicated a potential of high persistence of carbofuran (Saxena A M *et al* 1994 and Schocken, M. J., 1989; Belgium 2009a). The carbofuran residues from these three experiments were refitted and normalised by EFSA before the expert meeting of PRAPeR 62 (January 2009). Taking into account all of these data, the resulting range of DT_{50} values for carbofuran was 5.7 – 387 days (normalized to FOCUS reference conditions, SFO, n=17). The experts at the meeting of PRAPeR 62 (January 2009) discussed the reanalysis of the data and the derivation of degradation endpoints for carbofuran. This meeting (PRAPeR 62, January 2009) agreed with this data set and that the median of these DT_{50} values, which is 14 days, is appropriate to be used in the FOCUS modelling.

No degradation parameters were available for soil metabolites dibutylamine and 3-keto-carbofuran. The additional report prepared for the resubmission (Belgium 2009a) contained summaries of acceptable studies regarding the degradation of these metabolites and additionally for the minor soil metabolites 3-hydroxy-carbofuran and carbofuran-phenol. The study summaries of 3-keto-carbofuran, 3-hydroxy-carbofuran and carbofuran-phenol had already been available for the peer-reviews of the resubmissions of benfuracarb and carbofuran. The degradation endpoints to be used in the further assessments of these metabolites (DT_{50} in soil 3.01 days, 0.41 day and <1.0 day for 3-keto-carbofuran, 3-hydroxy-carbofuran and carbofuran-phenol, respectively) were discussed and agreed during the meetings of experts of these peer-review processes (PRAPeR 62, January 2009 and PRAPeR 67, April 2009). Details regarding these discussions can be found in the Reports of PRAPeR Expert Meetings (EFSA 2009c; EFSA 2009b) and in the EFSA conclusions for benfuracarb and carbofuran resubmissions, prepared in 2009 (EFSA 2009d, EFSA 2009e).

The degradation of metabolite dibutylamine was investigated in three aerobic soils (pH 5.8-7.5, OC content 1.08-1.79%, clay content 4.7-42.6%) at 20°C and pF 2.0 - pF 2.5 soil moisture content. The DT_{50} values of dibutylamine were calculated to be between 0.06 and 2.13 days. The geometric mean of the three values was 0.42 day. It should be highlighted that there were some concerns regarding this degradation study and the derivation of the DT_{50} values for dibutylamine (for details of this point see comments 4(6) and 4(7) in the reporting table). No further evaluation of the study or no new derivation of degradation endpoints were performed during the peer-review. Therefore a data gap was set by EFSA for re-evaluation of the degradation endpoints of dibutylamine based on the recommendations of FOCUS kinetic guidance. However, it should also be noted that the low persistence in standard laboratory conditions and the low risk to aquatic organisms is apparent for this metabolite. Even if a more appropriate degradation endpoint (expected to be longer than the existing one) was used, no significant increase would be expected regarding the FOCUS PEC values. Therefore this data gap can be regarded as not essential for the finalization of the assessment at EU level.

Brief summaries of some field dissipation studies performed with carbosulfan in EU are available. Half life of carbosulfan in these trials ranges between 0.35 to 31.3 days. Half life of metabolite carbofuran in these trials ranges between 1.3 to 71.9 days. EFSA noted (2006) that in the context of the carbofuran discussion, the meeting of MS experts (EPCO 31, September 2005) was not able to determine the reliability of these studies. A position paper from the applicants was available (June 2005) but has still not been assessed and peer reviewed. Also some summaries of field studies of carbofuran performed in USA were available in the dossier. The meeting of MS experts (EPCO 31) agreed that to assess these studies with respect to EU conditions more background information would be needed.

However, detailed summaries of the field studies were still not available in the additional report, the rapporteur Member State expressed that the studies of the US sites and the EU trial from which the field DT_{50} of 71.9 days for carbofuran and the 31.3 days for carbosulfan come from, are of limited quality and are not appropriate to derive accurate dissipation endpoints. Some information regarding this EU trial was included in the additional report (Belgium 2009), for PECsoil calculations for carbofuran, therefore the longest value of 27 days was used from those available field DT_{50} values, which had not been excluded. This is in line with the agreement of the meeting of experts PRAPeR 62, where this issue had already been discussed (EFSA 2009c).

PEC in soil were calculated for carbosulfan, carbofuran and dibutylamine based on the field worst case half lives of the agreed data set from the EU field trials (DT50 carbosulfan = 9.8 d, DT50 carbofuran = 27 d, DT50 dibutylamine = 54 d) and the representative uses in sugar beet (Belgium 2009b).

4.1.3. Mobility in soil of the active substance and its metabolites, degradation or reaction products.

A batch adsorption / desorption study with carbosulfan and its metabolites carbofuran and dibutylamine in four soils was summarised in the original DAR (Belgium 2004). In this study carbosulfan shows to be slight to low mobile in soil, carbofuran very high mobile and dibutylamine medium to high mobile in soil. The rapporteur Member State concluded in the DAR that this study is of limited quality. The meeting of MS experts (EPCO 31, September 2005) agreed that the study was not valid due to serious methodological flaws and therefore identified a data gap for a valid adsorption study for carbosulfan and dibutylamine. A separate study for dibutylamine in one soil was also summarised in the original DAR (Belgium 2004). However, this study was of limited quality as well, therefore it was not used in the further assessments. For the metabolite carbofuran an acceptable study on four soils (from a different notifier Dianica; Mamouni, 2002) is available in the dossier of carbofuran as active substance. This study was included in the additional report for carbosulfan (Belgium 2009). Based on this study carbofuran may be classified as very high mobile compound (K_{Foc} = 17 – 28 mL / g).

The additional report included new batch adsorption/desorption studies for carbosulfan on four soils and for the metabolites dibutylamine, 3-keto-carbofuran, 3-hydroxy-carbofuran and carbofuran-phenol on three soils. It should be noted, that the validity of the results obtained from the study of dibutylamine was questioned, since concerns regarding the water solubility and the vapour pressure of this metabolites was not sufficiently clarified and the equilibrium time was prolonged for 48 hours in this study (for details of this point see comments 4(20), 4(31) and 4(32) in the reporting table). The RMS was content with the results of the study.

Calculated adsorption K_{FOC} values for carbosulfan varied from 12895 to 33314 mL/g, (mean 20081 mL/g) (1/n 0.88 – 0.98, mean 0.94). Calculated adsorption K_{FOC} values for dibutylamine varied from 250 to 684 mL/g, (mean 409 mL/g) (1/n 0.64 – 0.79, mean 0.73).

The study summaries of 3-keto-carbofuran, 3-hydroxy-carbofuran and carbofuran-phenol had already been available for the peer-reviews of the resubmissions of benfuracarb and carbofuran. The endpoints for adsorption to be used in the further assessments of these metabolites (K_{doc} 330.5 mL/g with 1/n of 1, K_{doc} 55 mL/g with 1/n of 1 and K_{Foc} 1031 mL/g with 1/n of 0.9 for 3-keto-carbofuran, 3-hydroxy-carbofuran and carbofuran-phenol, respectively) were discussed and agreed during the meeting of experts of these peer-review processes (PRAPeR 62, January 2009 and PRAPeR 67, April 2009). Details regarding these discussions can be found in the Reports of PRAPeR Expert Meetings (EFSA 2009b; EFSA 2009c) and in the EFSA conclusions for benfuracarb and carbofuran resubmissions, prepared in 2009 (EFSA 2009d, EFSA 2009e).

A soil TLC study and two aged soil column leaching studies of limited quality are available. Moreover an aged column leaching study of carbofuran is available in the dossier of carbofuran.

A lysimeter study performed with two lysimeters in loamy sand soil is available. In this study carbosulfan was applied to bare soil at rate equivalent to 1.05 Kg a.s. / ha. The average concentration in the leachate for the two years that lasted the experiments was 0.82 – 0.85 µg carbosulfan equivalents / L leachate. However, annual average concentrations and detailed characterization of the residue is missing in this study. Evaluation meeting agreed that the levels of soil metabolite dibutylamine need to be determined in the lysimeter leachate samples and that the two new lysimeters performed with carbofuran (carbosulfan metabolite) should be submitted and assessed. These studies were submitted by the applicant in June 2005 but were not evaluated and peer reviewed during the first peer-review on the original submission of the carbosulfan dossier. For dibutylamine a position paper was provided by the applicant in June 2005 but this paper was also not evaluated and peer reviewed. In the additional reports prepared for carbofuran and carbosulfan, RMS included the summaries and the evaluation of the two lysimeter studies performed with carbofuran. These studies were already discussed at the meeting of experts from Member States for carbofuran (PRAPeR 67) and it was agreed that these studies are not conclusive regarding the leaching potential of carbofuran or its metabolites, therefore are regarded as only supplemental information. For dibutylamine a rate of degradation study and a batch adsorption/desorption study were available for the resubmission procedure. These data allow the estimations of FOCUS PECgw for this metabolite.

4.2. Fate and behaviour in water

4.2.1. Surface water and sediment

Degradation of carbosulfan in sterile buffer solutions at 25ºC is pH dependent. Carbosulfan hydrolyses with half lives lower than 1 d at pH 5 and 7 and with a half life of 7 d at pH 9. Main hydrolysis products are carbofuran and dibutylamine. Carbofuran subsequently degrades to carbofuran-7-phenol.

Photolysis in water had not been investigated for carbosulfan in the original dossier. A data gap was already identified in the physical and chemical properties section of the DAR. The study was provided by the applicant and evaluated by the rapporteur Member State in the addendum to section

B.2 of the DAR (September 2005). This study shows that photolysis may contribute to the environmental degradation of carbosulfan. Hydrolysis metabolite carbofuran-7-phenol is also found to be the major metabolite in the irradiated samples of this study (16.7 % AR after 23.9 h). Two regions of polar degradation products (amounting to 66.7 % AR) were found but not characterized.

The environmental relevance of these metabolites is uncertain and was not peer reviewed by the meeting of MS experts since the study was still not evaluated at the time in the environment meeting (EPCO 31, September 2005) took place. The study summary was included in the fate and behaviour chapter (B.8) of the additional report (2009). EFSA notes that it can be considered as unlikely, that the parent molecule or the degradation products of carbosulfan as precursor of these photolytic degradation products, will occur in the top layer of the natural water bodies in significant levels. Therefore formation of these unidentified polar products in natural water bodies is assumed to be low.

Carbosulfan is not readily biodegradable according the available study.

Dissipation in water / sediment was investigated in one study with two dark aerobic water sediment systems ($pH_{sediment}$ 7.1 – 7.2; pH_{water} 7.3 – 7.8) at 20 ºC and 10 ºC and at two different levels (0.2 and 0.4 mg a.s / unit).

Carbosulfan was low persistent in all experiments performed (DT50 whole system 20 ºC = 4.2 – 5.4 d; DT50 whole system 10 ºC = 10 d).

Main metabolites formed were carbofuran (max. 34.7 % AR in water (at 10°C); max. 20.1 % AR in sediment) and carbofuran-phenol (max. 23.2% AR in water; max. 6.22% AR in sediment). A non characterized metabolite (Unknown 3) also appears at levels above 10 % AR in the sediment of some systems (max. 20.11% AR after 7 d at 10°C). This compound consisted in a single well defined chromatographic peak. The amount of bound residues increased steadily up to 30.5 – 43.0 % AR at the end of the experiments (102 d).

For the resubmission, in the additional report, the residues of carbosulfan and the metabolites carbofuran and carbofuran-phenol were refitted and degradation endpoints were (re)calculated for the experiments conducted at 20°C. Regarding carbosulfan, the resulting range of DT_{50} values for the whole systems was 3.63-5.57 days (derived from SFO or FOMC kinetics, where FOMC kinetics was used pseudo SFO DT_{50} was calculated and used in further assessments). Whole systems DT_{50} of carbofuran ranged between 14-51.3 days. The endpoints regarding carbofuran-phenol derived from this study seemed to be unreliable therefore these were not used further. It is noted that dissipation/degradation endpoints for the water and sediment phase were also calculated, however these were not used in the further evaluation (for these calculations χ^2 errors were reported, but figures for the visual fits were not provided).

A separated study was performed to obtain higher amounts of Unkown 3 for its identification. The study was unsuccessful and only a tentative structure was proposed based on the mass spectrometry of the samples in the original study. This tentative structure contains the carbamate moiety and may be expected to produce carbofuran when degraded. Based on the tentative structure, this metabolite Unkown 3 is regarded as an intermediate transformation product between carbosulfan and carbofuran (in aquatic environment). Since the application method is soil incorporation (furrow application) and carbosulfan degradates rapidly in soil, it is unlikely that this compound can occur in surface water in significant level.

Applicant provided aerobic and anaerobic water sediment studies for the metabolite carbofuran that have not been summarized in the DAR. Evaluation meeting agreed that an addendum need to be produced to summarize the carbofuran studies used in the assessment of carbosulfan. The addendum is still awaited (2006), however EFSA may confirm that these are the same studies presented by applicant FMC in the carbofuran dossier and summarized by the rapporteur Member State in the carbofuran DAR. For the resubmission of carbofuran, the residues of carbofuran and carbofuran-phenol were refitted and degradation endpoints were (re)calculated for the aerobic experiments. These calculations had already been available for the peer-review of the resubmission of carbofuran. The degradation endpoints to be used in the further assessments were discussed and agreed during the meeting of experts of the carbofuran peer-review (EFSA 2009b). Details regarding these discussions can be found in the Report of PRAPeR Expert Meeting and in the EFSA conclusion for carbofuran resubmission, prepared in 2009 (EFSA 2009e). These refitted values are included in Appendix A of this conclusion together with other relevant results obtained from the peer-reviewed additional reports of carbofuran or benfuracarb.

For the first peer-review, PECSW/SED were calculated by the applicant based on an *ad hoc* modelling exercise. Spray drift (Marshal 25 CS), drainage, run-off and erosion (Marshal 10G and Marshal 25 CS) are potential routes of exposure of surface water. However, none of these modelling exercises follows FOCUS SW scheme. Since the input parameters selected to calculate PECSW and the assumptions made were not fully justified, the rapporteur Member State considered that more appropriate PECSW calculations were necessary to finalize the assessment of the EU representative uses and proposed the use of FOCUS SW scheme. No PECSW were proposed for dibutylamine. Evaluation Meeting confirmed the rapporteur Member State data requirement for FOCUS SW PECSW/SED and agreed that PECSW for dibutylamine need to be calculated. FOCUS SW calculations and a position paper for dibutylamine were provided by the applicant in June 2005 but was not evaluated and peer reviewed during the first peer-review.

FOCUS surface water modelling was evaluated up to step 3 for carbosulfan, carbofuran and 3-keto-carbofuran, up to step 2 for 3-hydroxy-carbofuran and dibutylamine and up to step 1 for carbofuran-phenol in the additional report. Since many input parameters were commented and deviated from the conclusions of the meetings of PRAPeR 62 and PRAPeR 67 (EFSA 2009b, EFSA 2009c), when the input parameters for FOCUS modelling for carbofuran and its metabolites had already been discussed. In the addendum prepared for the additional report (Belgium 2009b) a new FOCUS step 3 modelling was included for carbosulfan and for all the metabolites using Q_{10} of 2.2. Moreover for carbofuran-phenol, PECsw/PECsed values were calculated using the method, which was recommended by the meeting of experts at PRAPeR 67. In this modelling, the input parameters which were criticized were changed to the agreed values or worst case values were used, with the exception of the soil DT_{50} of carbosulfan (5 days was used instead of 4.8 days). This can be regarded as worst case for the parent, but best case for the metabolites. On the other hand it is noted that other parameters such as the formation fraction of the metabolites are considered as worst case parameters. It should also be noted that the degradation in soil or the adsorption parameters of dibutylamine are uncertain (for details see point 4.1.2 and 4.1.3 of this conclusion), therefore the available PECsw/PECsed values are uncertain as well. However the low risk to aquatic organisms is apparent for this metabolite. On the whole, the results of these calculations (Belgium 2009b) are considered as acceptable for use in the risk assessment and are included in Appendix A of this conclusion. It should be highlighted that since the mode of application was set to soil incorporation to 7 cm below the soil surface, the result of this modelling are represent only those situations when the granules containing the active substance are placed directly in the sowing row (to at least 2 cm below the soil surface) and than the furrows are covered by the soil.

4.2.2. Potential for ground water contamination of the active substance its metabolites, degradation or reaction products

For the previous peer-review of carbosulfan, the applicant presented an estimation of the potential for ground water contamination based on the FOCUS GW scheme (PRZM). The 80th percentile of the annual average concentration in the leachate at 1m depth was calculated for the MARSHAL 10 G and MARSHALL 25CS representative uses. For carbosulfan, the concentrations calculated were below 1 ng / L. The rapporteur Member State considered that half life and Koc employed for carbofuran in the calculation were not justified and proposed a data requirement for new PECGW. This data requirement was confirmed by the Evaluation Meeting that additionally required calculation of PECGW for metabolite dibutylamine. New FOCUS GW calculations for carbofuran and a position paper for dibutylamine were provided by the applicant in June 2005 but were not evaluated and peer reviewed by the completion of the first peer-review. Additionally, experts meeting (EPCO 31) indicated that potential ground water contamination by soil metabolite 3-keto-carbofuran should be addressed. For this a data gap was set by the meeting of experts.

FOCUS modelling for estimation PECgw were performed in the additional report (Belgium 2009a) for carbosulfan, carbofuran, dibutylamine, 3-keto-carbofuran and 3-hydroxy-carbofuran. Additionally carbofuran-phenol was also modelled. However many input parameters of these simulations were commented and deviated from the conclusions of the meetings of PRAPeR 62 and PRAPeR 67 (EFSA 2009b, EFSA 2009c) when the input parameters for FOCUS modelling for carbofuran and its metabolites had already been agreed. In the addendum prepared for the additional report (Belgium 2009b) new FOCUS modelling was included. In this modelling, the input parameters which were criticized were changed to the agreed values or worst case values were used, with the exception of the soil DT_{50} of carbosulfan (5 days was used instead of 4.8 days) and a slight difference in the used K_{Fom} value of carbosulfan (11678 mL/g was used instead of 11648 mL/g, affects only FOCUS PEARL calculations). This difference of the DT_{50} value can be regarded as worst case for the parent, but best case for the metabolites. On the other hand it is noted that other parameters such as the formation fraction of the metabolites are considered as worst case parameters. It should also be noted that the degradation in soil or the adsorption parameters of dibutylamine are uncertain (for details see point

4.1.2 and 4.1.3 of this conclusion), therefore the available PECgw values are uncertain as well. However the low potential for leaching to ground water is apparent for this metabolite.

In these simulations (included in the addendum of the additional report; Belgium 2009b) the applied for representative use of soil incorporation (incorporation depth 7cm, dose 750 g/ha) in sugar beet were modelled using FOCUS PEARL (version 3.3.3) and FOCUS PELMO (version 3.3.2) models with single annual and triennial application schemes using the following input parameters: carbosulfan single first order/pseudo SFO DT_{50} 5 days, K_{Foc} 20081 mL/g (K_{Fom} 11678 mL/g), 1/n=0.94; carbofuran single first order DT_{50} 14 days, K_{Foc} 22 mL/g, 1/n=0.96, formation fraction from carbosulfan 1; 3-hydroxy-carbofuran single first order DT_{50} 0.41 days, K_{doc} 43 mL/g, 1/n=1, formation fraction from carbofuran 1; 3-keto-carbofuran single first order DT_{50} 3.01 days, K_{doc} 331 mL/g, 1/n=1, formation fraction from 3-OH-carbofuran 1; carbofuran-phenol DT_{50} 1 day (from graphical estimation), K_{Foc} 1031 mL/g, 1/n=0.9, formation fraction from carbofuran 1; dibutylamine single first order DT_{50} 0.46 days, K_{Foc} 409 mL/g, 1/n=0.73, formation fraction from carbosulfan 1. The Q_{10} parameter applied in these simulations was 2.2.

Parent carbosulfan was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations of <0.001µg/L.

The main metabolite carbofuran was calculated to be present in leachate leaving the top 1m soil layer at 80th percentile annual average concentrations >0.1µg/L in case of 8 out of the 9 modelled FOCUS scenarios with the range of 0.22-4.09 µg/L using the PEARL model, and 7 out of the 9 modelled FOCUS scenarios with the range of 0.32-0.73 µg/L using the PELMO model, when annual applications were simulated. Only the Porto (PEARL) or Porto and Thiva (PELMO) FOCUS scenarios resulted PECgw <0.1µg/L (0.023 µg/L, 0.009 µg/L and 0.004 µg/L, respectively).

When triennial applications were simulated by FOCUS PEARL 7 out of the 9 modelled FOCUS scenarios exceeded the 0.1µg/L parametric drinking water limit with the range of 0.24-1.11 µg/L, and again Porto and Thiva FOCUS scenarios resulted PECgw <0.1µg/L (0.012 µg/L and 0.069 µg/L, respectively). When FOCUS PELMO was used for the simulation of triennial applications 5 out of the 9 modelled FOCUS scenarios exceeded the 0.1µg/L parametric drinking water limit with the range of 0.15-0.30 µg/L. Kremsmünster, Porto, Sevilla and Thiva FOCUS scenarios resulted PECgw <0.1µg/L (0.002 – 0.099 µg/L).

The PECgw for the metabolites 3-keto-carbofuran and 3-hydroxya-carbofuran exceeded the 0.1µg/L parametric drinking water limit only in a few cases of FOCUS simulations when annual applications were simulated. When triennial applications were simulated, 3-keto-carbofuran exceeded this trigger only in one case (FOCUS PEARL, Piacenza scenario) of the simulations.

The 80th percentile of the annual average concentrations of carbosulfan-phenol or dibutylamine in leachate leaving the top 1m soil layer did not exceed the trigger of 0.1µg/L in these FOCUS groundwater simulations.

It is noted that the simulations for the metabolites of carbofuran and dibutylamine can be regarded as worst case, as 100 % formation was assumed, while the observed maximum occurrences in soils were significantly lower. For carbofuran 100 % formation was assumed as well in these simulations. The calculated kinetic formation fractions of carbofuran ranged from 0.47 to 1 (see 4.1.2 of this conclusion).
Additionally it is also noted that in the additional report, FOCUS simulations with the reduced dose of 100 g/ha were also summarized however these simulations were not considered regarding the applied for representative uses.

4.3. Fate and behaviour in air

Volatilization studies from soil and plant surface are available in the carbosulfan dossier. These studies are not properly summarized in the carbosulfan DAR but the rapporteur Member State considers they show that carbosulfan will not pose a risk to the atmosphere.

Carbosulfan is not a volatile compound (vapour pressure 3.59 x 10^{-5} Pa at 25°C). Atmospheric half life for photochemical oxidations has been calculated as 2 h. It is noted that no information regarding this calculation is available in the Fate and Behaviour in Air chapter of the additional report or in the original DAR (Belgium 2004, Belgium 2009a). However the calculation is summarized in B.2 chapter of the original DAR.

It is not expected that carbosulfan may contaminate the air compartment or be prone to long range transport through air. Carbosulfan transform in the active substance carbofuran. No data on the fate in air of carbofuran is available in the carbosulfan dossier. Data in carbofuran dossier shows that contamination of the air compartment and long range transport thought air is not expected for carbofuran.

5. Ecotoxicology

Carbosulfan was discussed at the EPCO experts' meeting for ecotoxicology (EPCO 32) in September 2005. The discussion focused on confirming the data requirements originally proposed by the rapporteur Member State and on identifying additional data gaps for the proposed representative uses, since no additional information or studies provided had been evaluated by the rapporteur Member State. No summaries of studies on the metabolite carbofuran were included in the DAR. All toxicity values for the metabolite carbofuran in the DAR on carbosulfan and in this report are from the DAR on carbofuran. Carbosulfan was resubmitted, peer-reviewed and discussed in the PRAPeR expert meeting TC22 (teleconference) in September 2009 on the basis of the additional report (Belgium 2009a) and the addendum to Vol. 3, B9 from (Belgium 2009b). The only representative use retained in the resubmission was the use of the granular product Marshal 10G in sugar beet.

5.1. Risk to terrestrial vertebrates

A risk assessment for birds and mammals was conducted according to SANCO/4145/2000. The number of granules to reach the acute and dietary LD50 was calculated as 10.9 and 4.3 for a 15 g bird indicating a potential high risk to birds.

Wildlife observations/monitoring of poisoning incidents under the UK Wildlife Incident Investigation Scheme were submitted. However the information was considered of limited value in the risk assessment. The information was considered as not adequate to demonstrate a safe use of Marshal 10G.

The risk from accidental and intentional uptake of granules as grit was assessed as acceptable according to the EPPO scheme (EPPO-Standards, 2003). In addition a probabilistic risk assessment was provided by the applicant following the same approach as for carbofuran. The principle of the probabilistic risk assessment was agreed during the expert meeting as a relevant way to assess the acute risk. However the same shortcomings and uncertainties as for the probabilistic risk assessment for carbofuran granules were identified (e.g. not worst case assumptions, spills not taken into account, frequency of visits of field margins). For further details see conclusion on carbofuran (EFSA 2009e).

A study with house sparrows (*Passer domesticus*) was conducted in order to simulate exposure to Marshal 10G granules. No mortality was observed in the study. The experts considered extrapolation to a real field situation as problematic. The study did not cover end of row situations with spills of granules and it was not recorded whether the sparrows took up granules. Overall it was concluded that the outcome of the risk assessment according to the EPPO scheme indicates an acceptable risk. However since a few granules are sufficient to kill a bird the product should be applied with care and spills need to be avoided. The experts proposed labelling of the product with SPe5: "To protect

birds/wild mammals the product must be entirely incorporated in the soil; ensure that the product is also fully incorporated at the end of rows.

The risk to birds and mammals from exposure of residues in food items was driven by the toxicity of the metabolite carbofuran. A high risk to birds was indicated in the first-tier risk assessment for the uptake of sugar beet seedlings, earthworms and arthropods. Reduced PT and PD values were suggested in the refined risk assessment together with measured residues in food items. The RMS had some reservations using the residue trials in sugar beet since it was only conducted in northern EU but sugar beet production is also relevant in southern EU. The metabolite 3-hydroxy-carbofuran contains the carbamate moiety. The content of the 3-hydroxy-carbofuran was not measured in the field study with earthworms and arthropods and in the laboratory study with earthworms. Therefore the residue data underestimate the real exposure. The earthworms in the field study were stored alive overnight before analysis. This has probably reduced residue levels in earthworms.

Refinement of PD/PT values was suggested on the basis of general information on food composition but no specific data were provided to support the suggested refinements for the use in sugar beet. However, even with the proposed refinements the TERs were below the trigger for the proposed focal species wood pigeon (*Columba palumbus*), yellow wagtail (*Motacilla flava*), blackbird (*Turdus merula*), skylark (*Alauda arvensis*).

The acute risk to birds from uptake of contaminated food items was further refined by body burden modelling for yellow wagtail and wood pigeon according to the opinion on pirimicarb (PPR-Panel, 2005). Several parameters were highly uncertain or clearly not worst case (EFSA 2009e) Taking all uncertainties into account the experts decided that the refined risk assessment was not acceptable. A high risk to birds from residues in food items cannot be excluded and a data gap remains for further refinement of the risk to birds.

The number of granules that have to be ingested by a small mammal (15 g) to reach the LD_{50} is 46. Granules are not attractive to mammals and the acute risk from uptake of granules can therefore be considered as low. To reach the NOAEL for mammals 1.3, 2.2 and 4.3 granules have to be ingested by a 15 g, 25 g and 50 g mammal respectively. The risk to mammals from accidental uptake of granules (as part of soil ingestion) was assessed as low.

A high acute risk to insectivorous mammals and a high long-term risk to insectivorous and herbivorous mammals from uptake of residues in food items were indicated in the first tier risk assessment. The refined risk assessment was based on measured residues. The use of the measured residue values in the risk assessment was questioned (see above). TER calculations based on reduced PD/PT values were presented. These refinements include some uncertainty since they were not derived from targeted studies on sugar beet fields. However, even with these refinements the acute TER for insectivorous mammals and the long-term TER for insectivorous and herbivorous mammals were still below the trigger values of 10 and 5.

The risk from uptake of contaminated drinking water for birds and mammals was assessed as low according to the suggestions of the PPR-Panel on the science behind the guidance document on risk assessment for birds and mammals (PPR-Panel, 2008).

Overall it was concluded that a high risk to birds and mammals was indicated for the representative use evaluated. Data gaps remain to address the risk to birds and mammals.

5.2. Risk to aquatic organisms

The lowest endpoints for carbosulfan were observed in studies with fish and aquatic invertebrates. The TER values for all groups of aquatic organisms were above the trigger values of 100 and 10 with FOCUS step 3 PECsw.

Aquatic invertebrates were the most sensitive group of organisms tested with carbosulfan. The acute and long-term TERs exceeded the Annex VI trigger for fish, algae and sediment dwellers. The TERs were below the trigger for invertebrates based on the endpoints from laboratory studies in the FOCUS scenario D4 (pond and stream) which is based on drainage. The TER values were greater than the trigger in the drainage scenario D3 and in the run-off scenarios (R1, R3).

A mesocosm study was submitted in order to refine the effects endpoint. The experts agreed to the regulatory endpoint of 0.1 µg carbosulfan/L. The metabolite carbofuran was below the limit of quantification. Based on molecular weight ratio the endpoint for carbosulfan can be expressed as 0.058 µg carbosulfan/L. Based on this endpoint, the risk would be acceptable in the part scenario D4 (stream).

Overall it was concluded that the risk to aquatic organisms is low for environmental conditions represented by the FOCUS scenarios D3, D4 (stream), R1 and R3. A high risk was indicated for the scenario D4 (pond) (based on mesocosm endpoint, TER = 0.88, trigger = 1).

The risk from the metabolites 3-keto-carbofuran, 3-hydroxy-carbofuran, carbofuran-phenol and dibutyl amine was assessed as low.

Carbosulfan showed significant bioaccumulation with a maximum BCF value of 990 in whole fish. At the end of the 30 day depuration period 40%, 28% and 28% of the accumulated residues were still detected in fillet, viscera and whole fish respectively. Carbosulfan degrades rapidly in the aquatic environment to its metabolites with DT_{50} values (water phase) ranging from 0.54 to 3.16 days. Therefore the risk from bioaccumulation of carbosulfan was considered as low.

5.3. Risk to bees

Carbosulfan and carbofuran are very toxic to bees with acute oral and contact LD50 ranging from 0.038 µg carbofuran/bee to 1.035 µg carbosulfan/bee. No exposure of bees is expected from the use in sugar beet since sugar beets are wind pollinated and the production crop is harvested before flowering. Therefore the risk to bees from the representative use in sugar beets is considered to be low.

5.4. Risk to other arthropod species

The results obtained in laboratory studies with carbosulfan and the formulation Marschal 25 EC and Marshal 10G confirm that carbosulfan is toxic to non-target arthropods (*Typhlodromus pyri, Aphidius rhopalosiphi, Poecilus cupreus, Pardosa sp.*). A field study with carabid and staphylinid beetles using MARCHAL 10 G was assessed as not valid by the rapporteur Member State since no effects were observed in the positive control. No significant effects on *Poecilus cupreus* were observed in a new extended laboratory study. Significant adverse effects were observed in extended laboratory and aged residues studies with *Aleochara bilineata*. A new field study conducted in maize was submitted. No statistical significant adverse effects on soil dwelling arthropods were observed at the application rate of 750 g a.s./ha. Overall it was concluded that there was a low risk to non-target arthropods for the representative use.

5.5. Risk to earthworms

No valid laboratory studies with earthworms were made available. The risk to earthworms was assessed based on results from a field study performed with the formulation MARCHAL 25 CS at an application rate of 1.3 kg a.s./ha which is greater than the proposed application rate sugar beet (0.75 kg a.s./ha). The initial measured concentrations of carbosulfan and carbofuran were 0.6 mg/kg wet soil and 2.8 mg/kg wet soil. Reduction of earthworm populations (number of adult worms, biomass) were observed 1 month after application of carbosulfan. Recovery was observed 6 and 12 months after application. No studies are available with the granular formulation Marshal 10 G. It was questioned in the peer-review whether the study with Marshal 25 CS could be used to assess the risk from the granular formulation. Information was lacking whether broadcast application with even distribution of

the active substance leads to a worst case exposure compared to in-furrow application of granules. The experts were of the opinion that also new PECsoil calculations representing in-furrow application are needed to address the risk to earthworms. A study (Broadbent and Tomlin; 1982) was mentioned in the DAR (Belgium 2004), where more severe effects were observed in studies with even distribution of the test substance. The study was summarized and evaluated by the RMS in the addendum (Belgium 2009b). However the study could not be taken into account in the peer-review according to the restriction of the Commission Regulation No. (EC) 1095/2007.

No studies with soil organisms are available for the metabolite 3-keto carbofuran. The risk needs to be addressed since the active moiety is retained. Neither are studies with soil organisms available with the metabolite dibutylamine. For this metabolite studies are however not considered necessary since the metabolite does not contain the active moiety.

Overall it was concluded that no final conclusion can be drawn on the risk to earthworms. Further information is needed to confirm that broadcast application covers the risk from exposure to local higher concentrations of carbosulfan and carbofuran or field studies where the representative use is simulated are needed.

5.6. Risk to other soil non-target macro organisms

Laboratory studies with the formulation Marshal 10G and *Folsomia candida* and *Hypoaspis aculeifer* were submitted. The corrected NOECs were 0.15 and 10 mg a.s./kg soil. The corresponding TERs of 0.15 and 10 indicated a potential high risk to collembola. However no statistically significant effects on collembola were observed in the field study with non-target arthropods. Therefore the risk to soil dwelling arthropods was considered as low.

5.7. Risk to soil non-target micro-organisms

The studies with carbosulfan available in the original DAR were not considered acceptable. A study with Marshal 10 G was submitted in July 2005. The risk to soil micro-organisms was considered as low since no significant effects on nitrification and soil respiration were observed in a study with the formulation Marshal 10G at concentrations 5 times greater then the initial PECsoil (application rates up to 50 mg product/kg soil which corresponds to about 5 mg carbosulfan/kg soil).

5.8. Risk to other non-target organisms (flora and fauna)

No effects on seedling emergence were observed in a study with 2 monocotyledonous and 4 dicotyledonous plant species. Reduced shoot weight was observed in the study at high application rates (1.5 kg a.s./ha). The risk to non-target plants in the off-field area is considered as negligible due to the application method (in-furrow application of granules).

5.9. Risk to biological methods of sewage treatment

Data from a test with carbosulfan on effects on activated sludge respiration rate are available and indicate that the risk to biological methods of sewage treatment is low.

6. Residue definition in soil

Definitions for risk assessment: carbosulfan, carbofuran, 3-keto-carbofuran, 3-hydroxy-carbofuran and dibutylamine.
Definitions for monitoring: carbosulfan, carbofuran

Water

Ground water

Definitions for exposure assessment: carbosulfan, carbofuran, 3-keto-carbofuran, 3-hydroxy-carbofuran and dibutylamine.

Definitions for monitoring: carbosulfan, carbofuran; in case of carbofuran is found, it is recommended to analyse for 3-hydroxy-carbofuran and 3-keto-carbofuran as well

Surface water

Definitions for risk assessment: carbosulfan, carbofuran, 3-hydroxy-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol, dibutylamine.

Definitions for monitoring: carbosulfan, carbofuran (sediment and water); in case of carbofuran is found, it is recommended to analyse for 3-hydroxy-carbofuran (water only) and 3-keto-carbofuran (sediment and water) as well

Air

Definitions for risk assessment: carbosulfan and carbofuran.

Definitions for monitoring: carbosulfan and carbofuran.

Food of plant origin

Definition for risk assessment: carbosulfan; carbofuran plus 3-hydroxy carbofuran plus 3 keto carbofuran and their conjugates expressed as carbofuran (uses with soil application)

Definition for monitoring: 1) carbosulfan to be monitored separately from 2) carbamate structured metabolites, however no precise definition can currently be proposed due to outstanding data and information (preferably the same as for risk assessment pending information on the efficiency of the analytical method and the establishment of a conversion factor for 3-keto-carbofuran) (refer to 3.1.1)

Food of animal origin

Definition for risk assessment: 3-hydroxy carbofuran and 3-keto carbofuran, free and conjugated expressed as carbofuran

Definition for monitoring: no precise definition can currently be proposed due to outstanding data and information (preferably the same as for risk assessment pending information on the efficiency of the analytical method and the establishment of a conversion factor for 3-keto-carbofuran) (refer to 3.2)

Soil

Table Compound (name and/or code)	Persistence	Ecotoxicology
Carbosulfan	Very low to moderate persistent SFO/pseudoSFO DT_{50lab} 0.53 – 11.43 days, , normalized to 20°C and -10kPa soil moisture	The risk to soil dwelling arthropods and soil-micro-organisms was assessed as low. No final conclusion was drawn on the risk to earthworms.
Carbofuran	Low to high persistent SFO DT_{50lab} 5.7-387 days, normalized to 20°C and -10kPa soil moisture; $DT_{50field}$ 1.3 – 27 d (SFO)	No specific studies with carbofuran were submitted. However it can be assumed that carbofuran was formed in the studies dosed with carbosulfan in sufficient amounts that the risk is covered by the endpoints derived in the studies with carbosulfan
3-keto-carbofuran	Very low to low persistent Single first order DT_{50lab} 0.9-6.65 days, normalized to 20°C and -10kPa soil moisture	No studies with soil dwelling organisms available. The risk to soil dwelling organisms needs to be addressed since it contains the carbamate moiety and it is formed in amounts of > 10% in one study.
3-OH-carbofuran	Very low persistent Single first order DT_{50lab} < 1 day, normalized to 20°C and -10kPa soil moisture	No studies with soil dwelling organisms available. No data required due to the transient nature of the molecule.
Dibutylamine	Very low to low persistent Single first order DT_{50lab} 0.06 – 2.13 days[a)], normalized to 20°C and -10kPa soil moisture	No studies with soil organisms are available. Studies are not considered necessary since the metabolite does not contain the active moiety.

[a)]: endpoints are uncertain

Ground water

Compound (name and/or code)	Mobility in soil	> 0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
Carbosulfan	Immobile (K_{Foc} = 12895-33314 mL/g)	No	Yes	Relevant	Relevant

Carbofuran	Very high mobile (Koc = 17 – 28 mL / g)	FOCUS: Yes, trigger 0.1 µg/L exceeded for 7 of 9 scenarios (PELMO) or 8 of 9 scenarios (PEARL) with annual applications; 5 of 9 scenarios (PELMO), or 7 of 9 scenarios (PEARL) with triennial applications. Trigger 0.75 µg/L exceeded for 5 of 9 scenarios with annual applications or 1 of 9 scenarios with triennial applications (PEARL).	Yes	Relevant [c)] Very toxic (oral LD_{50} 7 mg/kg bw and inhalation LC_{50} 0.05 mg/L air) ADI and ARfD = 0.00015 mg/kg bw/day	Relevant
3-keto-carbofuran	Very high to low mobility (Kdoc = 47.5–504 mL/g)	FOCUS: Yes, trigger 0.1 µg/L exceeded for 1 of 9 scenarios (PELMO), or 3 of 9 scenarios (PEARL) with annual applications, 1 of 9 scenarios (PEARL) with triennial applications.[b)]	No data available	Relevant [c)] Toxic (oral LD_{50} 107 mg/kg bw) No studies available on genotoxicity	Very toxic to aquatic organisms. The risk to aquatic organisms was assessed as low.
3-hydroxy-carbofuran	Very high to high mobility (Kdoc = 43–62 mL/g)	FOCUS: Yes, trigger 0.1 µg/L exceeded for 1 of 9 scenarios (PEARL) with annual application.[b)]	No data available	Relevant [c)] Very toxic (oral LD_{50} 8.3 mg/kg bw) Genotoxic *in vitro* (Ames test and mouse lymphoma cells assay)	Very toxic to aquatic organisms. The risk to aquatic organisms was assessed as low.

Dibutylamine	Medium to low mobility (K_{Foc} = 250-684 mL/g) [a)]	No	No data available	Not relevant Harmful; Ames test negative; from the open literature, *in vivo* micronucleus assay was negative	More than one order of magnitude less toxic than carbosulfan and corbofuran. The risk to aquatic organisms was assessed as low

[a)]: endpoints are uncertain
[b)]: considered as worst case simulations
[c)]: refer to the EFSA Scientific Report (2009) 310, 1-132: Conclusion regarding the peer review of the pesticide risk assessment of the active substance carbofuran, issued on 16 June 2009

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Carbosulfan (water and sediment)	Very toxic to aquatic organisms (*D. magna* acute EC_{50} = 0.0015 mg/L). The risk to aquatic organisms was assessed as low for all FOCUS step3 scenarios.
Carbofuran (water and sediment)	Very toxic to aquatic organisms (*D. magna* acute EC_{50} = 0.00205 mg/L). The risk to aquatic organisms was assessed as low for the majority of the FOCUS step3 scenarios.
3-keto-carbofuran (water and sediment)	Very toxic to aquatic organisms *D. magna* acute EC_{50} = 0.049 mg/L). The risk to aquatic organisms was assessed as low.
3-OH-carbofuran (water only)	Very toxic to aquatic organisms *D. magna* acute EC_{50} = 0.023 mg/L). The risk to aquatic organisms was assessed as low.
Carbofuran-phenol (only water phase)	More than 3 orders of magnitude less toxic than carbosulfan (*D. magna* acute EC_{50} = 25 mg/L). . The risk to aquatic organisms was assessed as low.
Dibutylamine (water and sediment)	More than 3 orders of magnitude less toxic than carbosulfan (*D. magna* acute EC_{50} = 4.2 mg/L). The risk to aquatic organisms was assessed as low.

Air

Compound (name and/or code)	Toxicology
Carbosulfan	Toxic via inhalation (LC_{50} 0.61 mg/L air)
Carbofuran	Very toxic by inhalation (LC_{50} 0.05 mg/L air)

LIST OF STUDIES TO BE GENERATED, STILL ONGIOING OR AVAILABLE BUT NOT PEER REVIEWED.

A shelf-life study to demonstrate that the content of the relevant impurities 5-chlorocarbofuran and *N*-nitrosodibutylamine do not increasing upon storage (date of submission unknown, data gap identified by EFSA, refer to chapter 1).

ILV for the method to determine compounds in the residue definition for plants (Zietz (2008)) (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April, 2009), date of submission unknown; refer to chapter 1).

Data on efficiency of the hydrolysis step in the method (Zietz (2008)) for the determination of the residues in plants (relevant for all representative uses evaluated, data gap identified by PRAPeR 66 meeting (April, 2009), date of submission unknown; refer to chapter 1 and 3).

Method of analysis for 3-keto-carbofuran in water. For the other analytes in ground/drinking water the methods need to be validated with a lower LOQ due to the consumer risk assessment. (relevant for all representative uses evaluated, data gap identified by EFSA (October, 2009), date of submission unknown; refer to chapter 1).

Method of analysis for carbofuran in air (relevant for all representative uses evaluated, data gap identified by EFSA (October, 2009), date of submission unknown; refer to chapter 1).

The applicant to address the efficiency of the hydrolysis step to effectively release the carbofuran and 3- hydroxy carbofuran conjugates in the methods of analysis used in the supervised residue trials. (relevant for all representative uses evaluated; data gap identified by TC 21 meeting (September, 2009)no submission date proposed by the applicant, refer to 3.1)

A data gap was identified for submission of data addressing residues of carbofuran in succeeding crops. Identification of residues in rotational crops has to be provided. (relevant for all representative uses evaluated; (data gap identified by TC 21 meeting (September, 2009); no submission date proposed by the applicant, refer to 3.1.2)

Applicant to address the residue levels of the carbamate structured metabolites in refined sugar (data gap identified by TC 21 meeting (September, 2009); no submission date proposed by the applicant, refer to 3.1.2)

DT_{50} values of dibutylamine in soil has to be determined considering the recommendations of FOCUS kinetic guidance (relevant for all uses evaluated; date of submission unknown; gata gap identified by EFSA; data gap considered as not essential for the finalization of the EU assessment, refer to chapter 4.1.2).

The pesticidal activity of the metabolites 3-keto-carbofuran and 3-hydroxy-carbofuran needs to be addressed since these metabolites appear at concentrations >0.1 µg/L in the $FOCUS_{gw}$ modelling (relevant for all evaluated uses; submission date unknown; refer to point 4.2.2)

The risk to birds and mammals from ingestion of contaminated food items needs to be addressed. (relevant for the representative use assessed; data gap identified in the PRAPeR expert meeting TC22 (teleconference) in September 2009; refer to point 5.1)

Further justification is needed to clarify whether the earthworm field study performed with the formulation Marshal 25 CS (broadcast application) can be used for the risk assessment for

MARSCHAL 10 G (relevant for the representative use assessed; data gap identified in the PRAPeR expert meeting TC22 (teleconference) in September 2009; refer to point 5.1)

The risk to soil organisms from exposure to the metabolite 3-keto-carbofuran needs to be addressed since the active moiety is retained (relevant for the representative use assessed; data gap identified by EFSA, refer to point 5.5)

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The original conclusion from the review was reached on the basis of the evaluation of the representative use as an insecticide on sugar beet. The use on maize in the original conclusion has not been supported in the resubmitted dossier under Commission Regulation (EC) 33/2008. Full details of the GAP can be found in the list of end points. Carbosulfan can be used as an insecticide and nematicide. It should be noted that during the peer review process only the use as an insecticide was evaluated. The representative formulated product for the evaluation was "Marshal 10G", a granule (GR), registered in some Member States of the EU. It should be noted that the applicant no longer supports the second formulation, presented in the dossier and DAR ("Marshal 25CS"). Consequently also the uses on citrus and cotton are no longer supported. In the dossier submitted under Commission Regulation (EC) 33/2008 a reduced application rate on sugar beet was proposed by the applicant, this was rejected by the RMS as it was not considered a representative use.

There are methods available to monitor all compounds given in the respective provisional residue definitions for food of plant and animal origin, body fluids and tissues, however data gaps were identified for additional validation data for the hydrolysis step of the monitoring methods for plant matrices and for an ILV. If MRLs are to be set for animal products in the future then validation of the hydrolysis step in the methods would be needed. For the environmental matrices sufficient methods are available for soil for water the LOQ is not low enough for drinking water and also the method does not analyse for 3-keto-carbofuran for drinking and surface water. For air there is no method for carbofuran available (see data gap). Published multi-residue methods allowing determination of all compounds included in the proposed residue definitions in all matrix groups are not available.

Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible. Carbosulfan is toxic if swallowed and should be classified as T, R25 “Toxic if swallowed”. It is of low toxicity via dermal route and toxic via inhalation (classification as T, R23 is proposed). Carbosulfan is not a skin or eye irritant but is a skin sensitiser and should be classified R43 “May cause sensitisation by skin contact”. Carbosulfan gave negative results in *in vitro* and *in vivo* genotoxicity tests and did not show any carcinogenic potential. In the three-generation rat study, the relevant maternal and reproductive NOAEL was 1.2 mg/kg bw/day. In developmental toxicity studies in rats and rabbits, the relevant maternal and developmental NOAEL was 2 mg/kg bw/day. Carbosulfan displayed no potential for induced delayed neurotoxicity. In acute and subchronic neurotoxicity studies in rat decreased brain acetylcholinesterase activity was the critical finding, being the acute NOAEL 0.5 mg/kg bw and the subchronic NOAEL 1.2 mg/kg bw/day. All three reference values are based on the acute neurotoxicity study: ADI, AOEL and ARfD are 0.005 mg/kg bw/day, applying a safety factor of 100. According to the PHED model calculations, operator exposure is below the AOEL when operators use gloves during the loading and application operations. It is considered that bystander and worker exposure is likely to be negligible under the supported conditions of use.

Based on all available data the metabolic pathway of carbosulfan in soil applied uses can be considered as sufficiently investigated. Carbosulfan on one hand and the sum of carbofuran, 3-hydroxy-carbofuran and 3-keto carbofuran and on the other hand their conjugates were considered the

relevant residues to assess consumer exposure and consumer risk. However, a need to fully address residues and in particular their identity in succeeding crops was identified.

Supervised residue trials in sugar beet, indicated that residues were very low (between LOQ and LOD) and in all submitted trials below the LOQ. However, data to demonstrate the analytical method used in the residue trials has efficiently determined conjugated residues is still necessary in order to validate the residue data.

In livestock, carbosulfan undergoes an extensive metabolisation. 3-hydroxy-carbofuran and 3-keto carbofuran free and conjugated were considered the relevant residue in animal matrices to assess consumer exposure and consumer risk. On the basis of available data the ratio of free and conjugated residues in animal matrices could not be established, and therefore it was proposed to include the conjugates of 3-hydroxy carbofuran in the animal residue definition for monitoring. It has to be elaborated whether residues of 3-keto carbofuran (free and conjugated) can be taken into account by a conversion factor, or need to be included in the residue definition for monitoring.

The RMS has provided a comprehensive dietary exposure and risk assessment for consumers using both the EFSA PRIMo and the UK model for a review by the experts, which can be considered being indicative.

The sum of intakes of carbofuran and 3-hydroxy-carbofuran from the primary crop, rotational crops and food of animal origin was estimated and compared to the toxicological reference values for carbofuran. An **exceedance of the ADI** was noted for UK toddlers. Moreover, the acute consumer risk assessment indicates the **ARfD is significantly exceeded** for a number of crops, mainly succeeding crops, consumed by children and by adults/the general population. The results highlight the importance of further residue data on succeeding crops to enable refinement of the dietary risk assessment for consumers.

In order to further refine the risk assessment a data gap was identified for the applicant to address the residue levels of the carbamate structured metabolites in sugar. To mitigate the identified risk it was moreover suggested to restrict crop rotation to cereals only, but further data and assessment of the proposed scenario will be necessary. Based on the available data no further refinement of the consumer risk assessment is currently possible.

EFSA notes that significant contribution to the acute and chronic exposure might be expected through drinking water derived from groundwater if any restrictions that might be considered to mitigate leaching of residues of carbofuran were not effective.

The information available on the fate and behaviour in the environment, for the resubmission is already sufficient to carry out an appropriate environmental exposure assessment at the EU level. However appropriate summaries and assessments regarding most of the field dissipation studies were not available and the degradation endpoints of dibutylamine in soil were not determined considering the recommendations of FOCUS kinetic guidance. Moreover, the validity of the vapour pressure and the water solubility of this metabolite was not sufficiently clarified, therefore both the soil degradation and the adsorption/desorption properties are uncertain. Furthermore, these endpoints were used for the estimations of the exposure of the environment. For the applied for intended uses, the potential for groundwater exposure by the main metabolite carbofuran (an active substance itself) above the parametric drinking water limit of 0.1 µg/L is high over a wide range of geo-climatic conditions represented by FOCUS groundwater scenarios. The contamination of the groundwater by the soil metabolites 3-OH-carbofuran and 3-keto-carbofuran cannot be completely excluded regarding the available FOCUS simulations. Since these simulations can be regarded as worst case simulations (100% formations are assumed), it is recommended to repeat these simulations with more realistic estimations of the formation of these metabolites (see the Report of PRAPeR Expert meeting 67 for

suggestions). EFSA notes that it is likely that simulations with more realistic estimations of the formation of these metabolites might result PECgw < 0.1 µg/L for all FOCUS scenario for these metabolites. On the other hand it is also noted that the degradation parameter of the parent molecule used in these simulations is regarded as better case than the parameter, which should have been used. This applies to all the metabolites, including carbofuran.

Even at the drinking water limit of 0.1 µg/L that is applied to groundwater consumer exposure would be greater than 10% of the toxicological reference values for vulnerable consumer groups (toddlers and infants). Therefore a drinking water limit <0.1 µg/L is needed for the carbamate structured metabolites according to uniform principles. However, a method with a validated LOQ < 0.1 µg/L for each analyte is not available.

The risk to birds and mammals from uptake of granules was considered low provided that spills are avoided and the product is incorporated in soil. A high risk to birds and mammals was identified from residues in contaminated food items. The risk to birds and mammals needs to be addressed further. The risk to aquatic organisms was assessed as low for environmental conditions represented by the ROCUS scenarios D3, D4(stream), R1 and R3. A high risk was indicated for the scenario D4 (pond). Severe adverse effects were observed in laboratory studies with non-target arthropods. No statistical significant effects on non-target arthropods were observed in a field study indicating a low risk to non-target arthropods. No valid laboratory studies were available with earthworms. The risk assessment was based on a field study with broadcast application. In order to draw a final conclusion on the risk to earthworms it would be necessary to demonstrate that exposure in the field study is representative also for the in-furrow application of the granules. Alternatively a new field study where the representative use is simulated is needed.

Particular conditions proposed to be taken into account to manage the risk(s) identified

Appropriate personal protective equipment (gloves) is considered in order to have an estimated operator exposure below the AOEL according to the PHED data (treated area 15 ha/day, 75th percentile considered), refer to 2.12.

Strict restriction to the supported use in the GAP table (granule formulation to be dropped into seed furrow, at least to 2 cm below the soil surface, and than the furrow is covered by soil, use only once in every third year in the same field)

labelling of the product with SPe5: “To protect birds/wild mammals the product must be entirely incorporated in the soil; ensure that the product is also fully incorporated ate the end of rows.

CRITICAL AREAS OF CONCERN

An intake concern has been identified for consumers. The experts’ decision to include also the metabolite 3-keto-carbofuran free and conjugated in the residue definition for dietary risk assessment is likely to exacerbate the situation. With the data available, no refinement of the consumer intake and risk assessment is currently possible.

The potential for groundwater exposure by the metabolite carbofuran above the parametric drinking water limit of 0.1 µg/L is very high over a wide range of geo-climatic conditions represented by FOCUS groundwater scenarios. With annual application 8 out of the 9 modelled FOCUS scenarios resulted PECgw higher than the trigger of 0.1 µg/L. This number was 7 out of the 9 FOCUS scenarios with applications made once every three years

If consumers were exposed to the predicted levels of metabolites carbofuran, 3-hydroxy carbofuran and 3-keto carbofuran in ground water because any restriction to mitigate groundwater contamination

were not effective, this could result in a significant consumer intake which may even exceed the allocated toxicological reference values (in up to 4 out of the 9 presented FOCUS groundwater scenarios).

A high risk to birds and mammals from uptake of residues in contaminated food items.

Further data are required to address the risk to earthworms.

REFERENCES

Belgium, 2004: Draft Assessment Report

Belgium 2006: Final addendum to the DAR, compiled by EFSA in May 2006

EFSA 2006: Peer Review Report on Carbosulfan

Belgium, 2009a: Additional Report

Belgium 2009b: Final addendum to the Additional Report, compiled by EFSA in October 2009

EFSA 2009a: Peer Review Report on Carbosulfan

EFSA 2009b: Peer Review Report on Carbofuran

EFSA 2009c: Peer Review Report on Benfuracarb

EFSA 2009d: Conclusion on pesticide peer review regarding the risk assessment of the active substance benfuracarb. *EFSA Scientific Report* (2009) 239, 1-107

EFSA 2009e: Conclusion on pesticide peer review regarding the risk assessment of the active substance carbofuran. *EFSA Scientific Report* (2009) 310. 1-132

EPPO-STANDARDS (2003) Environmental risk assessment scheme for plant protection products. Chapter 11: Terrestrial Vertebrates. *EPPO Bulletin*, 211 - 238.

PPR-PANEL (2005) Opinion of the scientific Panel on Plant health, Plant protection products and their Residues on a request from EFSA related to the evaluation of pirimicarb. *The EFSA Journal*, 1-21.

PPR-PANEL (2008) Scientific Opinion of the Panel on Plant protection products and their Residues (PPR) on the Science behind the Guidance Document on Risk Assessment for birds and mammals. *The EFSA Journal*, 1-181.

FOCUS (2005) "Guidance Document on Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration" Report of the FOCUS Work Group on Degradation Kinetics, EC Document Reference Sanco/10058/2005 version 1.0, 431 pp

APPENDIX 1 (LIST OF END POINTS)

LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information, Methods of Analysis

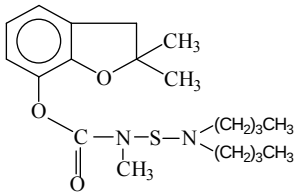
Rapporteur Member State	Month and year	Active Substance (Name)
Belgium	October 2009	Carbosulfan

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name)	Carbosulfan
Function (*e.g.* fungicide)	Insecticide
Rapporteur Member State	Belgium
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC)	2,3-dihydro-2,2-dimethylbenzofuran-7-yl (dibutylaminothio)methylcarbamate
Chemical name (CA)	2,3-dihydro-2,2-dimethyl-7-benzofuranyl [(dibutylamino)thio]methylcarbamate
CIPAC No	417
CAS No	[55285-14-8]
EEC No (EINECS or ELINCS)	EINECS 259-565-9
FAO Specification (including year of publication)	417/TC/S/F (1991), published in AGP: CP/315 (1995): Purity: "The Carbosulfan content shall be declared (not less than 890 g/kg) and, when determined, the content obtained shall not differ from that declared by more than ± 25 g/kg" Impurities: Carbofuran - max. 20 g/kg Water - max. 2 g/kg
Minimum purity of the active substance as manufactured (g/kg)	Technical Carbosulfan (as manufactured, before addition of stabilizer) : min. 890 g/kg Stabilized technical Carbosulfan (MUP = manufacturing use product) : min. 865 g/kg
Identity of relevant impurities (of toxicological, environmental and/or other significance) in the active substance as manufactured (g/kg)	Carbofuran - max. 20 g/kg 5-chlorocarbofuran – max. 0.3 g/kg N-nitrosodibutylamine - max. 1 mg/kg

Molecular formula	$C_{20}H_{32}N_2O_3S$
Molecular mass	380.5 u
Structural formula	

Physical-chemical properties (Annex IIA, point 2)

<table>
<tr><td>Melting point (state purity)</td><td>No clearly defined freezing point (98.5%)</td></tr>
<tr><td>Boiling point (state purity)</td><td>219.3°C (98.5%)</td></tr>
<tr><td>Temperature of decomposition (state purity)</td><td>219.5°C (98.5%)
decomposition of carbosulfan occurs a few moments after the beginning of boiling</td></tr>
<tr><td>Appearance (state purity)</td><td>medium yellow viscous liquid, no odour to perhaps a barely noticeable amine odour (98.5%)</td></tr>
<tr><td>Vapour pressure (state temperature, state purity)</td><td>3.59 x 10^{-5} Pa at 25°C</td></tr>
<tr><td>Henry’s law constant</td><td>124.21 x 10-3 Pa.m^3.mol^{-1} (98.5%)</td></tr>
<tr><td>Solubility in water (state temperature, state purity and pH)</td><td>pH 9, 25°C : 0.11 mg/L (98.5%)
no effect of pH (no dissociation in water)</td></tr>
<tr><td>Solubility in organic solvents (state temperature, state purity)</td><td>
<table>
<tr><td></td><td>solubility at 23°C</td></tr>
<tr><td>hexane</td><td>miscible in all proportions</td></tr>
<tr><td>toluene</td><td>miscible in all proportions</td></tr>
<tr><td>acetone</td><td>miscible in all proportions</td></tr>
<tr><td>acetonitrile</td><td>miscible in all proportions</td></tr>
</table>
<table>
<tr><td></td><td>solubility at 20°C (g/L)</td></tr>
<tr><td>dichloromethane</td><td>> 250</td></tr>
<tr><td>methanol</td><td>> 250</td></tr>
<tr><td>ethyl acetate</td><td>> 250</td></tr>
</table>
</td></tr>
<tr><td>Surface tension (state concentration and temperature, state purity)</td><td>Not applicable (instability in water)</td></tr>
<tr><td>Partition co-efficient (state temperature, pH and purity)</td><td>25 °C: 7.42 (98.5%)
no effect of pH (no dissociation in water)</td></tr>
<tr><td>Hydrolytic stability (DT_{50}) (state pH and temperature)</td><td>pH 5, 25°C : DT_{50} = 0.2 hr</td></tr>
<tr><td></td><td>pH 7, 25°C : DT_{50} = 11.4 hr</td></tr>
<tr><td></td><td>pH 9, 25°C : DT_{50} = 173.3 hr (ca 7 d)</td></tr>
<tr><td>Dissociation constant (state purity)</td><td>No dissociation in water</td></tr>
<tr><td>UV/VIS absorption (max.) (if absorption > 290 nm state ε at wavelength)</td><td><u>in acetonitrile :</u>
λ_{max} 200 nm; ε = 4.342 x 10^4 $L.mol^{-1}.cm^{-1}$
λ_{max} 277.5 nm; ε = 3.144 x 10^3 $L.mol^{-1}.cm^{-1}$
<u>in acetonitrile/water 50/50</u></td></tr>
</table>

	at λ 292 nm : ε = 274 $L.mol^{-1}.cm^{-1}$
Photostability (DT_{50}) (aqueous, sunlight, state pH)	Suntest CPS (filtered xenon lamp): pH 9, 22 °C : DT_{50} = 14 hrs
Quantum yield of direct phototransformation in water at Σ > 290 nm	φ: 1.21 x 10^{-6}
Flammability (state purity)	flash point : 136.7°C (89.3%, nonstabilized) flash point : 158.9°C (85.9%, stabilized) auto-ignition temperature : 360°C (88.4%)
Explosive properties (state purity)	Not explosive (statement)
Oxidising properties (state purity)	Not oxidising (88.8%)

Summary of uses supported by available data (carbosulfan)

Crop and/ or situation	Member State or Country	Product name	F G or I	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Remarks:
(a)			(b)	(c)	Type (d-f)	Conc. of as (i)	method kind (f-h)	growth stage & season (j)	number min max (k)	interval between applications (min)	kg as/hL min max	water L/ha min max	kg as/ha min max	(l)	(m)
Sugar Beet **BEAVA**	**EU**	**Marshal 10G**	***F***	**Elateridae spp, Scutigerella spp.** **Atomaria linearis** **Aphis spp.** **Blaniulus spp. Oscinella frit** **Phyllocnistis spp**	G	**100 g/kg**	**mechanical incorpor-ation into soil**	**At drilling**	**1**	Na	**na**	**na**	**0.75 (proposed by FMC in its original submission)** **0.1 (not acceptable, see point 2.1.3 in level 2)**	**PHI : not applicable as applied at drilling**	**Granule dropped into seed furrow. Soil then folded over to cover.** Applied every 3 years Application every year is not acceptable [1]

[1] a risk was identified in section 3, further refinement is not possible without additional data and information

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)

(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated

(i) g/kg or g/l

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) PHI - minimum pre-harvest interval

(m) Remarks may include: Extent of use/economic importance/restrictions

Methods of Analysis

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

Technical as (principle of method)	HPLC-UV; CIPAC Method 417/TC/M/3: HPLC-UV (ISTD)
Impurities in technical as (principle of method)	*Non-relevant impurities and additive:* HPLC-UV, GC-MS, GPC-UV, GPC with Refractive Index detector carbofuran, 5-chlorocarbofuran~~,~~: HPLC-UV *N*-nitrosodibutylamine: HPLC-MS
Plant protection product (principle of method)	*active substance :* CS : HPLC-UV(total and free carbosulfan) GR : CIPAC Method 417/GR/M/3 (HPLC-UV (ISTD)) *relevant impurities (in GR formulation):* carbofuran, 5-chlorocarbofuran: HPLC-UV N-nitrosodibutylamine: HPLC-MS

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Open (preferably the same as for the risk assessment – pending the efficiency of the analytical method to release the conjugates of carbofuran, 3-OH-carbofuran and 3-keto-carbofuran and the establishment of a conversion factor for 3-keto-carbofuran).(PRAPeR 70/TC 21)
Food of animal origin		Open (preferably the same as for the risk assessment – pending the efficiency of the analytical method to release the conjugates of 3-OH-carbofuran and 3-keto-carbofuran and the establishment of a conversion factor for 3-keto-carbofuran) .(PRAPeR 70/TC 21)
Soil		carbosulfan; carbofuran
Water	surface	Carbosulfan; Carbofuran; 3-OH-carbofuran; 3-keto-carbofuran
	drinking/ground	Carbosulfan; Carbofuran; 3-OH-carbofuran; 3-keto-carbofuran
Air		Carbosulfan; Carbofuran

Monitoring/Enforcement methods

Food/feed of plant origin (principle of method and LOQ for methods for monitoring purposes)	HPLC-MS/MS (carbosulfan, carbofuran, 3-OH carbofuran); LOQ = 0.005 mg/kg (for each analyte; dry crops, commodities with high water content, commodities

	with high fat content) OPEN: efficiency of hydrolysis step + ILV
Food/feed of animal origin (principle of method and LOQ for methods for monitoring purposes)	Not required (no MRLs proposed) OPEN: efficiency of hydrolysis step
Soil (principle of method and LOQ)	HPLC-fluorescence detector (Carbosulfan, Carbofuran) and GC-MS (Dibutylamine); LOQ = 0.005 mg/kg LC-MS/MS (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 0.01 mg/kg (for each analyte)
Water (principle of method and LOQ)	HPLC-fluorescence detector (Carbosulfan, Carbofuran, 3-hydroxy carbofuran); LOQ = 0.1 µg/L (drinking water, surface water) HPLC-MS (carbofuran, 3-hydroxy carbofuran, carbofuran-phenol); LOQ = 0.1 µg/L (for each analyte; drinking water, groundwater, surface water); Open because the LOQ of the method is not sufficient because of the consumer risk assessment and also a method for 3-keto-carbofuran in surface and groundwater is not available.
Air (principle of method and LOQ)	HPLC-fluorescence detector(Carbosulfan); LOQ = 6 ng/m³ (warm, humid air) Open a method for carbofuran is not available.
Body fluids and tissues (principle of method and LOQ)	HPLC- fluorescence detector (Carbosulfan, Carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran); LOQ = 0.05 mg/kg (tissues, blood) LC-MS/MS (Carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran, carbofuran-7-phenol); LOQ = 50 µg/L (blood, urine), 0.01 mg/kg (tissues)

Classification and proposed labelling (Annex IIA, point 10)

with regard to physical/chemical data	None

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	High bioavailability (> 70 %) within 24 h
Distribution ‡	Large, highest level in excretory organs and carcass
Potential for accumulation ‡	No evidence of accumulation
Rate and extent of excretion ‡	Rapid and extensive (app. 90 %) within 24 h mainly via urine (63 - 78 %)
Metabolism in animals ‡	Extensive metabolism (> 80 %): hydrolysis at C-7 to form carbofuran-7-phenol and at N-S to form carbofuran and dibutylamine. Carbofuran-7-phenol and carbofuran are oxidized at C-3 generating 3-OH-metabolites. Dibutylamine is oxidized to CO_2 and volatiles.
Toxicologically relevant compounds ‡ (animals and plants)	Parent compound and metabolites (carbofuran and carbamate metabolites of carbofuran)
Toxicologically relevant compounds ‡ (environment)	Parent compound (carbosulfan), carbofuran, 3-OH-carbofuran, 3-keto-carbofuran

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	Rat: 101 mg/kg bw (♀); 180 mg/kg bw (♂) Rabbit: 42.7 mg/kg bw	**T, R25**
Rat LD_{50} dermal ‡	3700 mg/kg bw	
Rat LC_{50} inhalation ‡	0.61 mg/L air /1h (whole body, aerosol exposure = 164 mg/kg bw)	**T, R23**
Skin irritation ‡	Non- irritant	
Eye irritation ‡	Non- irritant	
Skin sensitisation ‡	Sensitising (guinea pig patch test)	**R43**

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Inhibition of acetylcholinesterase (rat) Changes in red blood cells parameters and spleen weight (dog)	
Relevant oral NOAEL ‡	90-day, rat: 2 mg/kg bw/day (20 ppm) 6-month, dog: 1.6 mg/kg bw/day (500 ppm)	
Relevant dermal NOAEL ‡	21-day, rabbit: 5 mg/kg bw/day	
Relevant inhalation NOAEL ‡	28-day, rat: 0.15 mg/m^3	

Genotoxicity ‡ (Annex IIA, point 5.4)

Carbosulfan is unlikely to be genotoxic	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Acetylcholinesterase inhibition, focal iris atrophy and degenerative retinopathy (rat) AChE inhibition in the brain, erythrocytes and plasma (mouse)	
Relevant NOAEL ‡	2-year, rat: 1 mg/kg bw/day (20 ppm) 2-year, mouse: 2.5 mg/kg bw/day (20 ppm)	
Carcinogenicity ‡	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Reduced number born pups at parental toxic doses (decreased body weight and food consumption)	
Relevant parental NOAEL ‡	1.2 mg/kg bw/day mg/kg bw/day (20 ppm)	
Relevant reproductive NOAEL ‡	1.2 mg/kg bw/day mg/kg bw/day (20 ppm)	
Relevant offspring NOAEL ‡	1.2 mg/kg bw/day mg/kg bw/day (20 ppm)	

Developmental toxicity

Developmental target / critical effect ‡	Rat: incomplete ossification at maternal toxic dose Rabbit: no developmental effects at maternal	

	toxic doses (decreased body weight and deaths)	
Relevant maternal NOAEL ‡	Rat: 2 mg/kg bw/day Rabbit: 5 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 2 mg/kg bw/day Rabbit: 10 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	NOAEL = 0.5 mg/kg bw, based on AChE inhibition in the brain	
Repeated neurotoxicity ‡	90-day, rat: NOAEL = 1.2 mg/kg bw/day (20 ppm), based on ↓ body weight gain, clinical signs of neurotoxicity, altered FOB, ↓ locomotor activity	
Delayed neurotoxicity ‡	LD_{50} hens= 376 mg/kg bw: no delayed neuropathy	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data-not required	
Studies performed on metabolites or impurities ‡		
Dibutylamine:	Rat oral LD_{50} 205 mg/kg bw/day Negative Ames test	**Xn; R22**
Carbofuran[10(a)]	Very toxic by inhalation and if swallowed Danger of very serious irreversible effects/risk for serious damage to eyes Harmful in contact with skin ADI: 0.00015 mg/kg bw/day ARfD: 0.00015 mg/kg bw	**T+; R26/28** **R39/41** R21
3-hydroxy-carbofuran[(a)]	Rat oral LD_{50} 8.3 mg/kg bw Positive in Ames test strain TA1537 with S9 mix Positive in TK locus in L5178Y mouse lymphoma cells with and w/o S9 mix	**T+, R28**
2-keto-carbofuran[(a)]	Rat LD_{50} oral: 107 mg/kg bw	**T, R25**

[10] [(a)] refer to the EFSA Scientific Report (2009) 310, 1-132: Conclusion regarding the peer review of the pesticide risk assessment of the active substance carbofuran, issued on 16 June 2009

Medical data ‡ (Annex IIA, point 5.9)

The 25 FMC employees included chemical operators, supervisors, engineers and maintenance personnel. From March 1999 to date (May 2005), carbosulfan technical has been manufactured at the same plant by a toll manufacturer. Based on the annual medical surveillance exams, no unexpected or unusual employee health effects were noted.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.005 mg/kg bw/day	Rat, acute neurotoxicity study	100
AOEL ‡	0.005 mg/kg bw/day	Rat, acute neurotoxicity study	100
ARfD ‡	0.005 mg/kg bw	Rat, acute neurotoxicity study	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation: Marshal 10G	0.2 % *in-vitro* absorption study on rat skin

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure for Marshal 10G according to the PHED model (granular formulation, soil incorporation, application rate 0.75 kg a.i./ha) was below AOEL, only if PPE (gloves) are worn during loading and application operations. Tractor mounted equipment — % of the AOEL With PPE, without RPE: 70 % With PPE and RPE during loading: 10 %
Workers	Exposure considered to be negligible
Bystanders	Exposure considered to be negligible

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

	RMS/peer review proposal	
Carbosulfan	**T**	"Toxic"
	R23/25	"Toxic by inhalation and if swallowed"
	R43	"May cause sensitization by skin contact"

Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	For peer review soil application to root and tuber vegetables (Sugar beet); in addition cereals (corn/rice); oilseeds (soya plants)
Rotational crops	DT90 (lab) carbofuran >1 year, DT90 (field) 91 days carbofuran; 10 % of the total pertinent residue (active substance and bio-available metabolites) is likely to be found in soil at 100 days (PRAPeR 62). Interim results of a confined accumulation study in rotational crops with carbofuran (spinach, radish and maize/wheat) demonstrated that the uptake of carbofuran by all plant parts was low but not negligible. Data on further identification of residues in rotational crops has to be provided.
Metabolism in rotational crops similar to metabolism in primary crops	Open
Processed commodities	No radiolabel hydrolysis study to simulate processing conditions available, however formation of novel metabolites not expected (PRAPeR 70) Potential presence / residue level of the carbamate metabolites (carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran) in refined sugar has to be addressed
Residue pattern in processed commodities similar to residue pattern in raw commodities	Open
Plant residue definition for monitoring	Open (preferably the same as for the risk assessment – pending the efficiency of the analytical method to release the conjugates of carbofuran, 3-hydroxy carbofuran and 3-keto carbofuran and the establishment of a conversion factor for 3-keto carbofuran based)(PRAPeR 70/TC 21)
Plant residue definition for risk assessment	Carbosulfan; Sum of carbofuran, 3-hydroxy carbofuran and 3-keto carbofuran, all free and conjugated, expressed as carbofuran equivalents
Conversion factor (monitoring to risk assessment)	Open

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Lactating goats and laying hens.
Time needed to reach a plateau concentration in milk and eggs	Eggs: within 5 days in both egg yolks and whites in the phenyl label and dibutylamine (DBA) label study HR $_{phenyl}$ [mg carbosulfan equiv./ kg] yolk 0.026 ; white 0.009 HR $_{DBA}$ [mg carbosulfan equiv./ kg] yolk 1.87 ; white 0.119 Milk: after 2 days of dosing both for the 2 labelling forms phenyl and dibutylamine HR $_{phenyl}$ [mg carbosulfan equiv./ kg] 0.07 HR $_{DBA}$ [mg carbosulfan equiv./ kg] 0.748
Animal residue definition for monitoring	Open (preferably the same as for the risk assessment – pending the efficiency of the analytical method to release the conjugates of 3-hydroxy carbofuran and 3-keto carbofuran and the establishment of a conversion factor for 3-keto carbofuran based on metabolism data).(PRAPeR 70/TC 21)
Animal residue definition for risk assessment	Sum of 3-hydroxy carbofuran and 3-keto carbofuran, both free and conjugated expressed as carbofuran.
Conversion factor (monitoring to risk assessment)	Open
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes; log $P_{o/w}$ carbosulfan (25 °C): 7.42

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

.....	**A carbofuran confined accumulation in rotational crops study (field rate: 0.6 kg as/ha)– Interim Report was provided** Interim results (TRR): 30-day interval Leafy crop: 0.031 mg/kg, R/T crop: root 0.006 mg/kg, leaves 0.008 mg/kg, Cereal crop: forage 0.015 mg/kg, straw 0.005 mg/kg, grain 0.001 mg/kg 60 day interval: Leafy crop: 0.009 mg/kg, R/T crop: root 0.004 mg/kg, leaves 0.006 mg/kg, Cereal crop: forage 0.014 mg/kg, results for straw, grain not available for the peer review 365 day interval:no results available for the peer review

Data on further identification of residues in rotational crops has to be provided.

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 introduction)

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

Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)

Residue levels in animal matrices were calculated on the basis of the metabolism studies. No residues above the LOQ of the analytical method were detected in the available feeding study in ruminants (LoQ for milk: 0.025 mg/kg, LoQ for cream and tissues: 0.050 mg/kg), however the LOQ is considered to high to be used for risk assessment purposes given the toxicological properties of the carbamate structured compounds.

As residues in rotational crops relevant in animal diet have not been considered but only the target crop (sugar beet), the available estimates are expected to slightly increase. It should however be noted that the validity of the residue data in sugar beet is still pending confirmation on whether or not conjugates of carbofuran and 3-hydroxy carbofuran were included in the reported results, and how residues of 3-keto carbofuran and conjugates will be addressed.

	Carbofuran and 3-hydroxy carbofuran, free and conjugated)		
	Ruminant	Poultry	Pig
Muscle	**n/a (TRR 0.006 mg/kg)**	0.038 µg/kg	n/a
Liver	**0.008 µg/kg**	0.18 µg/kg	n/a
Kidney	**0.047 µg/kg**	n/a	n/a
Fat	**n/a (TRR 0.01 mg/kg)**	0.056 µg/kg	n/a
Milk	**0.043 µg/kg**		
Eggs		0.038 µg/kg	

[1] State whether intake by specified animals is ≥ 0.1 mg/kg diet/day or not, based on a dry weight basis as given in table 1 of Guidance Document Appendix G

[2] Fill in results from appropriate feeding studies at appropriate dose rates according to Guidance Document Appendix G. State 'not required' when the conditions of requirement of feeding studies according to directive 91/414/EEC are not met.

Summary of critical residues data **(Annex IIA, point 6.3, Annex IIIA, point 8.2)**

Crop	Northern or Mediterranean Region	Trials results relevant to the critical GAP (a)	Recommendation/comments	MRL (mg/kg)	STMR (mg/kg) (b)
Sugar beet	**NE**	Pending clarification on issues of conjugates and 3 keto carbofuran residues (refer to EFSA conclusion 3.1.1) **root : -*carbosulfan* : 10 x <0.05 mg/kg -*carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.*: 11 x <0.1 mg/kg **Leaves : -*carbosulfan* : 12 x <0.05 mg/kg -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.: 12 x <0.1 mg/kg. **root: -*carbosulfan*: 2 x <0.005 mg/kg -*carbofuran + 3-OH-carbofuran, free and conjugated expressed as carbofuran equiv*: 2 x <0.01 mg/kg **Leaves/tops: -*carbosulfan*: 2 x <0.005 mg/kg - *carbofuran + 3-OH-carbofuran, free and conjugated expressed as carbofuran equiv*: 2 x <0.01mg/kg	Samples of leaves/tops and roots at different PHIs up to normal harvest time were analysed for carbosulfan and its metabolites carbofuran and 3-OH-carbofuran. Decay curves are given with last sampling 129 to 173 days after the application. Trials performed in accordance with the critical GAP	*Carbosulfan* : 0.05* mg/kg *Carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.*: 0.1* mg/kg **MRL on sugar beet root:** *Carbosulfan* : 0.005* mg/kg *Carbofuran + 3-OH-carbofuran* , free and conjugated, *expressed*	*Carbosulfan* : 0.05 mg/kg *Carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.*: 0.1 mg/kg /
	SE	**root : -*carbosulfan* : 4 x <0.05 mg/kg			

		-carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.: 4 x <0.1 mg/kg **Leaves : *-carbosulfan* : 4 x <0.05 mg/kg -carbofuran + 3-OH-carbofuran expressed as carbofuran equiv.: 4 x <0.1 mg/kg **root: *-carbosulfan*: 7 x<0.005 mg/kg *- carbofuran + 3-OH-carbofuran, free and conjugated expressed as carbofuran equiv*: 7 x <0.01 mg/kg **Leaves: *-carbosulfan*: <0.05[(1)]-<0.005-<0.005-<0.05[(1)]-<0.005-<0.005-<0.05[(1)] mg/kg *- carbofuran + 3-OH-carbofuran, free and conjugated expressed as carbofuran equiv*: <0.1[(1)]-<0.01-<0.01-<0.1[(1)]-<0.01-<0.01-<0.1[(1)]-mg/kg [(1)]: These residue values were displayed for transparency but were not considered for MRL setting.		*as carbofuran equiv.*: 0.01* mg/kg, pending clarification on issues of cojugates and 3 keto carbofuran residues (refer to EFSA conclusion 3.1.1)	

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

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

a) Carbosulfan

ADI	0.005mg/kg bw/day
TMDI (% ADI) according to WHO European diet	*EFSA PRIMo rev. 2A* 0.1 % (WHO cluster diet B)
TMDI (% ADI) according to national (to be specified) diets	*EFSA PRIMo rev. 2A* 2.3 % (UK toddler)
IEDI (WHO European Diet) (% ADI)	Not applicable
NEDI (specify diet) (% ADI)	Not applicable
Factors included in IEDI and NEDI	Not applicable
ARfD	0.005 mg/kg bw/day
IESTI (% ARfD)	*EFSA PRIMo rev. 2A* 6.4 % (children) 2.6 % (general population)

B) Sum of Carbofuran, 3-OH-carbofuran and 3-keto-carbofuran, free and conjugated, expressed as carbofuran equivalents
(RA pending confirmation on whether residues determined in residue trials fully include conjugates, and on residue data on 3-keto-carbofuran)

ADI	0.00015 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	43.9 % (WHO cluster diet B)
TMDI (% ADI) according to national (to be specified) diets	*Scenario 1: EFSA PRIMo rev. 2A* 172.9 % (UK toddler) *Scenario 2: UK Model* 98 % (UK toddler)
IEDI (WHO European Diet) (% ADI)	no refinement possible with available data
NEDI (specify diet) (% ADI)	no refinement possible with available data
Factors included in IEDI and NEDI	not applicable
ARfD	0.00015 mg/kg bw/day
IESTI (% ARfD)	*Scenario 1: EFSA PRIMo rev. 2A* Highest % ARfD : 1806.8 % - Scarole (broad-leaf endive) (children) Highest % ARfD : 738.1 % - Chinese cabbage (general population) *Scenario 2: UK Model* Exceedances of the ARfD were observed for all the categories of UK consumers when consuming sugar beet roots (173% to 518%); root vegetables (except for UK adults) and leafy vegetables

grown as rotated crops. There is no acute intake concerns for cereals grown in rotation to sugar beet

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

Residue levels of the carbamate structured metabolites in refined sugar should be addressed (sufficiently low LOQ).
In an available study no residues of any carbamate (<0.01 mg/kg) or phenol (<0.02 mg/kg) metabolite were found in the roots, cossettes or dehydrated pulp samples. No carbamate residues (<0.01 mg/kg) were found in the molasses or sugar. However, low residue levels of 3-keto-7-phenol (0.02-0.03 mg/kg) were recovered in the molasses and sugar.

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

Carbosulfan	Sugar beet root	0.005*
Carbofuran, 3-hydroxy carbofuran, 3-keto carbofuran	Sugar beet root	Pending; residue definition for monitoring to be confirmed as the same as for risk assessment, pending the efficiency of the hydrolysis step release the carbofuran, 3-hydroxy carbofuran and 3-keto-carbofuran conjugates and the establishment of a conversion factor for 3-keto carbofuran.)

Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days	0.55-7.3 % after 28-120 d, [^{14}C-phenyl ring]-label (n= 6) 46.5-46.7 % after 28 d, [^{14}C-dibutylamine]-label (n= 2)
Non-extractable residues after 100 days	34.4-90.3 % after 28-120 d, [^{14}C-phenyl ring]-label (n=6) 29.9-35.1 % after 28 d, [^{14}C-dibutylamine]-label (n= 2)
Relevant metabolites - name and/or code, % of applied (range and maximum)	Carbofuran : 34.6- 69.3% at 3-21 days (n= 6) 3-keto-carbofuran: 6.6 % AR at 28 d (end of the study) (EPCO 31 agreed that this metabolite needs to be further assessed) Dibutylamine: 15.4-21.5% at 0-3 days (n=2) Moreover EPCO 31 (for carbofuran and benfuracarb) agreed that the minor transient metabolite 3-OH-carbofuran needs to be further assessed

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation	No reliable data available
Soil photolysis	No data available Studies performed with metabolite carbofuran show that this metabolite is stable to photolysis in soil.

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

Laboratory studies

Carbosulfan	Aerobic conditions							
Soil type	X[1]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} (d)	f. f. k_f/k_{dp}	DT_{50} (d) * 20°C pF2/10kPa	St. (X^2)	Method of calculation
Loamy sand	-	5.8	20/40	4.02	-	4.02	3.96	SFO
Silt loam	-	7.1	20/40	-	-	8.72	11.08	**FOMC**
Loam	-	7.3	20/40	-	-	9.77	15.99	**FOMC**
Loam	-	7.2	20/40	-	-	11.43	15.88	**FOMC**
Sandy clay loam	-	7.0	23/(60% FC)	6.2 & -	-	6.00**	8.95 & 1.71	SFO & FOMC
Silt loam	-	6.1	23/(60% FC)	0.42	-	0.53	2.25	SFO
Silt loam	-	7.1	10/40	21.7	-	-	10.86	SFO
Geometric mean						4.81		

*: where FOMC kinetic was used, the values in the table are pseudo DT_{50} value calculated from FOMC DT_{90} divided by 3.32

**: geometric mean taken from 2 same soils

Carbofuran	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50} (d)	f. f. k_f/k_{dp}	DT_{50} (d) 20°C pF2/10kPa	St. (X^2)	Method of calculation
Carbofuran as test item								
Sandy loam	-	5.7	25/75% FC	13.72	-	17.87	7.9	SFO
Silt loam	-	5.8	20/40	14.75	-	14.01	10.3	SFO
Silt loam	-		10/40	86.36	-	-	3.1	SFO
Sandy loam	-	6.5	20/40	8.97	-	7.71	14.8	SFO
Clay loam	-	7.5	20/40	14.12	-	13.56	8.5	SFO
Loam	-	5.7	20/40	19.17	-	17.25	2.1	SFO
Sandy loam	-	5.7	25/75% FC at 1/3 bar	307	-	151	2.6	SFO
Sandy loam	-	7.7	25/75% FC at 1/3 bar	111	-	54.6	9.1	SFO
Sandy loam	-	7.1	25/82% FC	362	-	387	1.4	SFO
Carbofuran as metabolite of carbosulfan								
Loamy sand	-	5.8	20/40	6.92	1	6.92	13.8	SFO
Silt loam	-	7.1	20/40	11.61	0.6	9.39	21.1	SFO
Loam	-	7.3	20/40	13.04	0.59	11.46	7.8	SFO
Loam	-	7.2	20/40	25.99	0.47	22.54	14.8	SFO
Silt loam	-	6.1	23/(60% FC)	17.47	0.76	22.19	4.4	SFO
Carbofuran as metabolite of benfuracarb								
Sandy loam	-	6.5	20/40	6.70	0.91	5.70	20.1	SFO
Sandy loam	-	5.8	20/40	20.39	0.79	20.39	15.9	SFO
Loam	-	7.1	20/40	11.42	0.83	10.39	15.7	SFO
Clay	-	6.7	20/40	23.38	0.91	11.69	16.8	SFO
Overall median						14.01		

3-OH-Carbofuran	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
loamy sand	-	5.7*	20/40	<1/<1	-	<1	na	graphical
sandy loam	-	6.3*	20/40	0.27/0.88	-	0.22	1.0	SFO
clay	-	6.9*	20/40	0.51/1.70	-	0.3	1.0	SFO
Geometric mean						0.41		

* in $CaCl_2$

3-keto-Carbofuran	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
loamy sand	-	5.7*	20/40	4.41/14.6	-	4.41	0.994	SFO
sandy loam	-	6.3*	20/40	8.12/27.0	-	6.65	0.984	SFO
clay	-	6.9*	20/40	1.54/5.13	-	0.9	0.998	SFO

Geometric mean					3.01		

* in $CaCl_2$

Carbofuran-phenol	Aerobic conditions							
Soil type	X[1]	pH	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
loamy sand		5.7*	20/40	<1/<1	-	<1	na	graphical
sandy loam		6.3*	20/40	<1/<1	-	<1	na	graphical
clay		6.9*	20/40	<1/<1	-	<1	na	graphical
Geometric mean						<1		

* in $CaCl_2$

dibutylamine	Aerobic conditions							
Soil type	X[1]	pH*	t. °C / % MWHC	DT_{50} (d) **	f. f. k_{dp}/k_f	DT_{50} (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Silt loam		7.51	20/pF 2-2.5	0.06	-	-	0.9929	SFO
Clay		7.2	20/pF 2-2.5	0.58	-	-	0.9408	SFO
Sand		5.81	20/pF 2-2.5	2.13	-	-	0.9258	SFO
Geometric mean				0.42				

* in $CaCl_2$

**: values are uncertain and the derivation of endpoints did not follow FOCUS recommendations

	DT_{50lab} (20°C, anaerobic): no relied on information is available
	Degradation in the saturated zone: not required.
Field studies (state location, range or median with n value)	DT50f, carbosulfan, Netherlands, Spain, Italy, bare soil, 0.35-9.8 d (n= 5, r^2 =0.88-0.997) single first order (Field studies where carbosulfan was applied as parent (Marshal 25CS, Marshal 5G, 10G) DT50f, carbofuran, Netherlands, Spain, Italy, bare soil, 1.3 d -27 d (n= 5, r^2 =0.88-0.997) single first order (Field studies where carbosulfan was applied as parent (Marshal 25CS, Marshal 5G, 10G) and carbofuran appeared as metabolite, FMC) DT50f, dibutylamine, Netherlands, Spain, Italy, bare soil, 2.2 d -54 d (n= 5, r^2 =0.82-0.997) single first order (Field studies where carbosulfan was applied as parent (Marshal 25CS, Marshal 5G, 10G) and dibutylamine appeared as metabolite, FMC)
	DT90f: carbosulfan, Netherlands, Spain, Italy, bare soil, 1.2-33 d (n= 5, r^2 = 0.880-0.997) 1st order DT90f: carbofuran, Netherlands, Spain, Italy,

	bare soil, 4.4-91 d (n= 5, r^2 = 0.880-0.997) 1st order DT90f: dibutylamine, Netherlands, Spain, Italy, bare soil, 7.4-181 d (n= 5, r^2 = 0.82-0.997) 1st order
Soil accumulation and plateau concentration	No soil accumulation studies available, none required

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Carbosulfan

Parameter		Soil I	Soil II	Soil III	Soil IV	Arithmetic Mean
K_F	[mL/g]	142	316	267	467	-
K_{FOC}	[mL/g]	12895	16623	33314	17493	20081
K_{FOM}	[mL/g]	7479	9642	19324	10147	11648
1/n	-	0.88	0.98	0.91	0.97	0.94
r^2	-	0.988	0.993	0.990	0.985	-
pH dependence (yes or no)				No		

Carbofuran							
Soil Type	OC %	Soil pH*	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.19	5.8	-	-	0.425	19	0.94
Loam	1.22	7.27	-	-	0.299	24	0.92
Silty clay loam	2.67	5.42	-	-	0.456	17	1.01
Silt loam	1.97	5.8	-	-	0.549	28	0.95
Arithmetic mean						**22****	**0.96****
pH dependence (yes or no)			No				

* in $CaCl_2$
** endpoint used for the modelling

3-OH-Carbofuran							
Soil Type	OC %	Soil pH*	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.29	5.7	1.4	62	-	-	-
Sandy loam	1.02	6.3	0.4	**43****	-	-	-
Sandy clay	1.9	6.9	1.1	60	-	-	-
Arithmetic mean			0.97	55	-	-	-
pH dependence (yes or no)			No				

* in $CaCl_2$
** endpoint used for the modelling

3-keto-Carbofuran							
Soil Type	OC %	Soil pH*	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.29	5.7	1.1	47.5	-	-	-
Sandy loam	1.02	6.3	-	-	4.59	440	1.144
Sandy clay	1.9	6.9	-	-	9.65	504	0.489
Arithmetic mean			Koc: 330.5**				
pH dependence (yes or no)			No				

* in $CaCl_2$
** endpoint used for the modelling

Carbofuran-phenol							
Soil Type	OC %	Soil pH*	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Loamy sand	2.29	5.7	-	-	10.0	444	0.407
Sandy loam	1.02	6.3	-	-	18.9	1810	0.516
Sandy clay	1.9	6.9	-	-	16.0	838	0.751
Arithmetic mean					14.97	1031**	
pH dependence (yes or no)			No				

* in $CaCl_2$
** endpoint used for the modelling

dibutylamine ‡							
Soil Type	OC %	Soil pH*	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc[a] (mL/g)	1/n[a]
Silt loam	1.1	7.4	-	-	3.227	293	0.79
clay	1.79	7.2	-	-	12.235	684	0.77
Sandy clay loam	1.09	5.78	-	-	2.722	250	0.64
Arithmetic mean						409**	0.73
pH dependence (yes or no)			No				

Note: the equilibrium time was prolonged to 48 hrs
* in $CaCl_2$
** endpoint used for the modelling
[a]: values are uncertain

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching	Point covered by a Thin Layer Chromatography study (of limited quality) on 4 soils. Mobility has been determined by comparison with reference substances (2,4-D and DDT)
Aged residues leaching	Study of limited quality

	Precipitation (mm): 508 mm Leachate: 8-80.7% total residues/radioactivity in leachate No information on a.s. and metabolites residues
Lysimeter/ field leaching studies	Location: Germany, Lower Saxony, Borstel Study type: 2 lysimeters, 2years Soil : loamy sand Number of applications: 1 application Application rate:1.05 kg/ha carbosulfan on bare soil Average annual rainfall (mm): 800 mm Average annual leachate volume (mm): 493 mm Annual average concentrations: 0.82-0.85 µg equivalent a.s./L (no information on the leachate concentrations of carbosulfan, carbofuran and possible metabolites) Non reliable information available from the lysimeter studies of carbofuran

PEC (soil) (Annex IIIA, point 9.1.3)

Application rate	Crop: sugar beet 0% plant interception: granular application in the sowing bed, soil layer: 5 cm, soil density :1.5 kg/dm^3 Number of applications: 1 Application rate(s): 0.75 kg/ha of carbosulfan and a 100% formation fraction is assumed as a worst case for both carbofuran and dibutylamine (molecular mass of carbosulfan is 380.5; molecular mass of carbofuran is 221.3, molecular mass of dibutylamine is 129.3) worst case DT50f of 9.8 days, 27 days and 54 days, respectively for carbosulfan, carbofuran and dibutylamine (Coria del Rio, Spain, Marshal 10G).

PEC$_{(s)}$ (mg/kg soil)		Single application Actual (carbosulfan)	Single application Actual (carbofuran)	Single application Actual (dibutylamine)
Initial		**1. 000**	**0.581**	0.340
Short term	24h	**0.932**	**0.566**	0.336
	2d	**0.868**	**0.552**	0.331
	4d	**0.753**	**0.525**	0.323
Long term	7d	**0.610**	**0.486**	0.311
	28d	**0.138**	**0.283**	0.237
	50d	**0.029**	**0.161**	0.179
	100d	**<0.001**	**0.045**	0.094

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolysis of active substance and relevant metabolites (DT_{50}) (state pH and temperature)	pH5: 25°C DT_{50} 0.2 hr (1st order)

	Major hydrolysis products : Carbofuran and dibutylamine; Carbofuran decomposes to 7-phenol under basic conditions
	pH7: 25°C 11.4 hr (1st order) distilled water (pH 7.3) : DT_{50} = 18.2 hr (1st order)
	pH9: 25°C DT_{50} 173.3 hr (ca 7 d) (1st order)
Photolytic degradation of active substance and relevant metabolites	Xenon arc lamp with UV filter cut, carbosulfan DT_{50} = 14 hrs 7-phenol max. level of 16.7% after 23.9 hrs. Given the short hydrolysis half-time of Carbofuran at basic pH, this is most likely a hydrolysis product and not a photolytic product. polar degradation products (polar-1 and polar-2) accumulate to 66.7% at final sampling point
Readily biodegradable (yes/no)	No, 28% biodegradation after 28 days

Degradation in water / sediment

Carbosulfan	Distribution (max in water 67.4-84.5% at 0 d. Max. sed 17.6-30.4% after 2-7 d)									
Water / sediment system	pH water phase	PH sed	t. °C	DT_{50} whole sys.	St. (χ^2)	DT_{50}-DT_{90} water	St. (χ^2)	DT_{50}- DT_{90} Sed	St. (χ^2)	Method of calculation
Pond (Millstream A)	7.32	7.2	20	5.57	12.1	0.54	25.8	-	-	FOMC, DT90 divided by 3.32 for DT50 whole system
Pond (Swarkestone) B	7.77	7.1	20	3.89	6.4	3.16	9.2	4.73	16.7	SFO, non linear
Pond (Millstream D)	7.32	7.2	20	3.63	14.4	1.41	4.8	10.9	22.8	SFO, non linear
Worst case used for PEC modelling				5.57						

Note: Millstream A and D are the same system dosed with different application rates

Carbofuran	Distribution of carbofuran resulting from application of carbosulfan: max in water 24.4-33.2% at 7-14 d. Max. sed 11.8-20.1% after 1-14 d									
Water / sediment system	PH water phase	pH sed	t. °C	DT50-DT90 whole sys.	St. (χ^2)	DT_{50}-DT_{90} water	St. (χ^2)	DT_{50}- DT_{90} Sed	St. (χ^2)	Method of calculation
Pond (Cooper)[c]	6.11	5.3	25	70.07 *	6.8	-	-	-	-	SFO, non linear
Pond (Millstream) A **	7.32	7.2	20	51.29	6.7	-	-	-	-	SFO, non linear
Pond (Millstream) D **	7.32	7.2	20	25.75	20.4	-	-	-	-	SFO, non linear
Pond (Swarkestone) B **	7.77	7.1	20	13.99	9.0	-	-	-	-	SFO, non linear

River (Rheinsulz)[c]	8.2	7.45	20	9.04	14.8	-	-	-	-	SFO, non linear
Pond (Ormalingen)[c]	7.0	7.08	20	11.64	5.2	-	-	-	-	SFO, non linear
OVP [b]	8.04	8.3	20	13.9-46.3	0.96	8.2-27.2#	0.99	-	-	SFO
SW [b]	7.8	7.9	20	14.8-49.2	0.97	10.8-35.8#	0.99	-	-	SFO
Worst case used for PEC modelling				**70.07**						

*: normalised to 20°C
**: study with carbosulfan as test item
$DT_{50/90}$ for dissipation
[b] study with benfuracarb as test item
[c] study with carbofuran as test item
Note: Millstream A and D are the same system dosed with different application rates

Carbofuran-7-phenol	Distribution of Carbofuran-7-phenol resulting from application of carbosulfan: max in water 1.4-23% at 1-100 d. Max. sed 0.5-6.2% after 1-100 d									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (χ^2)	DT_{50}-DT_{90} water	St. (χ^2)	DT_{50}-DT_{90} Sed	St. (χ^2)	Method of calculation
River (Rheinsulz)[c]	8.2	7.45	20	1.69	22.0	-	-	-	-	SFO, non linear
Pond (Ormalingen)[c]	7.0	7.08	20	1.86	27.0	-	-	-	-	SFO, non linear
Pond (Millstream) A [a]	7.32	7.2	20	3.6	87.3	-	-	-	-	SFO, non linear
Pond (Millstream) D [a]	7.32	7.2	20	1.79	55.3	-	-	-	-	SFO, non linear
Pond (Swarkestone) B [a]	7.77	7.1	20	2.6	69.4	-	-	-	-	SFO, non linear
OVP [b]	8.04	8.3	20	20.5-68.1	0.99	-	-	20.5-68.1	0.99	SFO
SW [b]	7.8	7.9	20	4.8-16.1	0.89	-	-	4.8-16.1	0.89	SFO
Worst case default used for PEC modelling				**1000**						

[a]: study with carbosulfan as test item
[b] study with benfuracarb as test item
[c] study with carbofuran as test item

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization (end of the study)*	Non-extractable residues in sed. max	Non-extractable residues in sed. (end of the study)
Pond (Millstream) A	7.32	7.2	30.38% after 102 d	42.99% after 102 d	42.99% after 102 d
Pond (Millstream) D	7.32	7.2	20% after 102 d	42.53% after 102 d	42.53% after 102 d
Pond (Swarkestone) B	7.77	7.1	20.32% after 102 d	35.5% after 60d	30.53% after 102 d

*: sum of volatile radioactivity (mainly CO_2)

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

Parent	See below
Parameters used in FOCUSsw step 1 and 2	
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: 'SWASH' (Surface Water Scenarios Help), version 1.1, FOCUS TOXSWA v 2.2.1
Application rate	Crop: sugar beet 0% plant interception: granular application in the sowing bed, soil layer: 5 cm, soil density: 1.5 kg/dm^3 Number of applications: 1 Application rate(s): 750 g a.s./ha, incorporation depth: 7 cm
Main routes of entry	Drainage, runoff

Input data for carbosulfan

Variable	Carbosulfan	
	Value	Reference
DT_{50} in water (days)	1000	Focus default value
DT_{50} in sediment (days)	5.57	Max. DT50 water/sediment system
DT50 water sediment system (days)	5.57	Max DT50 water sediment
DT_{50} in soil (days)	5	Price et al (2007a) – rounded, the geometric mean is 4.8 d
Koc (mL/g)	20081	Völkel (2007b) arithmetic mean
Freundlich coefficient	0.94	Völkel (2007b)
Vapour pressure (Pa) at 25°C	3.59 10^{-5}	Alvarez, 1995
Water Solubility (mg/L) at 25°C	0.11	Anon, 2006
Molecular Weight (g/mol)	380.5	
Plant Uptake Value	0.0	Non systemic
Crop Wash-off Factor PRZM input*	0.0007	0.016 x water solubility $^{0.3832}$

Input data for carbofuran

Variable	Carbofuran	
	Value	Reference
DT_{50} in water (days)	70.07	Max DT50 water sediment
DT_{50} in sediment (days)	1000	Focus default value
DT50 water sediment system (days)	70.07	Max DT50 water sediment
DT_{50} in soil (days)	14.01	median Price *et al* (2007a), Price *et al* (2007b) and Ford (2007), Saxena (1994), Schocken

		(1989)
Koc (mL/g)	22	Arithmetic mean Mamouni (2002)
Freundlich coefficient	0.96	Arithmetic mean Mamouni (2002)
Formation fraction in soil	1	Price *et al* (2007a) – Worst case
Vapour pressure (Pa) at 25°C	8.0×10^{-5} [b]	Alvarez (1995)
Water Solubility (mg/L) at 20°C	322	Bal *et al* (2002)
Molecular Weight (g/mol)	221.3	
Plant Uptake Value	0.0	Non systemic
Crop Wash-off Factor PRZM input*	0.146	0.016 x water solubility$^{0.3832}$

Input data for 3-keto-carbofuran

Variable	3-keto-carbofuran	
	Value	Reference
DT_{50} in water (days)	1000	Default Focus value
DT_{50} in sediment (days)	1000	Default Focus value
DT50 water sediment system (days)	1000	Default Focus value
DT_{50} in soil (days)	3.01	Geometric mean (Willems, 2005b)
Koc (mL/g)	331	arithmetic mean (Van Noorloos and Willems, 2005c)
Freundlich coefficient	1	PRAPeR 62
Formation fraction in soil	1	Worst case assumption
Vapour pressure (Pa) at 25°C	2.02×10^{-3}	Data from Arysta LifeScience
Water Solubility (mg/L) at 25°C	4464	Data from Arysta LifeScience
Molecular Weight (g/mol)	235.24	
Plant Uptake Value	0.0	Non systemic
Crop Wash-off Factor PRZM input	0.401	0.016 x water solubility$^{0.3832}$

Input data for 3-hydroxy-carbofuran

Variable	3-hydroxy-carbofuran	
	Value	Reference
DT_{50} in water (days)	1000	Default Focus value
DT_{50} in sediment (days)	1000	Default Focus value
DT50 water sediment system (days)	1000	Default Focus value
DT_{50} in soil (days)	0.41	Geometric mean (Willems, 2005a)
Koc (mL/g)	43	Worst case.

		Van Noorloos and Willems, 2005a)
Freundlich coefficient	1	PRAPeR 62
Formation fraction in soil	1	Worst case assumption
Vapour pressure (Pa) at 25°C	6.71×10^{-5}	Data from Arysta LifeScience
Water Solubility (mg/L) at 25°C	6207	Data from Arysta LifeScience
Molecular Weight (g/mol)	237.3	
Plant Uptake Value	0.0	Non systemic
Crop Wash-off Factor PRZM input	0.455	0.016 x water solubility$^{0.3832}$

Input data for 7-phenol-carbofuran

Variable	7-phenol-carbofuran	
	Value	Reference
DT_{50} in water (days)	1000	Default Focus value
DT_{50} in sediment (days)	1000	Default Focus value
DT50 water sediment system (days)	1000	Default Focus value
DT_{50} in soil (days)	1	PRAPeR 67
Koc (mL/g)	1031	Arithmetic mean Van Noorloos and Willems (2005c)
Freundlich coefficient	0.9	PRAPeR 62
Formation fraction in soil	1	A worst case assumption of 100% formation
Vapour pressure (Pa) at 25°C	0.28	Data from Arysta LifeScience
Water Solubility (mg/L) at 25°C	1096	Data from Arysta LifeScience
Molecular Weight (g/mol)	164.2	
Plant Uptake Value	0.0	Non systemic
Crop Wash-off Factor PRZM input*	0.234	0.016 x water solubility$^{0.3832}$

Input data for dibutylamine

Variable	Dibutylamine	
	Value	Reference
DT_{50} in water (days)	1000	FOCUS default value
DT_{50} in sediment (days)	1000	FOCUS default value
DT50 water sediment system (days)	1000	FOCUS default value
DT_{50} in soil (days)	0.46	Geometric mean (Völkel, 2007a) Note: the geometric mean should be 0.42 d (non FOCUS kinetics, not normalized)
Koc (mL/g)	409	Arithmetic mean (Völkel, 2007c)
Freundlich coefficient	0.73	Idem

Formation fraction in soil	1.00	Worst case assumption of 100% formation
Vapour pressure (Pa) at 25°C	202 x 10^{-3}	Data from Arysta LifeScience
Water Solubility (mg/L) at 25°C	4050	MSDS
Molecular Weight (g/mol)	129.2	
Plant Uptake Value	0.0	Non systemic
Crop Wash-off Factor PRZM input	0.386	0.016 x water solubility$^{0.3832}$

Calculated PEC values for carbosulfan and its metabolites (FOCUS Step 3) in surface water

Scenario	Compound	Max PECsw (µg/L)	Date of max PECsw	Max PECsed (µg)	Date of max PECsed
D3 ((Ditch)	Carbosulfan	0.00E+00	1-janv-92	0.00E+00	1-janv-92
D4 ((Pond)	Carbosulfan	0.00E+00	9-déc-85	0.00E+00	31-déc-85
D4 ((Stream)	Carbosulfan	0.00E+00	9-déc-85	0.00E+00	9-déc-85
R1 ((Pond)	Carbosulfan	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R1 ((Stream)	Carbosulfan	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R3 ((Stream)	Carbosulfan	0.00E+00	1-oct-80	0.00E+00	1-oct-80
D3 ((Ditch)	Carbofuran	1.11E-02	29-janv-93	2.00E-02	15-avr-93
D4 ((Pond)	Carbofuran	6.58E-02	30-janv-86	9.03E-02	6-mars-86
D4 ((Stream)	Carbofuran	4.62E-02	16-déc-85	4.10E-02	28-janv-86
R1 ((Pond)	Carbofuran	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R1 ((Stream)	Carbofuran	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R3 ((Stream)	Carbofuran	0.00E+00	1-oct-80	0.00E+00	1-oct-80
D3 ((Ditch)	DBA	0.00E+00	1-janv-92	0.00E+00	1-janv-92
D4 ((Pond)	DBA	0.00E+00	9-déc-85	0.00E+00	1-janv-85
D4 ((Stream)	DBA	0.00E+00	5-déc-85	0.00E+00	9-déc-85
R1 ((Pond)	DBA	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R1 ((Stream)	DBA	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R3 ((Stream)	DBA	0.00E+00	1-oct-80	0.00E+00	1-oct-80
D3 ((Ditch)	7-P-C*	1.30E-05	29-janv-93	4.07E-04	4-avr-93
D4 ((Pond)	7-P-C*	8.50E-05	31-janv-86	1.85E-03	1-mai-86
D4 ((Stream)	7-P-C*	7.50E-05	1-janv-85	9.67E-04	1-févr-86
R1 ((Pond)	7-P-C*	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R1 ((Stream)	7-P-C*	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R3 ((Stream)	7-P-C*	0.00E+00	1-oct-80	0.00E+00	1-oct-80
D3 ((Ditch)	3-H-C	2.11E-04	29-janv-93	4.28E-04	16-avr-93
D4 ((Pond)	3-H-C	1.39E-03	30-janv-86	2.39E-03	20-mars-86
D4 ((Stream)	3-H-C	8.85E-04	17-déc-85	8.12E-04	28-janv-86
R1 ((Pond)	3-H-C	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R1 ((Stream)	3-H-C	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R3 ((Stream)	3-H-C	0.00E+00	1-oct-80	0.00E+00	1-oct-80
D3 ((Ditch)	3-K-C	6.57E-04	30-janv-93	4.70E-03	1-mai-93
D4 ((Pond)	3-K-C	0.00E+00	3-sept-85	1.07E-06	1-mai-86
D4 ((Stream)	3-K-C	0.00E+00	6-juin-85	0.00E+00	25-avr-86
R1 ((Pond)	3-K-C	0.00E+00	1-mars-84	0.00E+00	1-mars-84

R1 ((Stream)	3-K-C	0.00E+00	1-mars-84	0.00E+00	1-mars-84
R3 ((Stream)	3-K-C	0.00E+00	1-oct-80	0.00E+00	1-oct-80

DBA: dibutylamine; 7-P-C: carbofuran phenol; 3-H-C: 3-Hydroxy-carbofuran; 3-K-C: 3-Keto-carbofuran

*The maximum FOCUS Step 3 PECsw and PECsed for carbofuran were multiplied using a MW correction factor (164.2/221.3 = 0.74) and the maximum % occurrence of carbofuran-phenol in water-sediment (total AR of 30% following the Yeomans (1995 and 1996) study). It resulted in PECsw of 0.0146 µg/L carbofuran-phenol and PECsed 0.02 µg/kg carbofuran-phenol.

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, monitoring, lysimeter)	FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUS-PELMO and FOCUS PEARL Scenarios: Chateaudun, Hamburg, Jokionen, Kremsmünter,Okehampton, Piacenza, Porto , Seville,Thiva Crop: sugar beet
Application rate	Application rate and method: 750 g carbosulfan/ha, 7 cm soil incorporation No. of applications: 1 application every year or 1 application in every 3 years(incorporation at planting) Time of application: 14 days before emergence

Test Substance Properties	Carbosulfan	Carbofuran	7-Phenol-Carbofuran	3-Hydroxy-Carbofuran	3-Keto-Carbofuran	Dibutylamine
Molar Mass in g/ mol	380.5	221.3	164.2	237.3	235.24	129.24
Vapour pressure in Pa at 25°C	3.59E-05	8E-05	0.28	6.71-5	2.02E-3	202E-3
Formation fraction in soil (%)	Parent	~~74~~ 100	100	100	100	100
Solubility in mg/ L at 20°C	0.11 (25°C)	322	1096 (25°C)	6207 (25°C)	4464 (25°C)	4050 (25°C)
Plant Uptake Factor	0	0	0	0	0	0
Half-life in days	5*	14.01	1	0.41	3.01	0.46***
K_{oc}	20081	22	1031	43	331	409
K_{om}	11648**	12.8	598	24.9	192	237
Freundlich Exponent	0.94	0.96	0.9	1	1	0.73

*: The correct value is 4.8 days

**: The correct value is 11678 mL/g

***: The correct value (geomean) of the not-normalized (non FOCUS kinetics) values is 0.42 days

80th Percentile Annual Average Groundwater FOCUS PEARL PECs (0.750 kg a.s./ha)

Location	Application Scheme	Carbosulfan PEC (µg/L)	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)	Di-butylamine PEC (µg/L)
Châteaudun	Sugar beets	0.000000	**1.225409**	0.035144	0.088191	0.001973	0.000000
Hamburg	Sugar beets	0.000000	**1.028318**	0.032707	**0.146515**	0.042727	0.000000
Jokioinen	Sugar beets	0.000000	**0.821221**	0.022919	0.043852	0.001091	0.000000
Kremsmünster	Sugar beets	0.000000	**0.704388**	0.020660	0.067154	0.001453	0.000000
Okehampton	Sugar beets	0.000000	**0.878747**	0.026573	0.085684	0.002987	0.000000
Piacenza	Sugar beets	0.000000	**1.624691**	0.051615	**0.288788**	0.069760	0.000000
Porto	Sugar beets	0.000000	0.023426	0.000635	0.000990	0.000012	0.000000
Sevilla	Sugar beets	0.000000	**4.089490**	**0.108894**	**0.165707**	0.004480	0.000000
Thiva	Sugar beets	0.000000	**0.224951**	0.006738	0.019950	0.000445	0.000000

80th Percentile Triennial Average Groundwater FOCUS PEARL PECs (0.750 kg a.s./ha)

Location	Application Scheme	Carbosulfan PEC (µg/L)	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)	Di-butylamine PEC (µg/L)
Châteaudun	Sugar beets	0.000000	**0.443631**	0.012746	0.031513	0.000737	0.000000
Hamburg	Sugar beets	0.000000	**0.348197**	0.011076	0.050104	0.014285	0.000000
Jokioinen	Sugar beets	0.000000	**0.341390**	0.009272	0.016263	0.000428	0.000000
Kremsmünster	Sugar beets	0.000000	**0.240606**	0.007150	0.018877	0.000410	0.000000
Okehampton	Sugar beets	0.000000	**0.273675**	0.008275	0.026922	0.000918	0.000000
Piacenza	Sugar beets	0.000000	**0.670068**	0.021069	**0.104181**	0.024858	0.000000
Porto	Sugar beets	0.000000	0.012370	0.000330	0.000367	0.000005	0.000000
Sevilla	Sugar beets	0.000000	**1.105556**	0.028859	0.037376	0.001058	0.000000
Thiva	Sugar beets	0.000000	0.068885	0.002069	0.006071	0.000139	0.000000

80th Percentile Annual Average Groundwater FOCUS PELMO PECs (0.750 kg a.s./ha)

Location	Application Scheme	Carbosulfan PEC (µg/L)	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)	Di-butylamine PEC (µg/L)
Châteaudun	Sugar beets	0.000	**0.400**	0.012	0.025	0.001	0.000
Hamburg	Sugar beets	0.000	**0.524**	0.016	0.070	0.019	0.000
Jokioinen	Sugar beets	0.000	**0.429**	0.010	0.013	0.000	0.000
Kremsmünster	Sugar beets	0.000	**0.318**	0.009	0.017	0.001	0.000
Okehampton	Sugar beets	0.000	**0.629**	0.019	0.054	0.002	0.000
Piacenza	Sugar beets	0.000	**0.725**	0.022	**0.102**	0.023	0.000
Porto	Sugar beets	0.000	0.009	0.000	0.000	0.000	0.000
Sevilla	Sugar beets	0.000	**0.388**	0.010	0.007	0.000	0.000
Thiva	Sugar beets	0.000	0.004	0.000	0.000	0.000	0.000

80th Percentile Triennial Average Groundwater FOCUS PELMO PECs (0.750 kg a.s./ha)

Location	Application Scheme	Carbosulfan PEC (µg/L)	Carbofuran PEC (µg/L)	3-Hydroxy-Carbofuran PEC (µg/L)	3-Keto-Carbofuran PEC (µg/L)	7-Phenol Carbofuran PEC (µg/L)	Di-butylamine PEC (µg/L)
Châteaudun	Sugar beets	0.000	**0.146**	0.004	0.009	0.000	0.000
Hamburg	Sugar beets	0.000	**0.172**	0.005	0.021	0.006	0.000
Jokioinen	Sugar beets	0.000	**0.145**	0.004	0.006	0.000	0.000
Kremsmünster	Sugar beets	0.000	0.099	0.003	0.005	0.000	0.000
Okehampton	Sugar beets	0.000	**0.251**	0.007	0.016	0.001	0.000
Piacenza	Sugar beets	0.000	**0.303**	0.009	0.043	0.009	0.000
Porto	Sugar beets	0.000	0.002	0.000	0.000	0.000	0.000
Sevilla	Sugar beets	0.000	0.017	0.000	0.000	0.000	0.000
Thiva	Sugar beets	0.000	0.002	0.000	0.000	0.000	0.000

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air	Not studied - no data requested
Quantum yield of direct phototransformation	φ: 1.21 x 10^{-6}
Photochemical oxidative degradation in air	DT_{50} of 2.0 hours derived by the Atkinson method of calculation (calculated assuming 1.5 x 10^6 OH radicles/cm^3 and the rate constant estimated at 65.19x10^{-12} cm^3 x $molecules^{-1}$x sec^{-1})
Volatilisation	from plant surfaces (BBA guideline): 1.9 % after 6-24 hours
	from soil (US-FIFRA guideline): 6.32E^{-05} - 6.41E^{-03} (µg/ cm^2 x hr) under the test conditions

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Not required

Definition of the Residue (Annex IIA, point 7.3) Relevant to the environment	Soil Definition for risk assessment: carbosulfan, carbofuran , 3-keto-carbofuran, 3-OH-carbofuran, dibutylamine Definition for monitoring: carbosulfan, carbofuran Surface water Definition for risk assessment: carbosulfan, carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol (=7-phenol), dibutylamine Definition for monitoring: carbosulfan, carbofuran, in case of carbofuran is found, it is recommended to analyse for 3-OH-carbofuran and 3-keto-carbofuran as well Sediment Definition for risk assessment: carbosulfan, carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, carbofuran-7-phenol (=7-phenol), dibutylamine definition for monitoring: carbosulfan, carbofuran, in case of carbofuran is found, it is recommended to analyse for 3-keto-carbofuran as well Groundwater Definition for risk assessment: carbosulfan, carbofuran, 3-keto-carbofuran, 3-OH-carbofuran, dibutylamine Definition for monitoring: carbosulfan, carbofuran, in case of carbofuran is found, it is recommended to analyse for 3-OH-carbofuran and 3-keto-carbofuran as well Air Definition for risk assessment and monitoring: carbosulfan, carbofuran

Monitoring data, if available (Annex IIA, point 7.4)	
Soil (indicate location and type of study)	Not available
Surface water (indicate location and type of study)	Not available
Ground water (indicate location and type of study)	Not available
Air (indicate location and type of study)	Not available

Classification and proposed labelling (Annex IIA, point 10)	
with regard to fate and behaviour data	Candidate for R53

Effects on Non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Anas platyrhynchos	carbosulfan	acute	**LD_{50} = 10**	-
Phasianus colchicus	carbosulfan	acute	LD_{50} = 20	-
Colinus virginianus	carbosulfan	acute	LD_{50} = 82	-
Anas platyrhynchos	carbosulfan	short-term	**LC_{50} = 3.99**	304
Phasianus colchicus	carbosulfan	short-term	LC_{50} = 567	1275
Colinus virginianus	carbosulfan	short-term	LC_{50} = 239	1100
Anas platyrhynchos	carbosulfan	long-term	**NOEL = 2.5**	30
Colinus virginianus	carbosulfan	long-term	NOEL = 10.8	150
Anas platyrhynchos	Marshal 25CS	acute	LD_{50} between 8 and 16	-
Anas platyrhynchos	carbofuran	acute	LD_{50} = 0.76	-
Anas platyrhynchos	carbofuran	acute	**$LD_{50,m}$ = 0.71** $LD_{50,f}$ = 0.86	-
Colinus virginianus	carbofuran	acute	$LD_{50,m}$ = 8.0 $LD_{50,f}$ = 8.0	-
Coturnix coturnix japonica	carbofuran	acute	$LD_{50,m}$ = 4.9 $LD_{50,f}$ = 3.5	-
Phasianus colchicus	carbofuran	acute	$LD_{50,m}$ = 4.0 $LD_{50,f}$ = 6.2	-
Anas platyrhynchos	carbofuran	short-term	LC_{50} (5 d) = 10 LC_{50} (5 d) = 17 **LC_{50} (14 d) = 1.6** **LC_{10} (14 d) = 0.64**	91 79 21 -
Colinus virginianus	carbofuran	short-term	LC_{50} (5 d) = 114 LC_{50} (14 d) = 15.8 LC_{50} (7 d) = 20.8	855 158 1000
Anas platyrhynchos	carbofuran	long-term	**LC_{10} (14 d) = 0.64**	-
Mammals ‡				
rabbit	carbosulfan	acute	**LD_{50} = 42.7**	-
rat	carbosulfan	long-term	**NOAEL = 1.2**	-
rat	carbofuran	acute	**LD_{50} = 5.3** – 5.6	-
rat	carbofuran	long-term	**NOAEL = 0.1**	-

Additional higher tier studies ‡
Wild-caught house sparrows were placed in small aviaries in the laboratory. The floor of each aviary was covered by dark brown organic soil (ground peat). This soil initially contained no grit particles. Appropriately-sized grit particles were scattered evenly on the soil surface at a specified density and 50 Marshal®10G granules/m^2 were placed on the soil surface along two simulated seed furrows. House sparrows exposed to 50 Marshal®10G granules/m^2 on the soil surface for a six-hour period experienced no mortalities or other adverse affects. The RMS considers that the results of this study cannot be easily extrapolated to the actual field situation.

Note : The reproductive endpoint for birds is based on a short-term dietary study (14 d) with *Anas platyrhynchos* ducklings.

Note : After PRAPeR 68, RMS included its position in the addendum (update May 2009) of carbofuran on the lower NOAEL = 0.1 mg a.s./kg b.w./day

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Crop and application rate : sugar beet, 1 x 0.750 kg a.s./ha in-furrow

Risk assessment for birds for consumption of granules (carbosulfan):

LD_{50}, LC_{50} and NOEC of carbosulfan expressed in number of granules for different sizes of birds (based on a weight of 1 granule of 0.14 mg and 0.014 mg a.s./granule)

Time scale	Number of granules for a 15 g bird	Number of granules for a 25 g bird	Number of granules for a 50 g bird	Number of granules for a 200 g bird	Number of granules for a 500 g bird
Acute LD_{50}	10.9	18.1	36	145	362
Dietary LC_{50}	4.3	7.2	14	58	144
Long-term NOEC	2.7	4.5	9	36	90

Accidental ingestion of Marshal 10G granules (as part of soil ingestion) by birds when seeking food :

Species	End-point	Toxicity Value	RWC Daily Dry Soil Dose ($DDSD_{rwc}$)	ETR ($DDSD_{rwc}$/ Toxicity endpoint)	Acceptable ETR (≤ 1 is low risk)
Acute – Short-term Exposure					
for individual species data (*)	LD_{50}	$LD_{50}^{5th\ percentile}$ = 5.32 mg a.s./kg b.w. [11]	0.3548	0.07	Yes

[11] Calculation of the Species Sensitivity Distribution (SSD) for the LD_{50} values
LD_{50} (*Anas platyrhynchos*) = 10 mg a.s./kg b.w.
LD_{50} (*Phasianus colchicus*) = 20 mg a.s./kg b.w.
LD_{50} (*Colinus virginianus*) = 82 mg a.s./kg b.w.
HD_5 median estimate = 5.32 mg a.s./kg b.w.; this value is only used for the EPPO calculations

Dietary – Medium-term Exposure					
Mallard ducklings	LC_{50} (14 day)	3.99 mg a.s./kg b.w./day	0.0713	0.10	Yes
Reproduction – Long-term Exposure					
Mallard duck (24 week study)	NOEL (18 week)	2.5 mg a.s./kg b.w./day	0.0378	0.086	Yes

Potential ingestion of Marshal 10G granules by birds as a source of grit :

Scenario	Size of birds	Field boundary Exposure		Mid field Exposure		End of Row Exposure	
		ETR	Acceptable	ETR	Acceptable	ETR	Acceptable
Acute – Short-term Exposure							
Realistic worst-case	Small	0.0081	Yes	0.0022	Yes	0.1419	Yes
Most likely case	Small	0.0024	Yes	0.0006	Yes	0.0421	Yes
Dietary – Medium-term Exposure							
Realistic worst-case	Small	0.0613	Yes	0.0165	Yes	1.0783	No
Most likely case	Small	0.0182	Yes	0.0049	Yes	0.3197	Yes
Reproduction – Long-term Exposure							
Realistic worst-case	Small	0.0979	Yes	0.0263	Yes	1.7210	No
Most likely case	Small	0.0290	Yes	0.0078	Yes	0.5102	Yes

Risk assessment for birds for consumption of sugar beet seedlings, earthworms and arthropods (carbofuran):

Indicator species/Category	Time scale	Route	ETE	TER	Annex VI Trigger
Tier 1 (worst-case toxicological endpoints, measured residue in seedlings)					
medium herbivorous bird	acute	**leafy crop/early** sugar beet seedlings (PD = 100 %)	**0.93**	0.77	**10**
	short-term		**0.38**	4.21	**10**
	long-term		**0.38**	1.68	**10**
Tier 2 (worst-case toxicological endpoints, measured residue in seedlings, earthworms and arthropods, focal species determined in monitoring studies, no food avoidance considered, PT = 100 %)					
Wood pigeon	acute	sugar beet seedlings (PD = 30 %)	**0.25**	2.83	**10**
	short-term		**0.10**	**15.56**	**10**
	long-term		**0.10**	**6.22**	**10**
Yellow wagtail	acute	arthropods (PD = 70 %)	**0.98**	0.73	**10**
	short-term		**0.75**	2.15	**10**
	long-term		**0.31**	2.05	**10**
Blackbird	acute	earthworms (PD = 100 %)	**0.32**	2.24	**10**
	short-term		**0.25**	6.36	**10**
	long-term		**0.11**	5.85	**10**
Skylark	acute	sugar beet seedlings (PD = 33 %), arthropods (PD = 23 %), earthworms (PD = 6 %)	**0.84**	0.85	**10**
	short-term		**0.44**	3.62	**10**
	long-term		**0.32**	2.01	**10**

Note : Since the long-term endpoint is based on a short-term study, the trigger is increased to 10

Note : The PD values used in the TER calculations are only for illustrative purposes; PT = 1

Risk assessment for mammals for consumption of granules (carbosulfan):

LD_{50} and NOAEL of carbosulfan expressed in numbers of granules for different sizes of mammals (based on a weight of 1 granule of 0.14 mg and 0.014 mg a.s./granule)

Time scale	Number of granules for a 15 g mammal	Number of granules for a 25 g mammal	Number of granules for a 50 g mammal	Number of granules for a 200 g mammal	Number of granules for a 500 g mammal
Acute LD_{50}	46	77	154	618	1545
Long-term NOAEL	1.3	2.2	4.3	17	43

Accidental ingestion of Marshal 10G granules (as part of soil ingestion) by mammals when seeking food :

Species	End-point	Toxicity Value	RWC Daily Dry Soil Dose ($DDSD_{rwc}$)	ETR ($DDSD_{rwc}$/ Toxicity endpoint)	Acceptable ETR (≤ 1 is low risk)
Acute – Short-term Exposure					
rat	LD_{50}	42.7 mg a.s./kg b.w.	0.0848	0.008	Yes
Dietary – Medium-term Exposure					
rat	NOAEL (28 d)	2.2 mg a.s./kg b.w./day[12]	0.0173	0.030	Yes
Reproduction – Long-term Exposure					
rat	NOAEL	1.2 mg a.s./kg b.w./day	0.0091	0.029	Yes

Risk assessment for mammals for consumption of sugar beet seedlings, earthworms and arthropods (carbofuran):

Indicator species/Category	Time scale	Route	ETE	TER	Annex VI Trigger
Tier 1 (worst-case toxicological endpoints, measured residue in seedlings)					
insectivorous mammal	acute	**leafy crop/early** earthworms (PD = 100 %)	**0.41**	**13**	**10**
	long-term		**0.14**	0.71	**5**
insectivorous mammal	acute	**leafy crop/early** arthropods (PD = 100 %)	**2.24**	2.37	**10**
	long-term		**0.71**	0.14	**5**
herbivorous mammal	acute	**leafy crop/early** sugar beet seedlings (PD = 100 %)	**0.34**	**16**	**10**
	long-term		**0.14**	0.71	**5**
Tier 2 (worst-case toxicological endpoints, measured residue in seedlings, earthworms and arthropods, focal species determined in monitoring studies, no food avoidance considered, PT = 100 %)					
Common shrew	acute	earthworms (PD = 80 %), arthropods (PD = 20 %)	**0.80**	6.63	**10**
	long-term		**0.26**	0.38	**5**
Brown hare	acute	sugar beet seedlings (PD = 40 %)	**0.13**	**41**	**10**
	long-term		**0.05**	2	**5**

Note : The PD values used in the TER calculations are only for illustrative purposes. The PD values were uncertain since they were not derived from targeted studies in sugar beet fields; PT = 1

[12] This endpoint (Goldenthal, 1979) is only used for the EPPO calculations.

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

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Lepomis macrochirus	carbosulfan	96 h (static)	Mortality, LC_{50}	**0.015 mg a.s./L** (nom)[13]
Lepomis macrochirus	carbosulfan	96 h (static)	Mortality, LC_{50}	0.0149 mg a.s./L (nom)[14]
Oncorhynchus mykiss	carbosulfan	96 h (static)	Mortality, LC_{50}	0.0424 mg a.s./L (nom)[15]
Cyprinus carpio	carbosulfan	96 h (static)	Mortality, LC_{50}	0.055 mg a.s./L (nom)[16]
Oncorhynchus mykiss	carbosulfan	14 d (flow-through)	Growth, NOEC	**0.004 mg a.s./L** (mm)
Oncorhynchus mykiss	carbosulfan	21 d (semi-static)	Growth, NOEC	0.016 mg a.s./L (nom)
Pimephales promelas	carbosulfan	30 d (flow-through)	Growth, NOEC	0.00828 mg a.s./L (mm)
Oncorhynchus mykiss	carbofuran	96 h (static)	Mortality, LC_{50}	0.3625 mg/L (*) (nom)
Cyprinodon variegatus	carbofuran	35 d fish early life stage	Growth, NOEC	**0.006 mg/L** (mm)
Oncorhynchus mykiss	carbofuran	90 d fish early life stage	Growth, NOEC	0.0248 mg/L (mm)
Oncorhynchus mykiss	carbofuran	28 d fish early life stage	Growth, NOEC	0.022 mg/L (nom)
Oncorhynchus mykiss	7-phenol	96 h (static)	Mortality, LC_{50}	37 mg/L (m)
Oncorhynchus mykiss	7-phenol	96 h (static)	Mortality, LC_{50}	42 mg/L (nom)
Oncorhynchus mykiss	7-phenol	96 h (static)	Mortality, LC_{50}	**32.3 mg/L** (**) (nom)
Lepomis macrochirus	7-phenol	96 h (static)	Mortality, LC_{50}	39.1 mg/L (**) (nom)
Oncorhynchus mykiss	dibutylamine	96 h (static)	Mortality, LC_{50}	**18 mg/L** (nom)

[13] No analytical measurements were available for the acute toxicity tests with fish and carbosulfan, this adds some uncertainty
[14] See 3
[15] See 3
[16] See 3

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Aquatic invertebrates				
Daphnia magna	carbosulfan	48 h (static)	Mortality, EC_{50}	0.0024 mg a.s./L (nom)[17]
Daphnia magna	carbosulfan	48 h (static)	Mortality, EC_{50}	**0.0015 mg a.s./L** (nom)[18]
Daphnia magna	carbosulfan	21 d (semi-static)	Reproduction, NOEC	**0.0032 mg a.s./L** (nom)
Daphnia magna	carbofuran	48 h (static)	Mortality, EC_{50}	0.0386 mg/L (***) (nom)
Gammarus fasciatus	carbofuran	96 h (static)	Mortality, LC_{50}	0.0028 mg/L (mm)
Hexagenia limbata	carbofuran	96 h (static)	Mortality, LC_{50}	237 mg/L (mm)
Daphnia magna	carbofuran	21 d (flow-through)	Reproduction, NOEC	0.0098 mg/L (mm)
Ceriodaphnia magna	carbofuran	7 d (semi-static)	Reproduction, NOEC	**0.00016 mg/L** (mm)
Daphnia magna	7-phenol	48 h (static)	Mortality, EC_{50}	> 1 mg/L (nom)
Daphnia magna	7-phenol	48 h (static)	Mortality, EC_{50}	40 mg/L (mm)
Daphnia magna	7-phenol	48 h (static)	Mortality, EC_{50}	30 mg/L (****) (nom)
Ceriodaphnia dubia	3-OH-carbofuran	48 h (static)	Mortality, EC_{50}	**0.023 mg/L** (mm)
Ceriodaphnia dubia	3-keto-carbofuran	48 h (static)	Mortality, EC_{50}	**0.049 mg/L** (mm)
Daphnia magna	dibutylamine	48 h (static)	Mortality, EC_{50}	**4.2 mg/L** (nom)
Daphnia magna	Marshal 25CS	48 h (static)	Mortality, EC_{50}	0.0043 mg form/L (nom) (0.00104 mg a.s./L)
Daphnia magna	Marshal 10G	48 h (static)	Mortality, EC_{50}	0.01 mg form/L (nom) (**0.00105 mg a.s./L**)
Sediment dwelling organisms				
Chironomus riparius	carbofuran	28 d (static)	NOEC	0.004 mg/L (nom) **0.0032 mg/L** (mm) **0.0022 mg/kg** (nom)
Algae				
Pseudokirchneriella subcapitata	carbosulfan	96 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**> 20 mg a.s./L** (nom) **> 20 mg a.s./L** (nom)
Pseudokirchneriella subcapitata	7-phenol	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	> 1 mg/L (nom) > 1 mg/L (nom)

[17] No analytical measurements were available for the acute toxicity tests with daphnids and carbosulfan, this adds some uncertainty
[18] See 7

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Pseudokirchneriella subcapitata	7-phenol	120 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	72 mg/L (mm) > 99 mg/L (mm)
Pseudokirchneriella subcapitata	7-phenol	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**47 mg/L** (nom) 83 mg/L (nom)
Pseudokirchneriella subcapitata	dibutylamine	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	**24 mg/L** (nom) 31 mg/L (nom)
Pseudokirchneriella subcapitata	Marshal 25CS	72 h (static)	Biomass: E_bC_{50} Growth rate: E_rC_{50}	429 mg form/L (nom) (107 mg a.s./L) 805 mg form/L (nom) (201 mg a.s./L)
Higher plant				
Not required.				
Microcosm or mesocosm tests				

Outdoor mesocosm containing aquatic invertebrates, algae and macrophytes, 1 application, the test item is MARSHAL 25 CS (capsule suspension containing 250 g/L carbosulfan)
The NOEAEC of 0.4 µg carbosulfan/L is based on

- Effects on *Ceriodaphnia* : Complete recovery of the populations occurred at 0.4 µg a.s./L after 40 days.
- Effect on free-living gammarids : full recovery after 42 days at 0.1 and 0.4 µg a.s./L treatment levels
- Effects on chironomid larvae: complete recovery of the populations at 0.4 µg/L from day 12 up to study termination.

Other groups of organisms are affected at levels above 0.4 µg a.s./L.

The only supported formulation in the resubmission is Marshal 10G and the supported GAP is 1 x 750 g a.s./ha in sugar beet. The TER calculations for carbosulfan and its major metabolites, based on laboratory data, show acceptable risk based on FOCUS step 1, step 2 and step 3 calculations (see below). There is no further need for the endpoint of the mesocosm study in the refinement of the risk. However, for completeness the expert review of the notifier was inserted in the DAR. The reassessment of the mesocosm study and recalculation of the relevant ecotoxicological endpoints confirm that the NOEAEC of 0.0004 mg carbosulfan/L (initial residue) is still valid. With an assessment factor of 4 this leads to an EAC = 0.1 µg carbosulfan/L. Also, a NOEC of 0.1 µg carbosulfan/L could be derived with an assessment factor of 1. In conclusion, a RAC (regulatory acceptable concentration) of 0.1 µg carbosulfan/L was agreed by Member States during Peer Review.

[1] indicate whether based on nominal ($_{nom}$) or mean measured concentrations ($_{mm}$). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

* : the most critical endpoint for fish is *Lepomis macrochirus*, 96 h semi-static, **LC_{50} = 0.18 mg carbofuran/L** (nominal), Migchielsen M.H.J., 2002 (Dianica)

**** : FMC studies – See DAR of carbofuran**

***** : the most critical endpoint for aquatic invertebrates is *Daphnia magna*, 48 h static, EC_{50} = 0.041 mg Furadan 5G/L = 0.00205 mg carbofuran/L (mean measured), Forbis A.D., 1986 (FMC)**
The most critical endpoint for algae is *Pseudokirchneriella subcapitata*, 72 h static, E_bC_{50} = 6.5 mg carbofuran/L and E_rC_{50} = 19 mg carbofuran/L (nominal), Migchielsen M.H.J., 2002 (Dianica)

**** : The most critical endpoint for aquatic invertebrates is *Daphnia magna*, EC_{50} = 25 mg 7-phenol/L, 48 h static, Migchielsen M.H.J., 2002 (Dianica)
The most critical endpoint for sediment dwelling organisms is *Chironomus riparius*, NOEC = 10 mg 7-phenol/L, equivalent to NOEC = 1.36 mg 7-phenol/L, 25 d static, Memmert U., 2002

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

Crop and application rate : sugar beet, 1 x 0.750 kg a.s./ha in-furrow

FOCUS step 3 calculations for carbosulfan and its metabolites were updated in the section on fate and behaviour (July 2009), and the TER calculations based on FOCUS step 3 were also updated in the ecotox section. The TER calculations based on FOCUS step 1 and 2 are based on the original PEC values of April 2009.

Risk assessment for the active substance :

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
carbosulfan	*Lepomis macrochirus*	0.015	96 h	9.00	-	**1.67**	100
carbosulfan	*Oncorhynchus mykiss*	0.004	14 d	9.00	-	**0.44**	10
carbosulfan	*Daphnia magna*	0.0015	48 h	9.00	-	**0.17**	100
Marshal 10G	*Daphnia magna*	0.00105	48 h	9.00		**0.12**	100
carbosulfan	*Daphnia magna*	0.0032	21 d	9.00	-	**0.36**	10
carbosulfan	*Pseudokirchneriella subcapitata*	> 20	96 h	9.00	-	> 2222	10

FOCUS Step 2

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
carbosulfan	N	*Lepomis macrochirus*	0.015	96 h	1.01	**14.85**	100
	S				2.01	**7.46**	100
carbosulfan	N	*Oncorhynchus mykiss*	0.004	14 d	1.01	**3.96**	10
	S				2.01	**1.99**	10
carbosulfan	N	*Daphnia magna*	0.0015	48 h	1.01	**1.49**	100
	S				2.01	**0.75**	100
Marshal 10G	N	*Daphnia magna*	0.00105	48 h	1.01	**1.04**	100
	S				2.01	**0.52**	100
carbosulfan	N	*Daphnia magna*	0.0032	21 d	1.01	**3.17**	10
	S				2.01	**1.59**	10

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Lepomis macrochirus*	96 h	0.015	0.00001	1500000	100
D4	Pond				0.00001	1500000	100
D4	Stream				0.00001	1500000	100
R1	Pond				0.00001	1500000	100
R1	Stream				0.00001	1500000	100
R3	Stream				0.00001	1500000	100
D3	Ditch	*Oncorhynchus mykiss*	14 d	0.004	0.00001	400000	10
D4	Pond				0.00001	400000	10
D4	Stream				0.00001	400000	10
R1	Pond				0.00001	400000	10
R1	Stream				0.00001	400000	10
R3	Stream				0.00001	400000	10
D3	Ditch	*Daphnia magna*	48 h	0.0015	0.00001	150000	100
D4	Pond				0.00001	150000	100
D4	Stream				0.00001	150000	100
R1	Pond				0.00001	150000	100
R1	Stream				0.00001	150000	100
R3	Stream				0.00001	150000	100
D3	Ditch	*Daphnia magna* (Marshal 10G)	48 h	0.00105	0.00001	150000	100
D4	Pond				0.00001	150000	100
D4	Stream				0.00001	150000	100
R1	Pond				0.00001	150000	100
R1	Stream				0.00001	150000	100
R3	Stream				0.00001	150000	100
D3	Ditch	*Daphnia magna*	21 d	0.0032	0.00001	320000	100
D4	Pond				0.00001	320000	10
D4	Stream				0.00001	320000	10
R1	Pond				0.00001	320000	10
R1	Stream				0.00001	320000	10
R3	Stream				0.00001	320000	10

Risk assessment for the metabolite carbofuran :

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
carbofuran	*Lepomis macrochirus*	0.18	96 h	104.35	-	**1.72**	100
carbofuran	*Cyprinodon variegatus*	0.006	35 d	104.35	-	**0.057**	10
carbofuran	*Daphnia magna*	0.00205	48 h	104.35	-	**0.020**	100
carbofuran	*Ceriodaphnia dubia*	0.00016	7 d	104.35	-	**0.0015**	10
carbofuran	*Pseudokirchneriella subcapitata*	6.5	72 h	104.35	-	62	10
carbofuran	*Chironomus riparius*	0.0032	28 d	104.35	-	**0.031**	10

Test substance	Organism	Toxicity end point (mg/kg)	Time scale	PEC_{sed} (µg/kg)	PEC_{twa} (µg/kg)	TER	Annex VI Trigger
carbofuran	*Chironomus riparius*	0.0022	28 d	24.31	-	**0.090**	10

FOCUS Step 2

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
carbofuran	N	*Lepomis macrochirus*	0.18	96 h	16.81	**10.71**	100
	S				33.63	**5.35**	100
carbofuran	N	*Cyprinodon variegatus*	0.006	35 d	16.81	**0.36**	10
	S				33.63	**0.18**	10
carbofuran	N	*Daphnia magna*	0.00205	48 h	16.81	**0.12**	100
	S				33.63	**0.061**	100
carbofuran	N	*Ceriodaphnia dubia*	0.00016	7 d	16.81	**0.010**	10
	S				33.63	**0.0048**	10
carbofuran	N	*Chironomus riparius*	0.0032	28 d	16.81	**0.19**	10
	S				33.63	**0.10**	10

Test substance	N/S	Organism	Toxicity end point (mg/kg)	Time scale	PEC_{sed} (µg/kg)	TER	Annex VI Trigger
carbofuran	N	*Chironomus riparius*	0.0022	28 d	3.92	**0.56**	10
	S				7.84	**0.28**	10

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Lepomis macrochirus*	96 h	0.18	0.0111	16216	100
D4	Pond				0.0658	2736	100
D4	Stream				0.0462	3896	100
R1	Pond				0.00001	18000000	100
R1	Stream				0.00001	18000000	100
R3	Stream				0.00001	18000000	100
D3	Ditch	*Cyprinodon variegatus*	35 d	0.006	0.0111	541	10
D4	Pond				0.0658	91	10
D4	Stream				0.0462	130	10
R1	Pond				0.00001	600000	10
R1	Stream				0.00001	600000	10
R3	Stream				0.00001	600000	10
D3	Ditch	*Daphnia magna*	48 h	0.00205	0.0111	185	100
D4	Pond				0.0658	**31**	100
D4	Stream				0.0462	**44**	100
R1	Pond				0.00001	205000	100
R1	Stream				0.00001	205000	100
R3	Stream				0.00001	205000	100
D3	Ditch	*Ceriodaphnia dubia*	7 d	0.00016	0.0111	14	10
D4	Pond				0.0658	**2**	10
D4	Stream				0.0462	**3**	10
R1	Pond				0.00001	16000	10
R1	Stream				0.00001	16000	10
R3	Stream				0.00001	16000	10
D3	Ditch	*Chironomus riparius*	28 d	0.0032	0.0111	288	10
D4	Pond				0.0658	49	10
D4	Stream				0.0462	69	10
R1	Pond				0.00001	320000	10
R1	Stream				0.00001	320000	10
R3	Stream				0.00001	320000	10

From the mesocosm study with Marshal 25CS (Foekema E.M. *et al*., 2002) a NOAEC of 0.4 µg carbosulfan/L was derived. With an assessment factor of 4, this leads to an EAC = 0.1 µg carbosulfan/L. Also, a NOEC of 0.1 µg carbosulfan/L could be derived with an assessment factor of 1. In conclusion, a RAC (regulatory acceptable concentration) of 0.1 µg carbosulfan/L was agreed by Member States during Peer Review.
Based on the laboratory toxicity endpoints for *Daphnia magna* (EC_{50} = 0.00205 mg carbofuran/L) and *Ceriodaphnia dubia* (NOEC = 0.00016 mg carbofuran/L) and the FOCUS step 3 PECsw values (750 g a.s./ha), TER values did not pass the trigger for 2 out of 6 scenarios, namely D4 pond and D4 stream (see above).
The RAC of 0.1 µg carbosulfan/L is equivalent with 0.058 µg carbofuran/L, based on molecular weight ratio carbofuran/carbosulfan of 221.3/380.5. With this RAC = 0.058 µg carbofuran/L, the scenario D4 stream (0.0462 µg carbofuran/L) would show acceptable risk, whereas scenario D4 pond (0.0658 µg carbofuran/L) is little above the EAC.
In conclusion, the endpoint of the mesocosm study could be applied to refine the risk assessment for aquatic invertebrates. At the application rate of 750 g a.s./ha, 5 out of 6 scenarios show acceptable risk (only scenario D4 pond does not pass the trigger of 4).

Scenario	**Water body type**	**Test organism**	**Time scale**	**Toxicity end point (mg/kg)**	**PEC_{sed} (µg/kg)**	**TER**	**Annex VI trigger**
D3	Ditch	*Chironomus riparius*	28 d	0.0022	0.0200	110	10
D4	Pond				0.0903	24	10
D4	Stream				0.0410	54	10
R1	Pond				0.00001	220000	10
R1	Stream				0.00001	220000	10
R3	Stream				0.00001	220000	10

Risk assessment for the metabolite 3-keto-carbofuran :

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
3-keto-carbofuran	*Ceriodaphnia dubia*	0.049	48 h	145.35	-	**0.34**	100

FOCUS Step 2

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
3-keto-carbofuran	N	*Ceriodaphnia dubia*	0.049	48 h	14.04	**3.49**	100
	S				28.08	**1.75**	100

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Scenario	**Water body type**	**Test organism**	**Time scale**	**Toxicity end point (mg/L)**	**PECsw (µg/L)**	**TER**	**Annex VI trigger**
D3	Ditch	*Ceriodaphnia dubia*	48 h	0.049	0.000657	74581	100
D4	Pond				0.00001	4900000	100
D4	Stream				0.00001	4900000	100
R1	Pond				0.00001	4900000	100
R1	Stream				0.00001	4900000	100
R3	Stream				0.00001	4900000	100

Risk assessment for the metabolite 3-OH-carbofuran :

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
3-OH-carbofuran	*Ceriodaphnia dubia*	0.023	48 h	147.46	-	**0.16**	100

FOCUS Step 2

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
3-OH-carbofuran	N	*Ceriodaphnia dubia*	0.023	48 h	0.01	2300	100
	S				0.02	1150	100

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PECsw (µg/L)	TER	Annex VI trigger
D3	Ditch	*Ceriodaphnia dubia*	48 h	0.023	0.000211	232227	100
D4	Pond				0.00139	35252	100
D4	Stream				0.000885	55367	100
R1	Pond				0.00001	4900000	100
R1	Stream				0.00001	4900000	100
R3	Stream				0.00001	4900000	100

Risk assessment for the metabolite 7-phenol :

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
7-phenol	*Oncorhynchus mykiss*	32.3	96 h	45.43	-	711	100
7-phenol	*Daphnia magna*	25	48 h	45.43	-	550	100
7-phenol	*Pseudokirchneriella subcapitata*	47	72 h	45.43	-	1035	10
7-phenol	*Chironomus riparius*	0.004	25 d	45.43	-	220	10

Test substance	Organism	Toxicity end point (mg/kg)	Time scale	PEC_{sed} (µg/kg)	PEC_{twa} (µg/kg)	TER	Annex VI Trigger
7-phenol	*Chironomus riparius*	1.36	25 d	468.40	-	**2.90**	10

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
7-phenol	*Oncorhynchus mykiss*	32.3	96 h	0.0146	-	2212329	100
7-phenol	*Daphnia magna*	25	48 h	0.0146	-	1712329	100
7-phenol	*Pseudokirchneriella subcapitata*	47	72 h	0.0146	-	3219178	10
7-phenol	*Chironomus riparius*	0.004	25 d	0.0146	-	684932	10

Test substance	Organism	Toxicity end point (mg/kg)	Time scale	PEC_{sed} (µg/kg)	PEC_{twa} (µg/kg)	TER	Annex VI Trigger
7-phenol	*Chironomus riparius*	1.36	25 d	0.02	-	68000	10

Risk assessment for the dibutylamine :

FOCUS Step 1

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	PEC_{twa} (µg/L)	TER	Annex VI Trigger
dibutylamine	*Oncorhynchus mykiss*	18	96 h	54.95	-	328	100
dibutylamine	*Daphnia magna*	4.2	48 h	54.95	-	**76**	100
dibutylamine	*Pseudokirchneriella subcapitata*	24	72 h	54.95	-	437	10

FOCUS Step 2

Test substance	N/S	Organism	Toxicity end point (mg/L)	Time scale	PEC_{sw} (µg/L)	TER	Annex VI Trigger
dibutylamine	N	*Daphnia magna*	4.2	48 h	0.01	420000	100
	S				0.03	140000	100

Bioconcentration				
	carbosulfan	Metabolite carbofuran	Metabolite 2	Metabolite3
$logP_{O/W}$	7.42	1.62 -1.80	-	-
Bioconcentration factor (BCF)[1] ‡	990 (whole fish), 730 (fillet), 1100 (viscera)	11 ± 2.3	-	-
Annex VI Trigger for the bioconcentration factor	100	100	-	-
Clearance time (days) (CT_{50})	**K_2 (day^{-1}) = 0.087 (fillet)** K_2 (day^{-1}) = 0.143 (viscera)	1.4 ± 0.20	-	-
(CT_{90})	-	4.6 ± 0.67	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	At the end of the 30 day depuration period, 60 %, 72 % and 72 % of the accumulated residues were eliminated from the fillet, viscera and whole fish respectively	4 – 20 % carbofuran	-	-

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
carbosulfan ‡	LD_{50} = 1.035 µg a.s./bee	LD_{50} = 0.18 µg a.s./bee
carbofuran ‡	LD_{50} = 0.05 µg a.s./bee	LD_{50} = 0.038 µg a.s./bee
Field or semi-field tests		
Not required.		

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Crop and application rate : sugar beet, 1 x 0.750 kg a.s./ha, in-furrow

The calculated Hazard Quotients are not relevant for granular incorporation use.
Due to the application technique (soil incorporation when sowing), foraging bees will not be significantly exposed directly to the granules.
Carbosulfan and its metabolites are transported systematically from the plant roots to the pollen and nectar. In the case of an extension of the use to blooming crops, the notifier should provide detailed information and further assessment of the risk to pollinating insects.
However, the risk to bees for the supported use is acceptable since the exposure to carbosulfan in sugar beets is not relevant. Sugar beet is not attractive for pollinating insects (no flower in the production crop).
In conclusion, the risk of carbosulfan and carbofuran is acceptable for the intended use.

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

Species	Life stage	Test substance, substrate and duration	Dose	End point	% effect	Trigger value
Laboratory tests						
Typhlodromus pyri	proto-nymphs	formulation containing 90.81 % carbosulfan, glass plates, 1 day	0.12 kg a.s./ha, initial	Corrected mortality Reproduction	96 % -	50 % 50 %
Aphidius rhopalosiphi	adults	formulation containing 90.81 % carbosulfan, glass plates, 2 days	0.12 kg a.s./ha, initial	Corrected mortality Reproduction	100 % -	50 % 50 %
Pardosa sp.	adult and subadult	Marshal 25 EC, sand, 7 days	0.375 kg a.s./ha, initial	Corrected mortality	100 % (1 d)	50 %
Extended laboratory tests						
Poecilus cupreus	adults	formulation containing 90.81 % carbosulfan, soil, 14 days	0.12 kg a.s./ha, initial	Corrected mortality Food consumption	76.7 % +89 %	50 % 50 %
Pardosa sp.	3 weeks old	formulation containing 90.81 % carbosulfan, soil, 14 days	0.12 kg a.s./ha, initial	Corrected mortality	100 % (1 d)	50 %
Poecilus cupreus	adults	Marshal 10G, soil, 14 days	0.67 mg a.s./kg d.w. soil, initial	Corrected mortality Food consumption	-3.45 % -6.19 %	50 % 50 %
			1.01 mg a.s./kg d.w. soil, initial (equivalent to 750 g a.s./ha)	Corrected mortality Food consumption	0.00 % -7.39 %	50 % 50 %

Species	Life stage	Test substance, substrate and duration	Dose	End point	% effect	Trigger value
			1.51 mg a.s./kg d.w. soil, initial	Corrected mortality Food consumption	3.45 % +0.80 %	50 % 50 %
Aleochara bilineata	adults	Marshal 10G, soil, 64 days	0.30 mg a.s./kg d.w. soil, initial	Reproduction	-3.60 %	50 %
			0.45 mg a.s./kg d.w. soil, initial	Reproduction	-10.3 %	50 %
			0.67 mg a.s./kg d.w. soil, initial	Reproduction	-10.4 %	50 %
			1.0 mg a.s./kg d.w. soil, initial (equivalent to 750 g a.s./ha)	Reproduction	-17.6 %	50 %
			1.5 mg a.s./kg d.w. soil, initial	Reproduction	-44.0 %	50 %
			EC_{50} = 1.68 mg a.s./kg d.w. soil			
Semi-field tests						
Pardosa sp	adult and subadult	Marshal 25 EC, sand, 7 days	0.375 kg a.s./ha, initial	Corrected mortality Food consumption	100 % (24 h); 46 % (5 d)* +7.5 %	50 % 50 %
Aged residue tests						
Aleochara bilineata	adults	Marshal 10G, soil, 28 days exposure	1.0 mg a.s./kg d.w. soil, (equivalent to 750 g a.s./ha)	Reproduction	-25 %	50 %

Corrected mortality : positive value = adverse effect, negative value = no adverse effect

Parasitism : negative value = adverse effect, positive value = no adverse effect
Food consumption : negative value = adverse effect, positive value = no adverse effect
Reproduction : negative value = adverse effect, positive value = no adverse effect
* for the newly introduced spiders

Field or semi-field tests
In the field study of Thompson A. R. (1989), the carabid and staphylinid beetles were evaluated. The study is considered as not acceptable. The main validity criterium of the study is not fulfilled: no negative effects were observed in the positive control at both 720 and 2200 g a.s./ha. A large scale field study (FMC Study No. A2007-6311) was conducted in summer 2006 to evaluate the magnitude and duration of any effects on populations of non-target surface-active and soil-dwelling arthropod species of an arable maize crop field in England following incorporation of Marshal 10G (10 % carbosulfan) into the seed furrow at time of drilling. The study was conducted in a maize crop in Cornwall, in southwest England. Surface-active arthropods were collected using pitfall traps. Soil-dwelling arthropods were collected using soil cores. Pitfall traps were set and soil cores collected two weeks and one week before treatment, one, two and three weeks after treatment and then on alternate weeks until four weeks before crop harvest (24 – 26 October, 2006). The final report of FMC Study No. A2007-6311 (designed to investigate the effects of Marshal 10G on non-target arthropods in maize) presented findings at the species and genus level for a range of taxonomic groups. For example, the population trends of the most abundant species of carabid and staphylinid beetle were presented over time for each treatment and the results interpreted with reference their ecology. Whilst this approach presents the response of the most abundant taxa, it does not include the response of those species found in low numbers in the samples. The RMS has requested that in addition to the species level interpretation, the raw data from pitfall trap and soil core sampling be summed and presented for the main groups found in the study. In particular, pitfall trap data was to be summed to provide information for Carabidae, Staphylinidae, other Coleoptera, Hymenoptera, Collembola, other Insect taxa, Arachnida, Acari, and Myriapoda. Soil core data was to be summed for Collembola, other Coleoptera, Acari and other taxa, respectively. The field study is acceptable. Both pitfall trap samplings and soil core analysis show no statistically significant adverse effects compared to the control at the application rate of 750 g a.s./ha.

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
Earthworms			
No acceptable laboratory study.			
Other soil macro-organisms			
Hypoaspis aculeifer	Marshal 10G	chronic 16 d	NOEC = 200 mg formulation/kg d.w. soil (20 mg a.s./kg d.w. soil) **$NOEC_{corr}$ = 10 mg a.s./kg d.w. soil**
Collembola			
Folsomia candida	Marshal 10G	chronic 28 d	NOEC = 4 mg formulation/kg d.w. soil (0.3 mg a.s./kg d.w. soil) **$NOEC_{corr}$ = 0.15 mg a.s./kg d.w. soil**

Test organism	Test substance	Time scale	End point
Soil micro-organisms			
Nitrogen mineralisation	Marshal 10G	28 d	+2.16 % effect at day 28 at 10.0 mg Marshal 10G/kg d.w. soil (7.5 kg Marshal 10G/ha) +11.5 % effect at day 28 at 50.0 mg Marshal 10G/kg d.w. soil (37.5 kg Marshal 10G/ha)
Carbon mineralisation	Marshal 10G	28 d	-4.13 % effect at day 28 at 10.0 mg Marsahl 10G/kg d.w. soil (7.5 kg Marshal 10G/ha) -7.71 % effect at day 28 at 50.0 mg Marshal 10G/kg d.w. soil (37.5 kg Marshal 10G/ha)
Field studies			
The application rate used in the earthworm field study (1.3 kg a.s./ha) is in the same range or higher than the proposed intended uses (750 g a.s./ha). Reduction of earthworm populations (number of adult earthworms, biomass) were observed in the carbosulfan treatment plots 1 month after application. Recovery was observed 6 months and 12 months after application. The actual concentrations of carbosulfan and carbofuran recovered in the soil (recalculated as 3.15 mg carbofuran/kg soil) cover the PECsoil (1.2 mg carbofuran/kg soil) for the proposed intended uses.			

Since the log P_{ow} of carbosulfan is 7.42, a correction factor of 2 is needed for the toxicological endpoints.

Toxicity/exposure ratios for soil organisms

Crop and application rate

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
No acceptable laboratory study.					
Other soil macro-organisms					
Folsomia candida	Marshal 10G	28 d	1.0	**0.15**	5
Hypoaspis aculeifer	Marshal 10G	16 d	1.0	10	5

[1] to be completed where first Tier triggers are breached
[2] indicate which PEC soil was used (e.g. plateau PEC)

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Marshal 10G has no effects on the seedling emergence of the tested species.

Marshal 10G did not cause phytotoxic effects at the tested rates, except for 2 out of 10 cucumber pots that exhibited signs of chlorosis on day 21.

Marshal 10G may reduce shoot weight of monocotyledons (*Allium cepa* (21.44 %) and *Avena sativa* (19.19 %)), and dicotyledons (*Brassica napus* (12.61 %), *Cucumis sativa* (26.44%), *Helianthus annuus* (11.42 %) and *Pisum sativum* (25.90 %) when exposed to soil treated with an application rate of 1500 G a.s./ha. *Cucumis sativus* (cucumber) showed signs of shoot weight reduction at the lower soil rate of 750 g a.s./ha (16.02 %). The effect was not significant for *Brassica napus*.

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	Endpoint
Activated sludge	EC_{50} > 1015 mg a.s./L

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

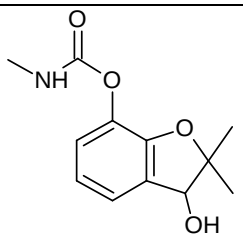
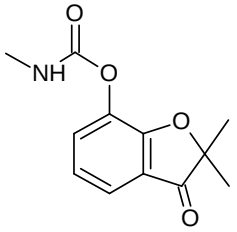
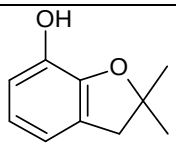
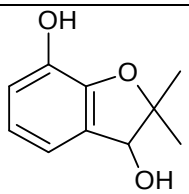
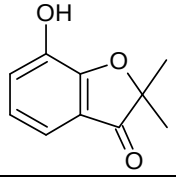
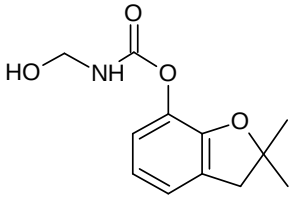
Compartment	
soil	carbosulfan, carbofuran, 3-keto-carbofuran, dibutylamine
water	carbosulfan, carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, 7-phenol , dibutylamine
sediment	carbosulfan, carbofuran, 3-OH-carbofuran, 3-keto-carbofuran, 7-phenol , dibutylamine
groundwater	carbofuran

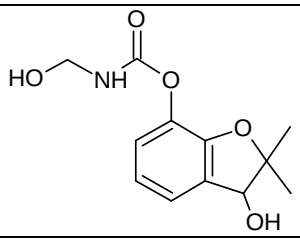
Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R50

	RMS/peer review proposal
Preparation	R50

APPENDIX 2 – USED COMPOUND CODES

Code/Trivial name	Chemical name	Structural formula
carbofuran	2,3-dihydro-2,2-dimethylbenzofuran-7-yl methylcarbamate	
3-OH-carbofuran 3-hydroxy carbofuran	3-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl methylcarbamate	
3-keto-carbofuran	2,2-dimethyl-3-oxo-2,3-dihydro-1-benzofuran-7-yl methylcarbamate	
carbofuran-7-phenol	2,2-dimethyl-2,3-dihydro-1-benzofuran-7-ol	
dibutylamine		
3-OH carbofuran-7-phenol	2,2-dimethyl-2,3-dihydro-1-benzofuran-3,7-diol	
3-ketocarbofuran-7-phenol	7-hydroxy-2,2-dimethyl-1-benzofuran-3(2*H*)-one	
N-OH methylcarbofuran	2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl (hydroxymethyl)carbamate	

3-OH-N-OH-methyl carbofuran	3-hydroxy-2,2-dimethyl-2,3-dihydro-1-benzofuran-7-yl (hydroxymethyl)carbamate	

GLOSSARY

AChE:	acetylcholinesterase
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ARfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
CHO	Chinese hamster ovary
d	day
DAR	draft assessment report
DBA	dibutylamine
DBNA	N-nitrosodibutylamine
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
EPCO	EFSA Peer Review Co-Operation
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOB	Functional observational battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
IEDI	international estimated daily intake

IESTI	international estimated short term intake
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LC_{50}	lethal concentration, median
LD_{50}	lethal dose, median; dosis letalis media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHED	Pesticide Handler's Exposure Data
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
POEM	Predictive Operator Exposure Model
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
SF	safety factor
STMR	supervised trials median residue
TER	toxicity exposure ratio

TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year